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SYSTEMATIC REVIEW

Diagnosis and Management of Obsessive Compulsive Disorders in Children

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Diagnosis and Management of Obsessive Compulsive Disorders in Children

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None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

The information in this report is intended to help healthcare decision makers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of healthcare services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of healthcare in the United States. The Patient-Centered Outcomes Research Institute (PCORI®) requested this report from the EPC Program at AHRQ. AHRQ assigned this report to the Brown Evidence-based Practice Center (Contract Number: 75Q80120D00001/75Q80121F32010).

AHRQ EPC reviews provide comprehensive, science-based information on common, costly medical conditions, and new healthcare technologies and strategies.

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If you have comments on this evidence report, they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov.

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In designing the study questions, the EPC consulted several Key Informants who represent the end-users of research. The EPC sought the Key Informant input on the priority areas for research and synthesis. Key Informants are not involved in the analysis of the evidence or the writing of the report. Therefore, in the end, study questions, design, methodological approaches, and/or conclusions do not necessarily represent the views of individual Key Informants.

Key Informants must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any conflicts of interest.

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In designing the study questions and methodology at the outset of this report, the EPC consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicted opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

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Prior to publication of the final evidence report, EPCs sought input from independent Peer Reviewers without financial conflicts of interest. However, the conclusions and synthesis of the scientific literature presented in this report do not necessarily represent the views of individual reviewers. AHRQ may also seek comments from other Federal agencies when appropriate.

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Diagnosis and Management of Obsessive Compulsive Disorders in Children

Abstract

Background. Obsessive compulsive disorder (OCD) is a common, chronic, and impairing psychiatric disorder that often begins in childhood or adolescence. Early identification and treatment of OCD is important to prevent a cascade of developmental disruptions lasting into adulthood. The 2012 American Academy of Child and Adolescent Psychiatry (AACAP) Practice Parameter recommends cognitive behavioral therapy that incorporates exposure and response prevention (ERP) as a first-line treatment for mild-to-moderate OCD in youth and recommends combined treatment with ERP (if feasible) and a selective serotonin reuptake inhibitor (SSRI) for some patients, particularly those with more severe symptoms. Clinical uncertainty exists regarding the optimal treatment strategies (and treatment combinations) that work best for specific populations and settings. In this report, we seek to evaluate the accuracy of brief assessment tools to identify OCD in symptomatic youth (Key Question [KQ] 1) and the effects and harms of treatment options for youth with OCD (KQ2).

Methods. We searched Medline®, Cochrane, Embase®, CINAHL®, and ClinicalTrials.gov from inception to May 15, 2024. After double screening, we extracted study data, assessed risk of bias, and conducted network and pairwise meta-analyses. We evaluated the strength of evidence (SoE) using standard methods. The protocol was registered in PROSPERO (registration number CRD42023461212).

Results. We found 117 studies (reported in 161 papers) that met inclusion criteria. Of these, 31 cross-sectional studies pertained to KQ1, diagnosis of OCD. For KQ 2, treatment of OCD, we included 71 randomized controlled trials, 2 nonrandomized comparative studies, and 13 single-arm studies that reported potential treatment effect modifiers. For KQ1, there is insufficient evidence regarding most brief assessment tools. Based on nine studies, the Child Behavior Checklist-Obsessive Compulsive subscale (CBCL-OCS) may have sufficiently high sensitivity and specificity to identify patients for specialist referral and diagnostic evaluation (moderate SoE). For KQ2, meta-analyses indicate that in-person ERP is more effective for OCD symptoms when compared to either waitlist (high SoE) or behavioral control (moderate SoE), and for remission when compared to waitlist (high SOE) or behavioral control (moderate SoE). ERP via telehealth is more effective than waitlist for OCD symptoms (high SoE) and remission (moderate SoE). SSRIs are more effective than placebo for OCD symptoms and global severity (high SoE). Clomipramine is probably more effective than placebo (moderate SoE). When used together, ERP and an SSRI are probably more effective than treatment with an SSRI alone for OCD symptoms (moderate SoE). ERP combined with an SSRI are as effective as ERP alone for OCD symptoms (high SoE). The side effects of SSRIs and clomipramine were inconsistently reported, precluding graded conclusions. Augmentation of ERP with D-cycloserine is as effective as ERP alone to reduce OCD symptoms (high SoE) or global severity (moderate SoE). The evidence was insufficient regarding potential effect modifiers.

Conclusion. The diagnosis of OCD relies on expert clinical evaluation, sometimes augmented by semi-structured interviews. The CBCL-OCS may be sufficiently accurate to indicate which youth should be further evaluated for OCD. ERP, delivered in-person or via telehealth, is an effective treatment for OCD in children and adolescents. ERP, alone or in combination with an SSRI, is probably more effective than treatment with an SSRI alone.

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Main Points

- **Diagnosis of Obsessive Compulsive Disorder (OCD):**
  - Nine brief assessment tools were identified, but only one had sufficient evidence to draw conclusions. Thus, the available evidence is insufficient regarding the diagnostic accuracy of most brief assessment tools.
  - The 8-question version of the Child Behavior Checklist-Obsessive Compulsive subscale (CBCL-OCS) probably has sufficient diagnostic accuracy to identify symptomatic patients for specialist referral and comprehensive diagnostic evaluation of OCD, with a summary area-under-the-curve of 0.84 (moderate strength of evidence [SoE]).
- **Treatment of OCD:**
  - Cognitive behavioral therapy with exposure and response prevention (ERP) is more effective than waitlist control (high SoE) and probably more effective compared to behavioral control for OCD symptoms (moderate SoE), and for remission compared to waitlist (high SoE) and behavioral control (moderate SoE).
  - Cognitive behavioral therapy with ERP provided via telehealth is more effective than waitlist control for OCD symptoms (high SoE) and probably more effective for remission outcome (moderate SoE).
  - Cognitive behavioral therapy with ERP provided via telehealth is as effective as in-person ERP for OCD symptoms (high SoE), and for remission (high SoE).
  - Treatment with a selective serotonin reuptake inhibitor (SSRI) is more effective than placebo control for OCD symptoms and global severity outcomes (high SoE).
  - Treatment with ERP is probably more effective than treatment with an SSRI alone for OCD symptoms (moderate SoE), but probably as effective as treatment with SSRI alone for remission (moderate SoE).
  - Treatment with ERP and an SSRI is more effective than treatment with an SSRI alone for OCD symptoms (moderate SoE).
  - Treatment with ERP combined with an SSRI is as effective as ERP alone for OCD symptoms (high SoE).
  - Treatment with the tricyclic antidepressant clomipramine is probably more effective than placebo for OCD symptoms (moderate SoE).
  - Treatment with an SSRI is as effective as clomipramine (a tricyclic antidepressant) for OCD symptoms (high SoE) and remission (high SoE).
  - Treatment with D-cycloserine to augment ERP is not more effective than ERP alone in reducing OCD symptoms (high SoE) and is probably not more effective in reducing global OCD severity (moderate SoE).
  - The side effects of SSRIs and clomipramine were inconsistently reported, precluding graded conclusions.
  - Studies were consistent in failing to find statistically significant associations between treatment effects and age, sex, baseline Child Obsessive Compulsive Impact Scale (COIS) score, baseline Family Accommodation Scale (FAS), or comorbid autism spectrum disorder or tics. Studies were inconsistent regarding the association between

treatment effect and baseline OCD severity as assessed by Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS).

Background and Purpose

OCD is a common, chronic, and impairing psychiatric disorder. People with OCD exhibit a wide range of compulsive rituals, avoidance behaviors, and other strategies to neutralize or avoid distress and obsessional triggers. Early identification and treatment of OCD is important to prevent a cascade of developmental disruptions lasting into adulthood that can affect both function and quality of life, particularly in academic and social functioning.

This review focuses on the diagnostic accuracy of brief OCD assessment tools and the treatment of OCD in children. The 2012 American Academy of Child and Adolescent Psychiatry (AACAP) Practice Parameter recommends CBT that incorporates ERP as a first-line treatment for mild-to-moderate OCD in youth, and recommends combined treatment with ERP (if feasible) and an SSRI for some children, particularly those with more severe symptoms. However, questions remain about what (combinations of) treatment strategies work best for specific populations and settings. In addition, new treatment modalities, such as neuromodulation and complementary interventions, have come into use since the 2012 Practice Parameter.

This comparative effectiveness review will summarize the findings from: (1) Studies related to the diagnostic accuracy of brief assessment tools compared to reference standard methods to identify OCD in symptomatic youth, and (2) Studies of psychological and/or pharmacological treatments of OCD.

The systematic review addresses two Key Questions (KQs):

KQ 1: How accurate are brief assessment tools compared to reference standard methods to identify OCD in symptomatic children and adolescents?

> KQ 1.a: How does diagnostic accuracy of brief assessment tools vary by patient, family, social, or other characteristics, or by respondent type?

KQ 2: What are the comparative effects and harms of treatment interventions, used alone or in combination, for OCD in children and adolescents?

> KQ 2.a: How do the effectiveness and harms vary with patient, family, social, or other characteristics?

Methods

In this systematic review, we used methods consistent with those outlined in the Agency for Healthcare Research and Quality Evidence-based Practice Center Program Methods Guidance (https://effectivehealthcare.ahrq.gov/topics/cer-methods-guide/overview). Our searches targeted comparative studies (i.e., randomized controlled trials [RCTs] and nonrandomized comparative

studies [NRCSs] with adjustment for potential confounders) for both KQs from database inception to May 15, 2024. For KQ 1 and for predictors of treatment response in KQ 2, we included single-arm studies. We extracted study data into the Systematic Review Data Repository Plus (SRDR+). With input from technical experts and key informants, we identified prioritized outcomes for each KQ. Where there was sufficient evidence, we conducted random effects network and pairwise meta-analyses. We assessed the risk of bias and evaluated the SoE using standard methods. The PROSPERO protocol registration number is CRD42023461212.

Results

We found 117 studies (reported in 161 papers or records) that met inclusion criteria. The studies were published between 1982 and 2024. Of these, 31 cross-sectional studies pertained to KQ1. For KQ 2, we included 71 RCTs and 2 NRCSs. Potential treatment effect modifiers were reported for 2 of the above RCTs and in 13 additional single-arm treatment studies.

Among the one-third of studies that reported data, more than 80 percent of children were White. Few studies reported on other potential social determinants of health, but among these, at least two-thirds of parents were living together with the child and about 60 to 90 percent of parents had at least a college degree.

Diagnosis: There are 31 studies that have evaluated tools that use either specific cut-points to classify an individual as having OCD or a prediction algorithm or model to predict the probability of OCD. Of these, 23 analyzed 9 brief assessment tools that determine whether a child should be further evaluated for OCD and were included in the analysis. For most of the 9 **brief assessment tools**, the evidence was sparse and insufficient to draw any conclusions. However, for the **8-question version of the CBCL-OCS**, based on 6 studies that provided sufficient data to include in meta-analysis), we found a summary area-under-the-curve of 0.84 (95 confidence interval 0.74 to 0.91) in 3,340 children, 11 percent of whom were diagnosed with OCD.

Treatment: We found 71 RCTs and 2 adjusted NRCSs evaluating OCD treatments. These included behavioral interventions in 31 studies, pharmacologic treatments in 24 studies, and combined behavioral and pharmacologic treatments in 17 studies and one study evaluating transcranial direct current stimulation. After removing small RCTs (N < 100 participants) that evaluated novel comparators, e.g., variations in ERP duration, intensity, location or medications other than SSRIs or clomipramine, we performed separate network meta-analyses by outcome, and concluded that each of these interventions (**ERP, remote ERP, SSRI, and clomipramine**) significantly reduces **OCD symptom severity** on the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS) or Yale-Brown Obsessive Compulsive Scale (Y-BOCS). The relative rate of **remission** with ERP is 3.8-fold higher (95% CI 1.9 to 7.8) than in control. ERP and SSRI both result in a net reduction in **global severity** as measured by the Clinical Global Impressions-Severity (CGI-S) scale, and **family accommodation** on the FAS scale is significantly reduced with ERP compared to control. Network meta-analyses indicated that remote ERP is equivalent to in-person ERP for OCD symptoms and may be equivalent for global severity outcomes. Treatment with ERP is more effective than treatment with SSRI alone, and treatment with ERP plus SSRI is probably more effective than treatment with an SSRI alone. Treatment with clomipramine (a tricyclic antidepressant) is probably more effective than control, and equivalent to treatment with an SSRI. In a pairwise meta-analysis of 5 studies evaluating D-cycloserine to augment ERP, we conclude that the combination of D-cycloserine and ERP is

not more effective than ERP alone in reducing OCD symptom severity and is probably not more effective in reducing global OCD severity. **Harms:** The side effects of SSRIs and clomipramine were inconsistently reported, precluding graded conclusions. No study collected or reported potential harms of behavioral interventions.

We found 15 studies (2 RCTs and 13 single-arm studies) that reported multivariable analyses of predictors of treatment response for ERP or a comparison of ERP with medication that was included in a multivariable model. The evidence was too sparse for any given predictor of treatment to form any conclusions. However, we found a consistent lack of association with treatment response for age (7 studies), sex (7 studies), baseline COIS (2 studies), baseline FAS (2 studies), comorbid autism spectrum disorder (3 studies), and comorbid tics (3 studies). For post-treatment CY-BOCS score, we found a consistent lack of association for age (6 studies), sex (5 studies), baseline functioning (2 studies), baseline FAS (3 studies), and comorbid tics (3 studies). Studies were inconsistent regarding the association between treatment effect and baseline OCD severity as assessed by CY-BOCS. There is some evidence that higher baseline scores mostly predicted higher post-treatment CY-BOCS scores (i.e., positive correlation between baseline and final scores), but also greater reduction in CY-BOCS scores.

Limitations

Multiple small studies reported novel comparisons sizes that did not support graded conclusions. Few studies reported on social determinants of health, but among those that did, study participants were mostly White with well-educated parents who lived together.

For the most robust CY-BOCS outcome network, various control conditions, waitlist, pill placebo, and behavioral control were treated as separate. To construct connected networks for remission and CGI-S, it was necessary to aggregate interventions into broader categories. Given the relatively sparse evidence within comparator-outcome categories, we did not perform subgroup analyses, or meta-regression of potential predictors and moderators of treatment effects.

Implications and Conclusions

The diagnosis of OCD relies on expert clinical evaluation, often augmented by semi-structured interviews. Brief assessment tools have been proposed to be used by primary care providers evaluating youth with symptoms of OCD to facilitate early identification and specialty referral for a comprehensive diagnostic evaluation and early initiation of treatment. The CBCL-OCS may be sufficiently accurate to indicate which youth should be further evaluated for OCD, but the available evidence is insufficient for other brief assessment tools.

We found evidence supporting the efficacy of ERP, delivered in-person or remotely, and for both SSRIs and clomipramine compared to placebo. ERP alone, or ERP in combination with an SSRI, is more effective than treatment with an SSRI alone.

The side effects of SSRIs and clomipramine were inconsistently reported in the included RCTs, precluding graded conclusions. However, based on evidence from other sources, the side effects of these drugs in children and adolescents are well known. No study collected or reported potential harms of behavioral interventions.

Treatment with D-cycloserine to augment ERP is not more effective than ERP alone in reducing OCD symptom severity and is probably not more effective in reducing global OCD severity.

Future research efforts should focus on: (1) inclusion of study participants who are representative of all youth affected by OCD, including non-white, low socioeconomic status children, and of sufficient size to allow subgroup analyses to determine what works for whom; (2) increased transparency in study reporting around dose of exposure, as well as therapist training and quality monitoring; (3) implementation research around the when/where/who/how of OCD treatment to be sure it is reaching everyone who needs it; and (4) development and evaluation of both pharmacologic and behavioral augmentation to ERP and novel interventions (e.g., neuromodulation).

1. Introduction

1.1 Background

Obsessive compulsive disorder (OCD) is a common, chronic, and impairing psychiatric disorder, defined by one or both of two cardinal features—obsessions and compulsions. Obsessions are persistent thoughts, urges, or images that are experienced as intrusive and unwanted, generally related to one or more domains that can range from fear of illness or death to uncomfortable experiences of incompleteness or disgust. People with OCD exhibit a wide range of compulsive rituals, avoidance behaviors, and other strategies to neutralize or avoid distress and obsessional triggers.[1]

For most people with OCD, symptoms begin in childhood or adolescence. An international study of patients with OCD reported that 21 percent had symptom onset in childhood (≤12 years) and 36 percent had symptom onset during adolescence (13-17 years).[2] Prevalence rates of pediatric OCD are generally found to be similar across youth from diverse racial and ethnic groups.[3-6] African Americans experience OCD at similar rates as the general population (White 2.6% vs. Black 2.3%[7]; White 1.6% vs. Black 1.6%[8, 9]), but are less likely to receive treatment or experience a remission.[6, 8]

Early identification and treatment of OCD is important to prevent a cascade of developmental disruptions lasting into adulthood that can affect both function and quality of life, particularly in academic and social functioning.[10-12] Untreated OCD is associated with depression, substance abuse, suicide attempts, and functional impairment in adulthood.[9, 11, 13-15] Establishing an OCD diagnosis can be more challenging in children than in adults due to overlap with developmentally typical childhood fears and rituals, and, especially in young children, developmentally limited cognitive ability to describe their experiences.[1, 16, 17] Furthermore, OCD in children is often comorbid with depression, anxiety disorders, attention deficit hyperactivity disorder (ADHD), and eating disorders.[18] Individuals with OCD may exhibit behaviors similar to those seen in autism, tic disorders, and other anxiety-related disorders, which frequently co-occur with OCD, making differential diagnosis challenging.[17]

The 2012 American Academy of Child and Adolescent Psychiatry (AACAP) Practice Parameter recommends that for children and adolescents undergoing psychiatric assessment for any condition, (1) "The psychiatric assessment … should routinely screen for the presence of obsessions and/or compulsions or repetitive behaviors," even when not part of the presenting complaint; (2) "If screening suggests [obsessive compulsive] symptoms may be present, clinicians should fully evaluate the child using [Diagnostic and Statistical Manual of Mental Disorders (DSM)] criteria and scalar assessment"; (3) Clinicians should use information from all available sources; and (4) "A complete psychiatric evaluation should be performed, … with attention to commonly occurring comorbid psychiatric disorders".[1] The reference standard for an OCD diagnosis is a clinical interview by an expert assessing current DSM criteria, often augmented, with a clinician rated diagnostic tool (e.g., Children's Yale-Brown Obsessive Compulsive Scale [CY-BOCS]), and in research settings with a semi-structured diagnostic interview (e.g., Anxiety Disorders Interview Scale-Child Version [ADIS-C] or MINI-KID [Mini International Neuropsychiatric Interview for Children and Adolescents]).[19]

Because practitioners may not have the expertise or the time to do the full diagnostic interview required for diagnosis, they identify only about 10 percent of cases of childhood OCD.[20] Systemic barriers to accessing experts in assessing OCD may lead to late or missed diagnosis of OCD in children. To address these issues, this review focuses on the diagnostic

accuracy of brief OCD assessment tools. The diagnostic accuracy of a given index test is a cross-sectional question: it addresses the extent to which a classification, based on a specific index test result, corresponds to how an individual would be classified by the reference standard.[21] An index test with sufficiently high diagnostic accuracy might allow primary care providers to make a provisional diagnosis of OCD, prompting expedited specialist referral for additional diagnostic assessment, and treatment.[22, 23] In the literature, these tools are sometimes referred to as "screeners". In this review, we avoid the use of the terms "screening" or "screener" to clearly indicate that our focus is on the accuracy of brief assessment tools for use with symptomatic children and adolescents (i.e., treatment seeking, or referred for clinical concern for a behavioral health concern).

In terms of treatment, the 2012 AACAP Practice Parameter recommends cognitive behavioral therapy that incorporates exposure and response prevention (ERP) as a first-line treatment for mild-to-moderate OCD in youth, and recommends combined treatment with ERP (if feasible) and a selective serotonin reuptake inhibitor for some patients, particularly those with more severe symptoms.[1] However, clinical uncertainty exists regarding the sequencing and combinations of treatment strategies that work best for specific populations and settings. Examples include individual versus family-focused versus parent-mediated, residential versus outpatient settings, through telemedicine as compared to in-person ERP, and ERP combined with medications or medication alone. In addition, new treatment modalities, such as neuromodulation and complementary interventions such as mindfulness, have come into use since the 2012 Practice Parameter.

OCD is thought to be a heterogeneous disorder with multiple potential causes. Individuals with OCD often have comorbidities (or co-occurring symptoms) including ADHD and tics. There is a robust emerging literature describing the neurocircuitry underlying OCD which suggests that shared biological mechanisms may underly the frequent co-occurrence of OCD, ADHD, and tics.[24]

The concept of an "autoimmune OCD" subtype has been proposed. Among patients with OCD some have presentations consistent with proposed definitions of pediatric acute-onset neuropsychiatric syndrome (PANS) and pediatric autoimmune neuropsychiatric disorder associated with streptococcal infections (PANDAS).[25, 26] In one study from a subspeciality pediatric OCD clinic, 7 of 136 (5.1%) children with OCD met proposed diagnostic criteria for PANS/PANDAS.[27] Evidence relating to the diagnostic criteria for PANS/PANDAS, and treatment of these patients with antibiotics or anti-inflammatory medications is outside the scope of this review.

1.2 Purpose of the Review

This comparative effectiveness review will inform a planned update of the 2012 AACAP Practice Parameter.[1] AACAP nominated this topic to the Patient-Centered Outcomes Research Institute (PCORI®), which contracted with the Agency for Healthcare Research and Quality to conduct the review.

Specifically, the systematic review summarizes the findings from: (1) Studies related to the diagnostic accuracy of brief assessment tools compared to reference standard methods to identify OCD in symptomatic youth, and (2) Studies of behavioral interventions, pharmacological treatments, and combined behavioral and pharmacological interventions for the treatment of OCD.

1. Introduction

The intended audience includes guideline developers, child psychiatrists and psychologists, pediatricians, family physicians, advanced practice providers, parents, and patients.

2. Methods

2.1 Review Approach

For all Key Questions (KQs), the systematic review (SR) followed Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Center Program methodology, as laid out in its Methods Guide, particularly as it pertains to reviews of comparative effectiveness, and meta-analyses.[28, 29] Appendix A provides full details for the search strategies, protocol development process, detailed inclusion and exclusion criteria, abstract screening, and data management. We registered the protocol for this SR in PROSPERO (registration number CRD42023461212).

2.2 Key Questions

KQ 1: How accurate are brief assessment tools compared to reference standard methods to identify obsessive compulsive disorder (OCD) in symptomatic children and adolescents?

> KQ 1.a: How does diagnostic accuracy of brief assessment tools vary by patient, family, social, or other characteristics, or by respondent type?

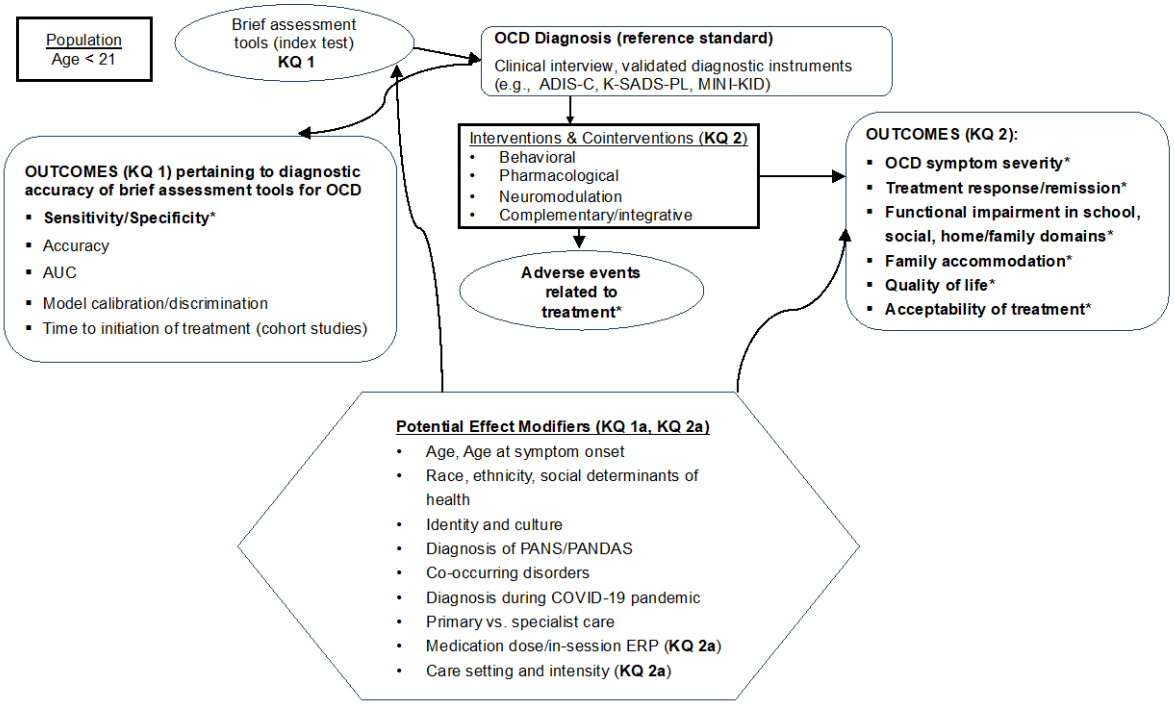
KQ 2: What are the comparative effects and harms of treatment interventions, used alone or in combination, for OCD in children and adolescents?

> KQ 2.a: How do the effectiveness and harms vary with patient, family, social, or other characteristics?

2.3 Logic Model

Based on discussions with Key Informants and Technical Expert Panel members, we developed a logic model for the two KQs (Figure 1).

Figure 1. Logic model for diagnosis and management of obsessive compulsive disorders in children



Abbreviations: ADIS-C = Anxiety Disorders Interview Schedule for Diagnostic and Statistical Manual of Mental Disorders 5 (DSM-5), K-SADS-PL = Kiddie Schedule for Affective Disorders and Schizophrenia, Present and Lifetime version , MINI-KID = Mini-International Neuropsychiatric Interview for Children and Adolescents, AUC = Area under the receiver operating characteristic curve, KQ = Key Question, OCD = Obsessive compulsive disorder, PANS = pediatric acute-onset neuropsychiatric syndrome, PANDAS = pediatric autoimmune neuropsychiatric disorder associated with streptococcal infections

*Prioritized outcome.

2.4 Study Selection

We searched for studies and existing systematic reviews in MEDLINE® (via PubMed®), the Cochrane Register of Clinical Trials, the Cochrane Database of Systematic Reviews, Embase®, CINAHL® and PsycINFO® and Education Resources Information Center (ERIC) databases on July 6, 2023, with an update search on May 15, 2024. Additional searches were conducted on September 1, 2023 in the ClinicalTrials.gov registry for ongoing and unpublished studies with study results. The reference lists of relevant existing systematic reviews were screened for additional eligible studies. Additional articles suggested to us from any source were screened with the same eligibility criteria as the studies identified in the database searches.

We took advantage of the machine learning capacities of Abstrackr (http://abstrackr.cebm.brown.edu/) to limit resources spent on abstract screening. We stopped double screening when the predicted likelihood of the remaining unscreened papers was below 0.40 (this threshold is based on experience with several dozen screening projects and an analysis in preparation for publication) and we had rejected at least 400 consecutive citations.

For KQ 1, we report studies that evaluate the diagnostic accuracy (predictive validity) of brief assessment tools for OCD in children and adolescents, compared to a reference standard (clinical interview by an expert assessing current Diagnostic and Statistical Manual for Mental

Disorders criteria, possibly augmented by a semi-structured interview using a validated assessment instrument).

For KQ 2, we included randomized controlled trials (RCTs) and nonrandomized comparative studies (NRCSs) that compared psychological and pharmacological interventions for OCD, alone or in combination, compared to control conditions (i.e., waitlist, pill placebo, behavioral interventions that did not include exposure and response prevention [ERP]), or another active intervention or co-intervention(s) or delivery method. Eligible NRCSs had to adjust for potential confounders. We evaluated outcomes as listed in the Study Eligibility Criteria section, focusing on listed prioritized outcomes related to OCD symptom severity, treatment response and remission, functional impairment, family accommodation, quality of life, and acceptability of treatment and adverse events related to treatment. Prioritized outcomes are in bold font (with asterisks) in the Study Eligibility Criteria table.

We extracted reported predictors and moderators of treatment effect from the included RCTs, and in addition from adjusted single-arm studies that reported predictors of treatment response.

For all Key Questions, we identified predictors and moderators of treatment effect from the included RCTs (see potential effect modifiers/subgroups of interest), and in addition from adjusted single-arm studies that reported predictors of treatment response. Studies excluded in full text along with their exclusion reasons are listed in Appendix B.

2.5 Data Extraction and Data Management

We extracted data into the Systematic Review Data Repository Plus (SRDR+) database (https://srdrplus.ahrq.gov) and Google Sheets as appropriate. Data extracted in Google Sheets were imported into SRDR+ at the end of the project. Each eligible study was extracted and assessed for risk of bias (RoB)/quality by one researcher. Extracted data, including RoB assessment, were confirmed by a second, independent researcher.

2.6 Assessment of Risk of Bias and Methodologic Quality

We evaluated each comparative study (RCT and NRCS) for RoB. All overall RoB assessments were determined by discussion of the team.

For RCTs, including cluster randomized trials, we completed the Cochrane Risk of Bias tool,[30] which addresses issues related to randomization and allocation concealment; blinding; deviations from intended intervention; missing data; outcome measurement; and reporting biases.

For NRCSs, we added assessments of specific elements from ROBINS-I[31] (Risk Of Bias In Non-randomized Studies - of Interventions) related to selection bias (comparability of groups) and relevant concepts addressed for RCTs (i.e., related to missing data, outcome measurement, analysis plan).[31]

In developing a RoB rating for comparative studies, we used the following heuristic: If allocation or randomization RoB was high, the overall RoB was high. If any other single element was at high RoB, the overall RoB was moderate. If two other elements were at high RoB, the overall RoB was high. If allocation, randomization, and blinding were all unclear, the overall RoB was (at best) moderate. If blinding of outcome assessor was at low RoB and blinding of participants was at high RoB, overall blinding was determined to be at low RoB. If blinding of the outcome assessor was unclear and blinding of participants was at high RoB, overall blinding was at high RoB. For NRCSs, given lack of randomization, all were at best moderate RoB.

Those with other methodological issues that increased the likelihood of residual confounder were deemed high RoB.

For single-arm studies reporting predictors of treatment effect, we assessed the adequacy of adjustment for potential confounders using three criteria: (1) whether all predictors in the model were described in the article, (2) whether results were given for all predictors in model, and (3) whether the number of variables in the model divided by number of participants was greater than 10. Where all 3 criteria were met, the analysis was considered to be adequate; otherwise, the analysis was considered inadequate.

For single test diagnostic accuracy studies, we assessed specific elements from the QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies 2).[32-34] Overall RoB rating was determined in consensus among the group using the following heuristics: If the study was a single-arm study (with no control group) or a case control study that did not enroll a random or consecutive sample, and did not report using a reference standard on all participants, the study was determined to have high RoB. If the study was not a case-control study and reported using a reference standard on all participants, RoB was low. If the study was a case-control design, but all other criteria were low, RoB was moderate.

2.7 Data Synthesis

Each study is described in summary and evidence tables presenting study design features, study participant characteristics, descriptions of interventions, outcome results, and RoB/methodological quality in Appendix C.

For diagnostic test studies, we extracted all relevant outcome measures (e.g., sensitivity, specificity, area under the curve receiver operating characteristics curve [AUC ROC]) at all reported thresholds.

For KQ 1, we conducted random-effects model meta-analyses of comparative studies if at least 6 studies were sufficiently similar in population, interventions, outcomes, and study design. The diagnostic meta-analysis models estimate 5 parameters: mean sensitivity, mean specificity, the standard deviations of the random effects of sensitivity and specificity, and the correlation between the random effects of sensitivity and specificity. We created summary ROC curves for tools where there were at least 5 studies with sufficient data using the diagmeta[35] package in R,[36] which uses a hierarchical restricted maximum likelihood (REML) linear random effects model.

For KQ 2, we analyzed continuous effect metrics on the original reported scales, such as Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS). We focus on common scales reported across studies, and do not use standardized effect sizes such as Cohen's d. For continuous outcomes, we compute net mean differences (NMD; the difference between arms of the within-arm changes in outcome). For categorical outcomes such as remission, we report effects on the risk ratio (RR) scale.

In the network graphs, the circles (nodes) represent interventions. The diameter of the circles is proportional to the number of patients who received each intervention. The lines connecting nodes (edges) represent the direct comparisons between pairs of interventions. The width of the edges are proportional to the number (shown in text on each line/edge) of studies that directly compared each pair of treatments.

For all networks, we assign separate control groups—wait list (WL), pill placebo (placebo) and behavioral control (behavCntrl)— to separate comparator nodes. In a sensitivity analysis, we combined these control group types into a common 'Control' node.

In each network, we found studies comparing a novel treatment or treatment adjunct with a reference treatment (often ERP). Comparisons between non-reference treatments rely on indirect evidence, limiting the reliability of these estimates. We removed these "hanging branches" during network construction. For those comparisons with fewer than 100 participants, we summarize narratively. When comprised of three or more studies, we synthesize these "hanging branches" via separate pairwise meta-analysis.

We conducted network meta-analysis (NMA), an extension of pairwise MA that synthesizes direct and indirect evidence in a single analysis of multiple comparisons. We fit frequentist random effects models using the R package netmeta.[37] REML was used to estimate the between study variance τ^2.

The effect estimates for each treatment contrast derive from two sources—studies that directly compare two treatments (direct evidence)—and also from studies in a connected path via one or more intermediate comparators (indirect evidence).[37] We report network effect estimates (which combine direct and indirect evidence) only for those comparisons informed by direct evidence from at least 2 study arms. For each comparison, the figures display separate direct and indirect estimates, the overall network estimate, and the predictive interval. The transitivity assumption is supported when the direct and indirect estimates are similar. We compared direct and indirect evidence for each pairwise comparison using the separate indirect from direct evidence (SIDE) method.[38]

The Q_B statistic under the assumption of a full design-by-treatment interaction random effects model was used to test the null hypothesis of global consistency of the random effects models.[30]

The prediction interval is the expected range of treatment effects in future similar studies and represents an indirect indicator of between study heterogeneity.[39]

We performed random effects pairwise MA using the R[36] package meta[40] for comparisons represented as "hanging branches" (nodes connected to the network by a single edge) that are informed by direct comparisons in 3 or more studies.

For sparsely reported outcomes (i.e., outcomes reported by fewer than 3 studies for a given comparison), we summarize the number of studies reporting each outcome, and report study specific effects in the appendix evidence tables. We summarize but do not detail these results in the main report.

We narratively describe differences in effects and harms by different factors, subgroups, or predictors. This includes NRCSs with adjustment for potential confounders, and single-arm studies of over 50 participants that performed any type of adjusted analysis with at least three variables in the model.

2.8 Grading the Strength of Evidence for Prioritized Outcomes

Following AHRQ Methods guidance, we considered the number of studies, their designs, limitations (i.e., RoB and overall methodological quality), the directness of the evidence, the consistency of study results, the precision of any estimates of effect, the likelihood of reporting bias, other limitations, and the overall findings across studies, and assigned a consensus strength of evidence (SoE) rating of high, moderate, low, or insufficient to estimate an effect, addressing each prioritized outcome for each KQ.

Outcomes with highly imprecise estimates (with 95% confidence intervals that extend beyond both 0.5 and 2.0 for categorical outcomes, or a confidence interval greater than half the

full range of the scale for continuous outcomes), highly inconsistent findings across studies (in terms of directions of effect), or with data from only one study were deemed to have insufficient evidence to allow for a conclusion. Data from a single study were deemed insufficient evidence to allow for a graded conclusion, with the exception that a relatively large (defined as N ≥100), well-conducted (defined as low RoB) study could provide low SoE.

This approach is consistent with the concept that for imprecise evidence "any estimate of effect is very uncertain," which is the definition of Very low-quality evidence per the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach.[41]

In accordance with AHRQ guidance for describing treatment effects,[1, 42, 43] we have incorporated qualifying language regarding SoE when communicating conclusions (e.g., in Key Points sections of the text) as follows: "probably" for conclusion statements with Moderate SoE and "may" for conclusion statements with Low SoE. Conclusions with High SoE do not include any qualifiers.

3. Results

3.1 Literature Search Results

The literature search yielded 12,907 records after deduplication. Detailed search strategies, inclusion and exclusion criteria, and a list of excluded studies (with reasons for their exclusion) are in Appendixes A and B. Appendix C Figure C-1 summarizes the results of the search and screening processes.

We retrieved and screened the full-text publications for 443 citations or records. We extracted data from 161 papers or records that met our inclusion criteria. Of these, 31 cross-sectional studies pertained to Key Question (KQ) 1 (of which 22 evaluated brief assessment tools and were included in the analysis). For KQ 2, we included 71 randomized controlled trials (RCTs) and 2 nonrandomized comparative studies (NRCSs). Predictors of treatment effects were reported for 2 of the above RCTs and in 13 additional single-arm study cohorts (reported in 19 papers).

3.2 Description of Included Evidence

Tables describing study designs, groups, and sample characteristics; RoB; and details of outcome data are in Appendix C, Results: Design, Arm, and Sample Details. Specifically, Appendix Tables C-1.1 to C-2.3.2 summarize the design, arm, and patient characteristics for each KQ. Appendix D Tables D-1.1 to D-2.2 summarize the risk of bias (RoB) for comparative studies for RCTs and NRCSs, and methodological quality for single arm studies. Detailed results are in Appendix E, Tables E–KQ1-1 to E–KQ2-40. References for all appendixes are in Appendix F. Appendix G contains the full data extractions for KQ1 and Appendix H contains the full data for the KQ2 studies that assesses predictors of treatment effectiveness.

We call attention to specific appendix table numbers in the relevant subsections.

3.3 Key Question 1

Key Question 1: How accurate are brief assessment tools compared to reference standard methods to identify obsessive compulsive disorder (OCD) in symptomatic children and adolescents?

> KQ 1.a: How does diagnostic accuracy of brief assessment tools vary by patient, family, social, or other characteristics, or by respondent type?

3.3.1 Key Points

- Nine brief assessment tools were identified, but only one had sufficient evidence to draw conclusions. Thus, the available evidence is insufficient regarding the diagnostic accuracy of brief assessment tools other than the Child Behavior Checklist-Obsessive Compulsive subscale (CBCL-OCS).
- Brief assessment tools: The 8-question version of the CBCL-OCS probably has sufficient diagnostic accuracy to identify symptomatic patients for specialist referral and

comprehensive diagnostic evaluation of OCD, with a summary area-under-the-curve of 0.84 (moderate strength of evidence [SoE]).

3.3.2 Evidence Identified

In the context of tools that use specific cut-points to classify an individual as having OCD or a prediction algorithm or model to predict the probability of OCD, 31 studies met eligibility criteria.[20, 22, 23, 44-71] Of these, 22 addressed brief assessment tools that determine whether a child should be further evaluated for OCD and were therefore included in this analysis. The nine studies that evaluated non-brief tools are summarized in Appendix E. The rest of this section describes the results for brief assessment tools.

Descriptions of the brief tools evaluated are in Table 1. In all studies the reference standard was a clinical diagnosis by a doctoral-level evaluator. The studies enrolled between 50 and 2,512 children (between 8 and 489 with OCD). The mean ages ranged from 9 to 15 years, with most children in early adolescence. The cohorts were generally equally distributed between males and females but ranged from 32 to 71 percent male. Among the studies that reported data on race and/or ethnicity, participants were predominantly White (88% to 98%). In the OCD group, 82 percent of studies drew their participants from outpatient psychiatric clinics, 2 described as OCD-specific; 2 drew from intervention research study populations, 1 from an inpatient psychiatric clinic, and 1was not reported. In the control group, 50 percent of studies drew their participants from outpatient psychiatric clinics, one OCD-specific; 4 drew from nonclinical populations (e.g., schools), 2 drew from intervention research study populations, 1 from an inpatient psychiatric clinic, and 4 did not have a control group. Full details of study design and cohort characteristics are in Appendix Tables C-1.1 to C-1.2. Most studies used a case-control design (91%), comparing a known group of children with OCD with a control group of either clinical controls or a mix of clinical and nonclinical controls. Studies that compared children with OCD only with nonclinical controls (i.e., children who were not being evaluated for OCD, such as general school children) and studies that had no controls were extracted for sensitivity only (i.e., evaluation only of the group of children with OCD). Overall RoB is reported in the results tables for each study. Full RoB data are in Appendix Table D-1.1.

Table 1. Brief assessment tools

Tool Acronym	Tool Components/Items	Tool Description Reporter (Parent/Child)	Tool Range*	No. Studies
Children's Florida Obsessive Compulsive Inventory (C-FOCI)[72]	25 questions addressing obsessions and compulsions that are frequent among young people with OCD	OCD-specific, brief, focused instrument: Symptom Checklist is a dichotomous tool that evaluates the presence/absence of obsessions (10 questions) and compulsions (10 questions). The severity checklist includes additional 5 questions to evaluates severity of symptoms (total 25 questions) Reported by parent and/or child	Symptom checklist: 0 to 20 Severity scale: 0 to 25	2[57, 71]
Child Behavior Checklist-Obsessive Compulsive subscales (CBCL-OCS)[23]	8 questions addressing fears/worries, obsessions, and compulsions	OCD-specific subscale: A subset of the full CBCL. The most common CBCL-OCS subscale consists of a subset of 8 items determined to be most predictive in an analysis by Nelson et al.[23] OCS-R (revised) contains 6 items, which are a subset of the 8 established by Nelson et al.[22] Reported by parent only	0 to 24	9[20, 23, 46, 48, 50, 52, 59, 64, 66]

3.3.2. Results, Key Question 1: Brief Assessment Tools, Evidence Identified

Tool Acronym	Tool Components/Items	Tool Description Reporter (Parent/Child)	Tool Range*	No. Studies
Obsessional Compulsive Inventory-Child (CHOCI)[62]	Questions addressing obsessions, compulsions, and impairment associated with both	OCD specific: Designed to assess the presence and severity of OCD in children and adolescents aged 7-17 years; derived from the CY-BOCS, but intended for self-report rather than clinician rating Reported by parent and/or child	Total impairment: 0 to 48 Total symptoms: 0 to 40	1[62]
Leyton Obsessional Inventory – Child Version (LOI-CV)[73]	44 items that assess obsessive symptoms. Short version consists of 20 items	OCD specific. Self-report questionnaire focused on obsessions. Reported by child only	1 to 132 (full version) 1 to 60 (short version)	3 (1 full version, [65] 3 short version[47, 65, 67]
Obsessive Compulsive Inventory – Child Version (OCI-CV)[74]	21 items addressing six domains: doubting/checking, obsession, ordering, doubting, neutralizing, and hoarding Doubting/Checking, obsessing, Hoarding, Washing, Ording, and neutralizing	OCD specific: Self-report severity scale for children aged 7-17 years old OCI-CV-R (revised) assesses all items except those related to hoarding (18 items) OCI-CV-5 assesses a five-item subset of the OCI-CV-R Reported by child only (self-report)	OCI-CV: 0 to 42 OCI-CV-R: 0 to 36 OCI-CV-5: 0 to 10	4 (2 OCI-CV,[58, 70] 1 OCI-CV-R,[22] 1 OCI-CV-5[44])
Spence Children's Anxiety Scale – OCD subscale (SCAS-OCD) [69]	6 items, assessing obsessions and compulsions	OCD specific subscale: Derived from the Spence Children's Anxiety Scale, assesses a subset of symptoms related to OCD for children ages 8 to 15 years Reported by parent and/or child	0 to 24	2[60, 69]
Short Obsessive Compulsive Disorder Screener (SOCS)[68]	7 items that address common symptoms (e.g., checking, touching, cleanliness/washing, repeating, and exactness)	OCD specific: Includes the 5 most discriminant items of the 44-item LOI. Two additional questions were designed to gauge the associated impairment and resistance, so there are total 7 questions Reported by parent only	0 to 14	2[56, 68]
Toronto Obsessive–Compulsive Scale (TOCS)[54]	21-item measure of obsessive and compulsive symptoms addressing 6 subscales: counting/checking, cleaning/contamination, hoarding, symmetry/order, rumination, and superstition	OCD specific: designed to measure OCD traits in the general population; designed to be administered by clinicians for children and adolescents Reported by parent and/or child	-63 to 63†	1[54]
Youth Self-Report OCD subscale (YSR OCD subscale)[64]	8 items that address obsessions, and compulsions	OCD specific subscale: A subset of the YSR, which assesses internalizing and externalizing problems, designed for children ages 11 to 18 years. Reported by child only	0 to 16	1[64]
Children's Florida Obsessive Compulsive Inventory (C-FOCI)[72]	17 questions addressing obsessions and compulsions that are frequent among young people with OCD	OCD-specific, brief, focused instrument: Symptom Checklist is a dichotomous tool that evaluates the presence/absence of obsessions and compulsions.	Symptom checklist: 0 to 17 Severity scale: 0 to 85	2

3.3.2. Results, Key Question 1: Brief Assessment Tools, Evidence Identified

Tool Acronym	Tool Components/Items	Tool Description Reporter (Parent/Child)	Tool Range*	No. Studies
Child Behavior Checklist-Obsessive Compulsive subscales (CBCL-OCS)[23]	8 questions addressing fears/worries, obsessions, and compulsions	OCD-specific subscale: A subset of the full CBCL. The most common CBCL-OCS subscale consists of a subset of 8 items determined to be most predictive in an analysis by Nelson et al.[23] OCS-R (revised) contains 6 items, which are a subset of the 8 established by Nelson et al..[22]	0 to 24	9
Obsessional Compulsive Inventory-Child (CHOCI)[62, 75]	19 questions addressing obsessions, compulsions, and impairment associated with both	OCD specific: Designed to assess the presence and severity of OCD in children and adolescents aged 7-17 years; derived from the CY-BOCS, but intended for self-report rather than clinician rating	Total impairment: 0 to 48 Total symptoms: 0 to 40	1
Leyton Obsessional Inventory – Child Version (LOI-CV)[73]	44 items that assess obsessive symptoms. Short version consists of 20 items	OCD specific. Self-report questionnaire focused on obsessions.	1 to 44 (full version) 1 to 20 (short version)	3 (1 full version, 2 short version)
Obsessive Compulsive Inventory – Child Version (OCI-CV)[74]	21 items addressing six domains: washing/checking, obsession, ordering, doubting, neutralizing, and hoarding	OCD specific: Self-report severity scale for children aged 7-17 years old OCI-CV-R (revised) assesses all items except those related to hoarding (18 items) OCI-CV-5 assesses a five-item subset of the OCI-CV-R	OCI-CV: 0 to 63 OCI-CV-R: 0 to 35 OCI-CV-5: 0 to 15	4 (2 OCI-CV, 1 OCI-CV-R, 1 OCI-CV-5)
Spence Children's Anxiety Scale – OCD subscale (SCAS-OCD) [69]	6 items, assessing obsessions and compulsions	OCD specific subscale: Derived from the Spence Children's Anxiety Scale, assesses a subset of symptoms related to OCD for children ages 8 to 15 years	0 to 24	2
Short Obsessive Compulsive Disorder Screener (SOCS)[68]	5 items that address common symptoms (e.g., checking, touching, cleanliness/washing, repeating, and exactness)	OCD specific: Includes the 5 most discriminant items of the 44-item LOI	0 to 14	2
Toronto Obsessive–Compulsive Scale (TOCS)[54]	21-item measure of obsessive and compulsive thoughts	OCD specific: designed to measure OCD traits in the general population; designed to be administered by clinicians for children and adolescents	-63 to 63†	1
Youth Self-Report OCD subscale (YSR OCD subscale)[64]	Addresses obsessions, and compulsions	OCD specific subscale: A subset of the YSR, which assesses internalizing and externalizing problems, designed for children ages 11 to 18 years.	0 to 11	1

Tools are listed in alphabetical order based on their acronyms.
Abbreviations: CV = child version; DSM = Diagnostic and Statistical Manual of Mental Disorders; ICD = International Classification of Diseases; OCD = obsessive compulsive disorder; R = revised.

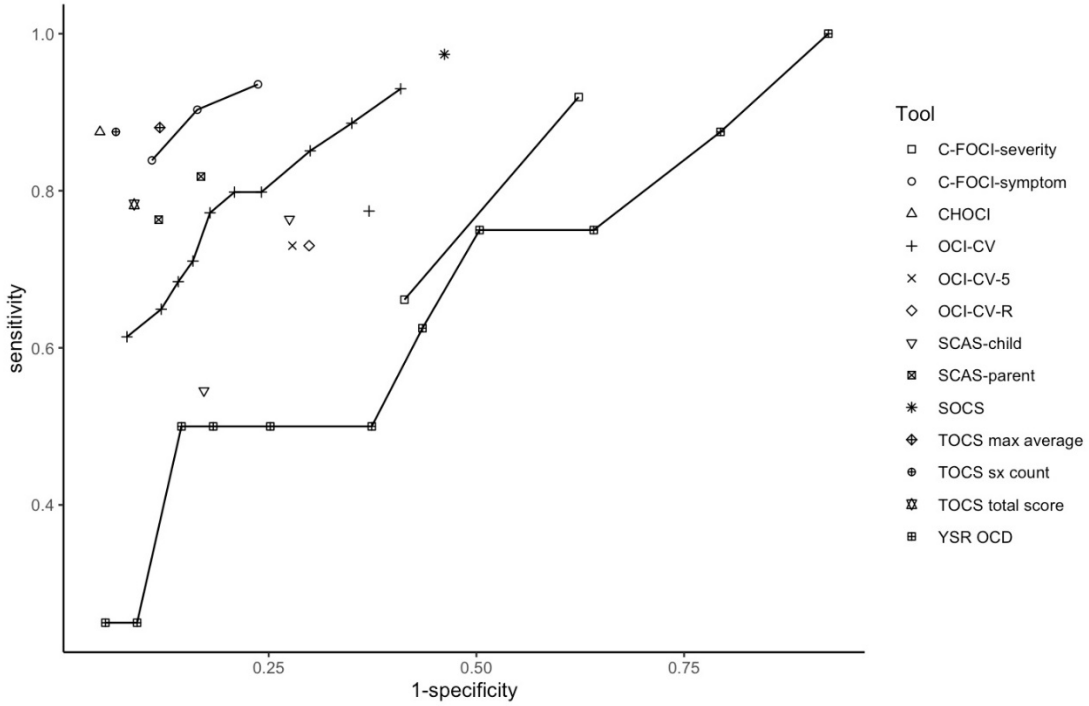
***** Higher scores reflect greater severity.
† Scores for each item range from −3 = far less often to 0 = average to +3 = far more often.

3.3.2.1 Brief Assessment Tools

Most of the brief assessment tools were evaluated in only one or two studies each, with the exception of the Child Behavior Checklist-obsessive compulsive subscale (CBCL-OCS); also called the Child Behavior Checklist-obsessive compulsive disorder (CBCL-OCD), which was

evaluated in nine studies. The small number of studies and inconsistent control groups mostly precluded comparisons across studies. Sensitivity and specificity results for each study are presented by tool in Figure 2 and by study in Table 2 Information for the CBCL-OCD is below.

Figure 2. Observed ROC curves for other tools



Datapoints connected by lines are from the same studies. Studies that did not provide specificity data are omitted.
Abbreviations: C-FOCI = Children's Florida Obsessive Compulsive Inventory; CHOCI = Child Obsessional Compulsive Inventory; OCD = obsessive compulsive disorder; OCI-CV = Obsessive Compulsive Inventory – Child Version; SCAS = Spence Children's Anxiety Scale (OCD subscale); ROC = receiver operating characteristic; SOCS = Short Obsessive Compulsive Disorder Screener; TOCS = Toronto Obsessive–Compulsive Scale; YSR-OCD = Youth Self-Report OCD subscale

3.3.2. Results, Key Question 1: Brief Assessment Tools, Evidence Identified

Table 2. Sensitivity and specificity for brief assessment tools

Tool	Study (N OCD/N Control) RoB	Cutoff	Sensitivity, %	Specificity, %
C-FOCI Symptom	Piqueras 2017[57] (94/NA) high	9	0.37 (0.27, 0.48)	NA
C-FOCI Symptom (Persian)	Zemestani 2021[71] (62/NA) high	9	0.94 (0.84, 0.98)	0.76 (0.71, 0.81)
C-FOCI Severity (Persian)	Zemestani 2021[71] (62/NA) high	6	0.92 (0.82, 0.97)	0.59 (0.53, 0.64)
CHOCI	Shafran 2003[62] (24/64) high	17	0.88 (0.47, 1)	0.95 (0.87, 0.99)
LOI-CV 20 question version	Stewart 2005[65] (81/NA) moderate	25	0.28 (0.18, 0.39)	NA
LOI-CV 20 question version	Storch 2011[67] (50/NA) moderate	25	0.14 (0.06, 0.27)	NA
LOI-CV 20 question version, measured using symptom frequency	Bamber 2002[47] (9 OCD only/NA) high	5	0.78 (0.40, 0.97)	NA
LOI-CV 20 question version, measured using symptom frequency	Bamber 2002[47] (14 OCD + depression/NA) high	5	0.79 (0.49, 0.95)	NA
LOI-CV 44 question version	Stewart 2005[65] (81/NA) moderate	30	0.52 (0.40, 0.63)	NA
OCI-CV	Rough 2020[58] (114/641) high	11	0.77 (0.68, 0.85)	0.82 (0.78, 0.86)
OCI-CV (Persian)	Zemenstani 2022[70] (62/NA) high	17.5	0.77 (0.65, 0.87)	0.63 (0.57, 0.68)
OCI-CV-R	Abramovitch 2022[22] (489/298) moderate	8	0.73 (0.69, 0.77)	0.70 (0.65, 0.75)
OCI-CV-5	Abramovitch 2022[44] (489/298) moderate	2	0.73 (0.69, 0.77)	0.72 (0.67, 0.77)
SCAS-OCD parent	Whiteside 2012[69] (76/85) moderate	7	0.76 (0.65, 0.85)	0.88 (0.79, 0.94)
SCAS-OCD parent	Sattler 2018[60] (33/279) high	8	0.82 (0.65, 0.93)	0.83 (0.78, 0.87)
SCAS-OCD child	Whiteside 2012[69] (76/85) moderate	7	0.76 (0.65, 0.86)	0.72 (0.61, 0.82)
SCAS-OCD child	Sattler 2018[60] (33/279) high	8	0.55 (0.36, 0.72)	0.83 (0.78, 0.87)
SOCS	Uher 2007[68] (114/13) low	6	0.97 (0.93, 0.99)	0.54 (0.25, 0.81)
SOCS	Piqueras 2015[56] (94/NA) high	6	76 (66, 84)	NA
TOCS max average	Lambe 2021[54] (184/227) moderate	1	0.88 (0.82, 0.92)	0.88 (0.83, 0.92)
TOCS symptom count	Lambe 2021[54] (184/227) moderate	2	0.88 (0.82, 0.92)	0.93 (0.89, 0.96)
TOCS total score	Lambe 2021[54] (184/227) moderate	1	0.78 (0.72, 0.84)	0.91 (0.87, 0.95)
YSR-OCD subscale	Skarphedinsson 2021[64] (8/131) moderate	9	0.50 (0.16, 0.84)	0.85 (0.78, 0.91)

Abbreviations: C-FOCI = Children's Florida Obsessive Compulsive Inventory; CHOCI = Child Obsessional Compulsive Inventory; LOI-CV = Leyton Obsessional Inventory – Child Version; OCD = obsessive compulsive disorder; OCI-CV = Obsessive Compulsive Inventory – Child Version; RoB = risk of bias; SCAS-OCD = Spence Children's Anxiety Scale – OCD subscale; SOCS = Short Obsessive Compulsive Disorder Screener; TOCS = Toronto Obsessive–Compulsive Scale; YSR-OCD = Youth Self-Report OCD subscale

The shading groups tools but does not provide any unique meaning.

In terms of discriminating among OCD, attention-deficit/hyperactivity disorder (ADHD), and autism spectrum disorder (ASD), Lambe (2021) reported area-under-the-curve (AUC) analyses for the Toronto Obsessive Compulsive Scale (**TOCS)** in a cohort of 350 children with OCD, 820 children with ADHD, and 794 children with ASD.[54] For OCD versus ADHD, the TOCS had an AUC of 0.86 (95% confidence interval [CI] 0.84 to 0.89). For OCD versus ASD, the TOCS had an AUC of 0.81 (95% CI 0.78 to 0.84). These results suggest that the tool may be better at differentiating OCD from ADHD than OCD from ASD.

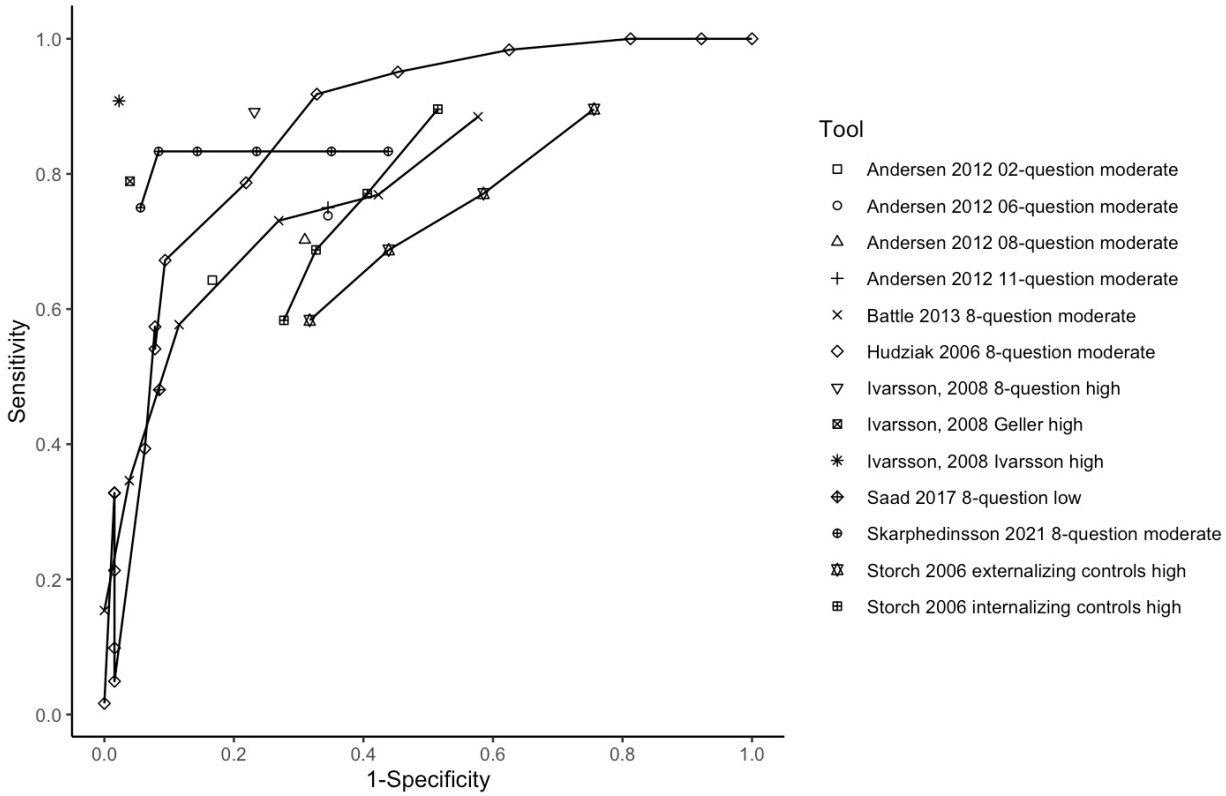
Nine studies evaluated the CBCL-OCS/OCD in 3746 participants.[20, 23, 46, 48, 50, 52, 59, 64, 66] Only one study was rated as low RoB,[59] four were rated as of moderate RoB,[20, 46, 48, 64] and two were rated as of high RoB.[52, 66] Individual ratings are listed with the study name in Figure 3. Both

3.3.2. Results, Key Question 1: Brief Assessment Tools, Evidence Identified

Nelson 2001 and Geller 2006 reported data only by percentile; thus, their data are not included in the figures.[23, 50] Both reported sensitivity and specificity for percentiles ranging from the 40th to the 90th. Sensitivities ranged from 0.98 in the 40th percentile to 0.30 in the 90th, and specificities ranged from 0.41 in the 40th percentile to 1.0 in the 90th percentile. Six studies evaluated the 8-question subscale developed by Nelson et al. in 2001.[23] The other three evaluated subsets of these questions. The prevalence of OCD in the nine studies ranged from 0.03 to 0.54, with a median of 0.49 (interquartile range [IQR] 0.33 to 0.49) and a mean of 0.39 (standard deviation [SD] 0.17).

Meta-analysis of the six studies[20, 46, 48, 52, 59, 64] that evaluated Nelson et al.'s 8-question subscale (in 3,340 children, 361 with OCD) showed a summary AUC of 0.84 (95% CI 0.74 to 0.91). The summary receiver operating (SROC) curve is shown in Figure 4.

Figure 3. ROC curves for the CBCL-OCS scale

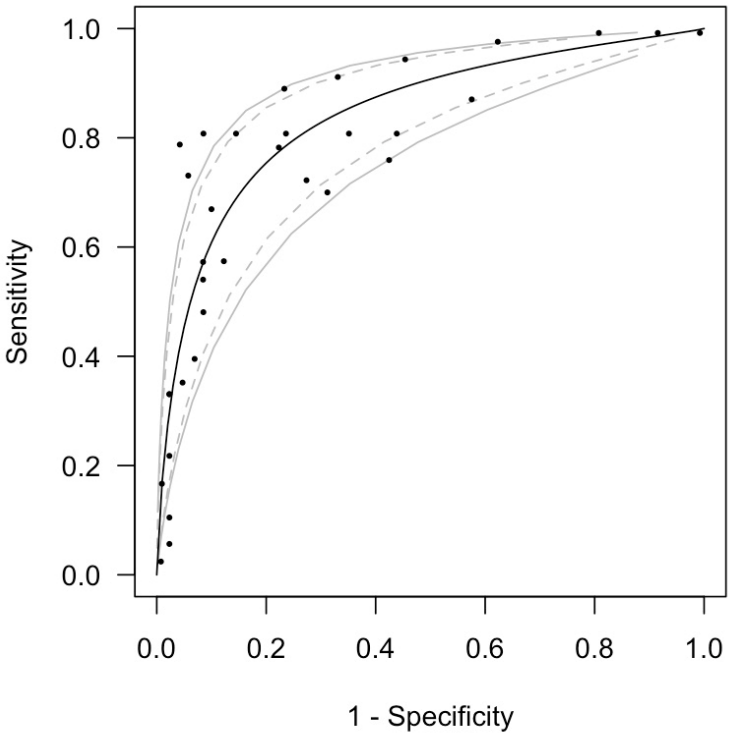


Listed studies present the study author, year, differentiating information as needed, and overall risk of bias rating.

Abbreviations: CBCL-OCS = Child Behavior Checklist-Obsessive Compulsive subscales, ROC = receiver operating characteristic

3.3.2. Results, Key Question 1: Brief Assessment Tools, Evidence Identified

Figure 4. SROC curve for the CBCL-OCS scale



The meta-analysis was done on only the 8-question version of the Child Behavior Checklist-Obsessive Compulsive subscales (CBCL-OCS). The solid black line is the summary receiver operating curve (SROC); the solid gray lines demark the 95% confidence region for sensitivity given specificity and the dashed gray lines demark the 95% confidence region for specificity given sensitivity. The dots represent the reported sensitivity and 1-specificity points from each of the 6 studies. See Figure 3 for details on the individual studies.

Several studies evaluated the CBCL-OCD scale for different subsets of questions, reporting generally very good AUCs, which ranged from 0.74 to 0.96. These were not included in the meta-analysis, as they were not directly comparable to the standard 8-question CBCL-OCS. Specifically, Andersen 2012 evaluated the CBCL-OCD scale for different subsets of questions (2, 6, 8, and 11) in 168 children (84 with OCD) and reported AUCs were between 0.74 and 0.79.[46] Ivarsson 2008 chose four CBCL-OCD scale items that, in a logistic regression, best predicted OCD.[52] In a cohort of 362 children (185 with OCD and 177 clinical controls, the AUC for these items was 0.96 (95% CI 0.94 to 0.98). They compared this with the 8-question scale developed by Nelson et al. in 2001 in the same cohort and reported an AUC for the 8-question scale of 0.91 (95% CI 0.87 to 0.94). Storch 2006 narrowed the criteria in the 8-question scale developed by Nelson et al. in 2001to 6 factors with the greatest predictive strength.[66] Then evaluated the 6-question CBCL-OCS subscale in participants with internalizing and externalizing disorders. It is unclear if this is because the comparator groups had disorders more similar to OCD than the other studies' comparator groups or because the scale had fewer elements.

3.3.3 Results, Key Question 1: Brief Assessment Tools, Evidence Profile for Key Question 1

3.3.3 Evidence Profile for Key Question 1

Overall, the current evidence is insufficient to justify broad conclusions about the performance and utility of tools and tools used to diagnose OCD other than the CBCL-OCD. See Table 3.

Table 3. Evidence profile for Key Question 1, diagnosis of OCD

Tool Type	Tool	N Studies (Patients)	RoB	Consistency	Precision	Directness	SoE	Conclusions
Brief assessment tools	CBCL-OCD	9 (4021); 6 (3508) using Nelson's CBCL 8 question version	Moderate	Consistent	Precise	Direct	Moderate	Summary AUC 0.84 (0.74 to 0.91)*

Tools with insufficient evidence are omitted.

*Based on the 6 studies evaluating the 8 question score

Abbreviations: AUC = area under the curve; CBCL-OCD= Child Behavior Checklist-Obsessive Compulsive Disorder subscale; RoB = risk of bias; SoE = strength of evidence

3.4 Key Question 2

Key Question 2: What are the comparative effects and harms of treatment interventions, used alone or in combination, for OCD in children and adolescents?

Key Question 2.a: How do the effectiveness and harms vary with patient, family, social, or other characteristics?

3.4.1 Key Points

- Cognitive behavioral therapy with exposure and response prevention (ERP) is more effective than waitlist control (high SoE) and probably more effective compared to behavioral control for OCD symptoms (moderate SoE), and for remission compared to wait list (high SoE) and behavioral control (moderate SoE).
- Cognitive behavioral therapy with ERP provided via telehealth is more effective than waitlist for OCD symptoms (high SoE), remission (moderate SoE), and family accommodation outcomes (SoE).
- Cognitive behavioral therapy with ERP provided via telehealth is as effective as in-person ERP for OCD symptoms (high SoE), and for remission (high SoE).
- Treatment with a selective serotonin reuptake inhibitor (SSRI) is more effective than placebo control for OCD symptoms and global severity outcomes (high SoE).
- Treatment with ERP is probably more effective than treatment with an SSRI alone for OCD symptoms (moderate SoE).
- Treatment with ERP combined with an SSRI is as effective as ERP alone for OCD symptoms (high SoE) and probably as effective for remission.
- Treatment with the tricyclic antidepressant clomipramine may be more effective than placebo control for OCD symptoms (moderate SoE).
- Treatment with an SSRI is as effective as clomipramine (a tricyclic antidepressant [TCA]) for OCD symptoms (moderate SoE).
- Treatment with D-cycloserine to augment ERP is not more effective than ERP alone in reducing OCD symptoms (high SoE) and is probably not more effective in reducing global OCD severity (moderate SoE).
- The side effects of SSRIs and clomipramine were inconsistently reported, precluding graded conclusions.
- Studies were consistent in failing to find statistically significant associations between treatment effects and age, sex, baseline Child Obsessive Compulsive Impact Scale (COIS) score, baseline Family Accommodation Scale (FAS), or comorbid autism spectrum disorder or tics. Studies were inconsistent regarding the association between treatment effect and baseline OCD severity as assessed by the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS).

3.4.2 Evidence Identified

We included 73 comparative studies, 71 RCTs[76-146] with information from 38 additional[147-184] papers or records and two NRCSs.[185, 186]

3.4.2 Results, Key Question 2: Treatment Interventions, OCD Severity, Clinical Remission, Functional Impairment, and Family Accommodation, Evidence Identified

Of these comparative studies, 24 evaluated pharmacologic treatments, 31 were studies of behavioral interventions, 17 studied combined behavioral and pharmacologic treatments and 1 evaluated transcranial direct current stimulation (tDCS) combined with fluoxetine versus fluoxetine alone.[144]

Among comparative studies, 33 were conducted in the U.S., 10 in Europe, 9 in China, 6 in the U.K., 6 in Iran, 3 in Australia, 2 in Brazil, 3 in Canada and 1 in Japan. The median end-of-treatment time for analyzed outcomes was 12 months (IQR: 8 to 13.5 months).

Fifty-eight percent (42/73) of the studies reported (or implied) race or other social determinants of health. Nine studies were conducted in China. Among studies not conducted in East Asia, between 60 and 100 percent of participants were White, with a median of 88 percent across studies and only 8 of 29 relevant studies (28%) including more than 20 percent children who were categorized as other than White. With the exception of one study with 20 participants, 2 of whom were categorized as Black, fewer than 7 percent of participants were Black.

Few studies reported other social determinants of health. Across 6 studies, 55 to 78 percent of parents had at least a college education. Among 5 studies, the parents of about 75 percent of participants were married and living together in 4 studies (62% in one additional study). In 3 studies that reported data related to income, 94 percent of parents were employed in one study, socioeconomic status was described as high in one study, and mean family income (in approximately 2005) was $96,055 in one study (about $150,000 in 2023 dollars).

3.4.2.1 Evidence Not Included in Network Meta-Analyses

The two NRCSs are described narratively in section 3.4.5.

We excluded 29 of 71 RCTs from the network meta-analyses. Of these, 10 RCTs are summarized as follows.

Three studies[110, 111, 128] provided family interventions in addition to ERP versus ERP alone. The CY-BOCS outcomes for these studies are described in Section 3.4.3.1.4.2.

Five trials [102, 109, 118, 123, 140] evaluated whether D-cycloserine augments the effect of ERP and reported CY-BOCS and Clinical Global Impressions-Severity (CGI-S) outcomes. We report pairwise meta-analyses of these studies in sections 3.4.3.1.4.1 (CY-BOCS outcome) and 3.4.3.3.2 CGI-S outcome (reported in 3 of 5 RCTs).

In two studies, participants were randomized based on their clinical response to an open-label intervention—responders to an SSRI (paroxetine), [88] and non-responders to ERP in phase I of the two phase Nordic long-term OCD treatment study (NordLOTS) trial.[122] These studies are described in section 3.4.5.

The remaining 19 RCTs are described in Appendix E—of these, 3 evaluated variations in ERP delivery, 3 augmented ERP with another behavioral intervention, 4 evaluated other behavioral interventions, 8 evaluated additional medications, and 1 evaluated tDCS.[144]

3.4.3 Network Meta-Analyses of RCTs—OCD Severity, Clinical Remission, Functional Impairment, and Family Accommodation Outcomes

We performed separate network meta-analyses (NMAs) for each prioritized outcome, resulting in four networks. In order of decreasing network size and complexity, these included: OCD severity (CY-BOCS or Yale-Brown Obsessive Compulsive scale [Y-BOCS])—12 direct

3.4.3 Results, Key Question 2: Treatment Interventions, OCD Severity, Clinical Remission, Functional Impairment, and Family Accommodation, Network Meta-Analyses of RCTs

comparisons (designs); remission—7 designs; global severity (CGI-S scale)—7 designs; and FAS—2 designs.

To enable organization of the interventions across studies and for the purpose of the NMAs, similar treatment interventions were categorized. (see Appendix Table C-2.2: Arm Details). In the network graphs (Figures 5-24), these intervention categories are represented by the nodes (circles).

For each outcome network, we report treatment effects and make a graded determination for SoE for those comparisons that are informed by direct evidence from at least two studies.

Treatment effects for all possible comparisons (many informed by indirect evidence only) are presented in a league table (Figure 6).

For "hanging branches" excluded from the network, we report pairwise meta-analyses when three or more studies contribute direct evidence.

Study-specific effects for all studies, including studies not included in the meta-analyses, are detailed in Appendix E, Evidence Tables E-KQ2-1 to E-KQ2-40.

3.4.3.1 OCD Symptom Severity: (C)Y-BOCS

Sixty-nine of the 71 RCTs reported the CY-BOCS or the Y-BOCS as a measure of overall OCD symptom severity. Both scales are clinician-rated, 10-item scales, with each item rated from 0 (no symptoms) to 4 (extreme symptoms), for a total range from 0 to 40.[187-189] A threshold score of 16 or greater is most commonly used as a study inclusion criteria. No study reported results on the CY-BOCS-II (Second Edition), which has an expanded scoring range with a ceiling of 50.[190]

Three non-inferiority trials, one in adults with OCD[191] and two trials enrolling youth,[119, 137] have considered a 4 or 5 point decrease in (C)Y-BOCS to represent a clinically important difference. When interpreting effects as net mean differences (NMD) on the (C)Y-BOCS scale, we refer to the interval from NMD of less than −4 to 4 as the zone of indifference.

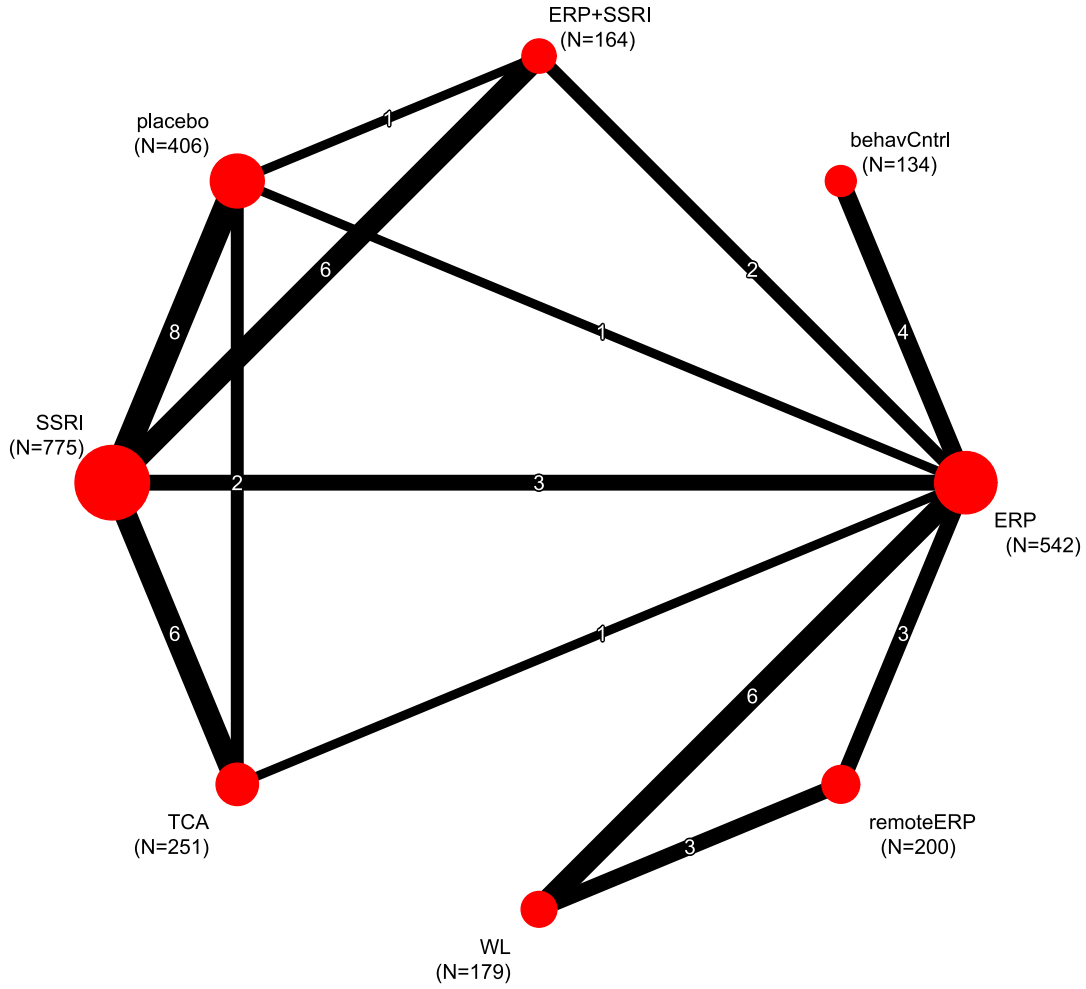
3.4.3.1.1 Network Meta-Analyses: (C)Y-BOCS

Figure 5 displays the network plot for studies reporting the (C)Y-BOCS outcome. The plot graphically describes the network topology for the 41 RCTs that enrolled 2651 participants and provide direct evidence for 12 (of 46 possible) pairwise comparisons between 5 interventions (SSRI, TCA, ERP, ERP via telehealth [remoteERP] and ERP+SSRI) and 3 separate control conditions—pill placebo (placebo), waitlist (WL), and behavioral control groups (behavCntrl). The median end-of-treatment time was 12 weeks, with an interquartile range from 9 to 14 weeks.

Among the 41 studies included in the (C)Y-BOCS network, we assessed the overall RoB as low in 21, moderate in 15 and high in 5 studies. The omnibus null hypothesis of consistency was rejected (P = 0.029).

3.4.3 Results, Key Question 2: Treatment Interventions, OCD Severity, Clinical Remission, Functional Impairment, and Family Accommodation, Network Meta-Analyses of RCTs

Figure 5. Network plot — CY-BOCS



The network presents all intervention categories (represented by circles/nodes) that were compared with one or more other intervention categories. The diameter of the circles is proportional to the number of participants (in parentheses) who received the intervention of interest. The lines connecting nodes (edges) represent the direct comparisons between pairs of interventions. The width of the edges are proportional to the number (shown in white text on each line/edge) of studies that directly compared each pair of treatments.

Abbreviations: behavCntrl = behavioral control; (C)Y-BOCS = (Children's) Yale-Brown Obsessive Compulsive Scale; ERP = cognitive behavioral therapy with exposure and response prevention; N = number of participants; placebo = pill placebo; remoteERP = synchronous or asynchronous ERP via telehealth; SSRI = selective serotonin reuptake inhibitors (various); TCA = tricyclic antidepressant (clomipramine); WL = waitlist

The net mean difference in (C)Y-BOCS (with 95 percent confidence intervals) for all pairwise contrasts are shown in Figure 6.

3.4.3 Results, Key Question 2: Treatment Interventions, OCD Severity, Clinical Remission, Functional Impairment, and Family Accommodation, Network Meta-Analyses of RCTs

Figure 6. League table: (C)Y-BOCS — all possible pairwise comparisons

	ERP	remoteERP	ERP+SSRI	TCA	SSRI	behavCntrl	placebo	WL
ERP		-1.1 (-3.5, 1.3)	0.3 (-2.7, 3.3)	-2.6 (-5.8, 0.6)	-2.7 (-5.4, 0.0)	-5.3 (-8.0, -2.7)	-7.1 (-10.2, -4.0)	-10.5 (-12.6, -8.4)
remoteERP	1.1 (-1.3, 3.5)		1.4 (-2.4, 5.2)	-1.5 (-5.6, 2.5)	-1.6 (-5.3, 2.0)	-4.3 (-7.9, -0.7)	-6.0 (-9.9, -2.1)	-9.4 (-11.9, -7.0)
ERP+SSRI	-0.3 (-3.3, 2.7)	-1.4 (-5.2, 2.4)		-3.0 (-5.8, -0.2)	-3.0 (-5.1, -1.0)	-5.7 (-9.7, -1.7)	-7.4 (-10.0, -4.9)	-10.8 (-14.5, -7.2)
TCA	2.6 (-0.6, 5.8)	1.5 (-2.5, 5.6)	3.0 (0.2, 5.8)		-0.1 (-2.1, 1.9)	-2.7 (-6.9, 1.5)	-4.5 (-6.8, -2.1)	-7.9 (-11.7, -4.0)
SSRI	2.7 (0.0, 5.4)	1.6 (-2.0, 5.3)	3.0 (1.0, 5.1)	0.1 (-1.9, 2.1)		-2.6 (-6.4, 1.2)	-4.4 (-6.1, -2.6)	-7.8 (-11.2, -4.3)
behavCntrl	5.3 (2.7, 8.0)	4.3 (0.7, 7.9)	5.7 (1.7, 9.7)	2.7 (-1.5, 6.9)	2.6 (-1.2, 6.4)		-1.7 (-5.8, 2.3)	-5.1 (-8.5, -1.7)
placebo	7.1 (4.0, 10.2)	6.0 (2.1, 9.9)	7.4 (4.9, 10.0)	4.5 (2.1, 6.8)	4.4 (2.6, 6.1)	1.7 (-2.3, 5.8)		-3.4 (-7.1, 0.3)
WL	10.5 (8.4, 12.6)	9.4 (7.0, 11.9)	10.8 (7.2, 14.5)	7.9 (4.0, 11.7)	7.8 (4.3, 11.2)	5.1 (1.7, 8.5)	3.4 (-0.3, 7.1)	

Table cells summarize the net mean difference in (C)Y-BOCS, with 95 percent confidence intervals, for each row by column treatment contrast. For example, the right-most upper cell displays the NMA estimate represents the ERP vs. WL comparison. Larger negative NMDs represent greater treatment effect. Shading is added to emphasize larger effects.

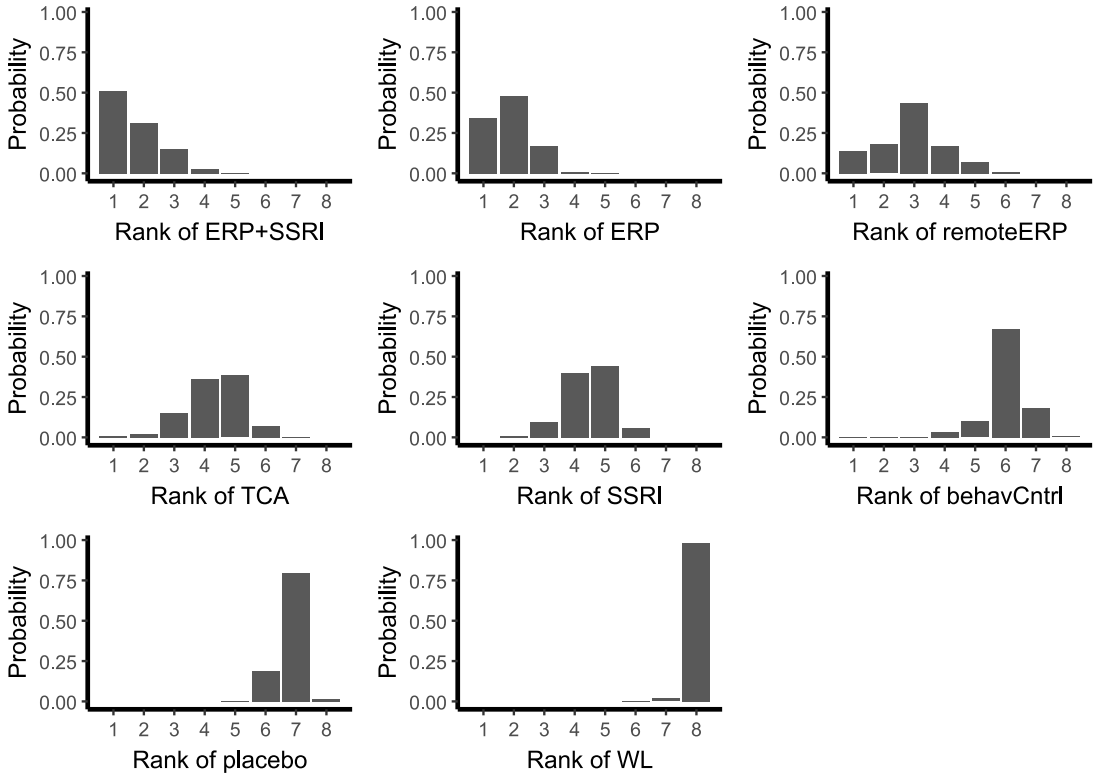
Abbreviations: behavCntrol = behavioral control; (C)Y-BOCS = Children's Yale-Brown Obsessive Compulsive scale; ERP = CBT with exposure and response prevention; NMA = network meta-analysis; NMD = net mean difference; N = number of participants; placebo = pill placebo; remoteERP = synchronous or asynchronous ERP via telehealth; SSRI = selective serotonin reuptake inhibitors (various); TCA = tricyclic antidepressant (clomipramine); WL = waitlist

We used the network meta-analysis methods to rank the 5 behavioral, pharmacological and combination treatments and 3 control conditions (behavioral control, pill placebo and waitlist). Figure 7 below, is a rank-o-gram, with histogram for each of 5 treatments and 3 control categories The height of each bar represents the probability given treatment is the best, the worst and all positions in between, based on the effect metric of decrease in total CY-BOCS NMD as the relative treatment effect metric.[192]

Treatments including ERP (ERP+SSRI, ERP and remoteERP) comprise the 3 highest ranked interventions, medications (TCA, SSRI) the mid-ranked interventions, with the 3 control conditions (behavioral control, pill placebo, wait list) with the lowest ranks.

3.4.3 Results, Key Question 2: Treatment Interventions, OCD Severity, Clinical Remission, Functional Impairment, and Family Accommodation, Network Meta-Analyses of RCTs

Figure 7. Rank-o-gram



Abbreviations: behavCntrl = behavioral control; ERP = cognitive behavioral therapy with exposure and response prevention; N = number of participants; placebo = pill placebo; remoteERP = synchronous or asynchronous ERP via telehealth; SSRI = selective serotonin reuptake inhibitors (various); TCA = tricyclic antidepressant (clomipramine); WL = waitlist

3.4.3.1.2 Estimates of Effects and Comparative Effects from NMA: (C)Y-BOCS

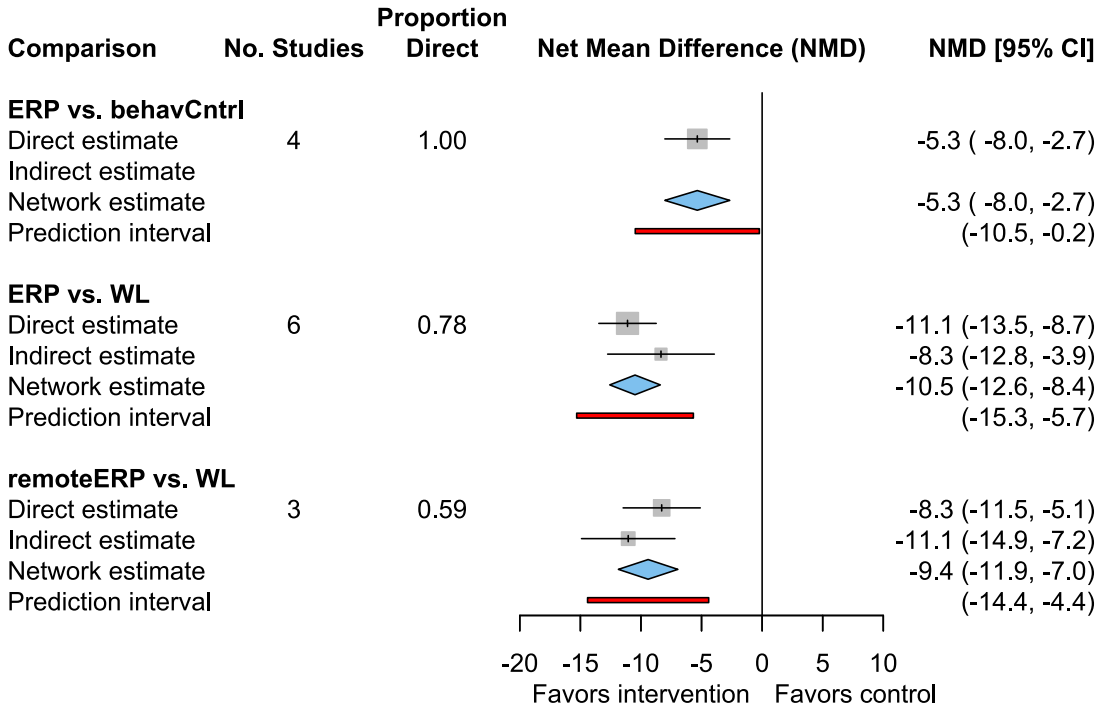
For each comparison with at least two studies contributing direct evidence, we provide figures illustrating these effects. The figures provide the number of studies contributing direct evidence, and the proportion of direct evidence, and display row-wise point estimates with 95 percent confidence intervals for the direct, indirect, and pooled effect estimates, to facilitate a visual comparison of the degree of similarity between direct and indirect estimates, i.e., local coherence. The P values associated with the null hypothesis of local coherence are provided in each figure note. The red bar represents the range of effect estimates that would be expected in a future study.

3.4.3.1.2.1 Effects of Behavioral Interventions: (C)Y-BOCS

Figure 8 displays 3 relative effect estimates—ERP versus behavioral control, ERP versus WL, and remote ERP versus WL.

3.4.3 Results, Key Question 2: Treatment Interventions, OCD Severity, Clinical Remission, Functional Impairment, and Family Accommodation, Network Meta-Analyses of RCTs

Figure 8. ERP versus behavioral control, ERP versus waitlist, and remoteERP versus waitlist: CY-BOCS



A P value for the null hypothesis of local coherence for ERP vs. behavControl cannot be calculated due to absence of indirect evidence. For ERP vs. WL, P = 0.279; For remote ERP vs. WL, P = 0.279.

Abbreviations: CI = confidence interval; CY-BOCS = Children's Yale-Brown Obsessive Compulsive Scale; ERP = CBT with Exposure and Response Prevention; No. = number of studies that contributed direct evidence for a comparison; NMD = net mean difference; remoteERP = synchronous or asynchronous ERP delivered via telehealth; WL = waitlist control

For ERP versus behavioral control, the NMD was −5.3 (95% CI −8.0 to −2.7). This estimate is statistically significant and compatible with effects ranging from clinically important, to effects of uncertain clinical importance. Four RCTs (with 298 participants) contributed direct evidence. Among these, 2 studies enrolled children 5 to 8 years-of-age and compared family-based ERP with family-based relaxation treatment that included psychoeducation, affective education to identify negative and positive feelings, and relaxation training [96, 114] One study enrolled children 8 to 17 years-of-age and compared ERP plus a structured family intervention versus a behavioral control including psychoeducation and relaxation training.[106] Another study enrolled both adolescents 12 to 18 years-of-age and compared ERP with stress management therapy.[145]

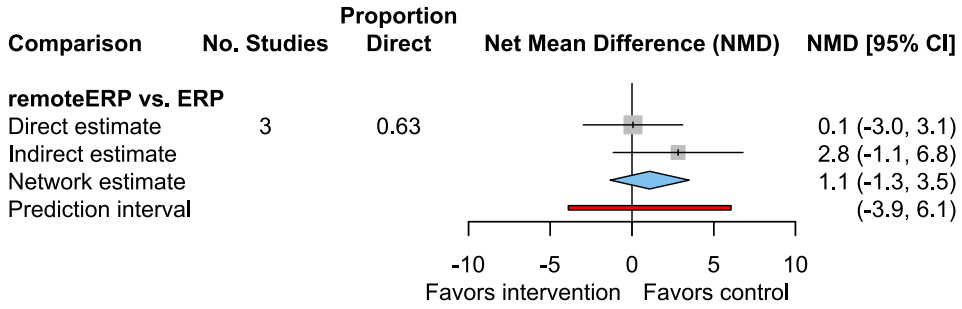
For ERP versus WL, the pooled NMD is −10.5 (95% CI −12.6 to −8.4). There were 6 RCTs (with 237 participants) that contributed direct evidence.[87, 89, 95, 103, 104, 124] This estimate is statistically significant, and the confidence interval is entirely compatible with clinically important effects.

For remote ERP versus WL, the NMD was −9.4 (95% CI −11.9 to −7.0). Three RCTs[107, 127, 141] compared remote ERP versus waitlist control in 158 participants. This estimate is statistically significant, and the 95 percent confidence interval is entirely compatible with clinically important effects.

Figure 9 displays the relative effect estimate for ERP versus behavioral control.

3.4.3 Results, Key Question 2: Treatment Interventions, OCD Severity, Clinical Remission, Functional Impairment, and Family Accommodation, Network Meta-Analyses of RCTs

Figure 9. Remote ERP versus ERP — CY-BOCS



For remoteERP vs. ERP the P value for the null hypothesis of local coherence is 0.279.

Abbreviations: behavCntrl = behavioral control; CI = confidence interval; ; CY-BOCS = Children's Yale-Brown Obsessive Compulsive Scale; ERP = CBT with Exposure and Response Prevention; No. = number of; NMD = net mean difference; remoteERP = remote synchronous or asynchronous ERP

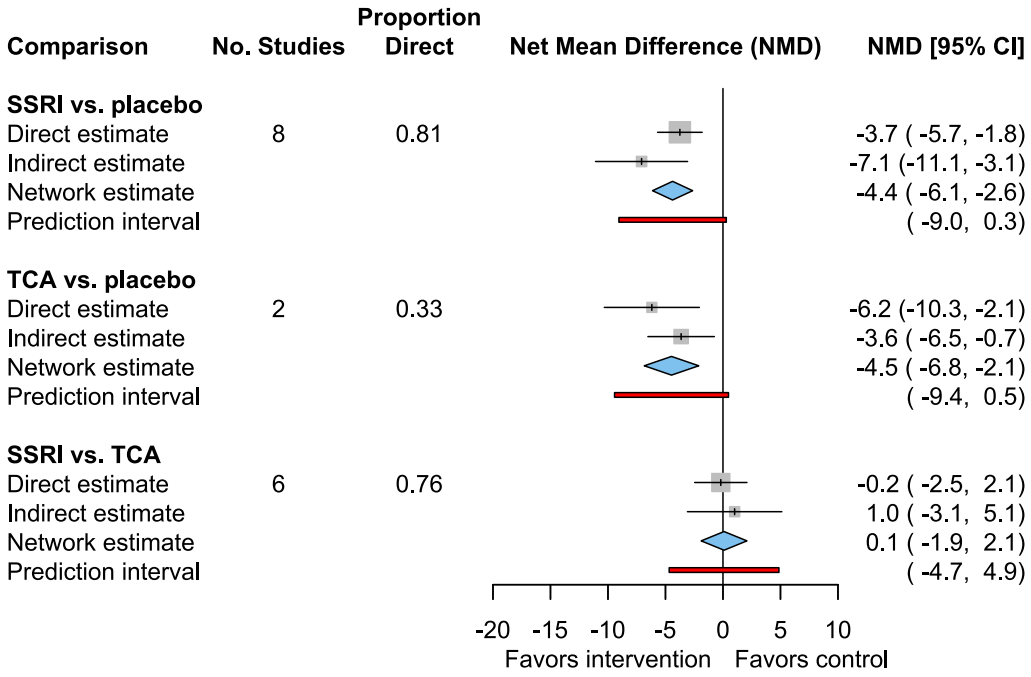
For remoteERP versus ERP, the NMD was 1.1 (95% CI −1.3 to 6.1). Three RCTs[119, 125, 137] compared remoteERP with ERP in 246 participants. The 95 percent confidence interval overlaps the null effect, and includes effects of uncertain clinical importance only.

3.4.3.1.2.2 Effects of Pharmacological Interventions — (C)Y-BOCS

Figure 10 illustrates the effects and comparative effects of pharmacological therapies, compared to placebo and each other. For each comparison, the figure shows the number of studies contributing direct evidence and the proportion of direct evidence. The direct, indirect, and pooled estimates of NMD associated 95 percent confidence intervals are displayed to visually compare the degree of similarity between direct and indirect estimates, i.e., local coherence. The red bar represents the range of effect estimates that would be expected in a future study.

3.4.3 Results, Key Question 2: Treatment Interventions, OCD Severity, Clinical Remission, Functional Impairment, and Family Accommodation, Network Meta-Analyses of RCTs

Figure 10. SSRI versus placebo, TCA versus placebo, and SSRI versus TCA — (C)Y-BOCS



P values for null hypothesis of local coherence: SSRI vs. placebo, P = 0.142; TCA vs. placebo; P = 0.322; SSRI vs. TCA, P = 0.615.

Abbreviations: CI = confidence interval; (C)Y-BOCS = (Children's) Yale-Brown Obsessive Compulsive Disorder Scale; SSRI = selective serotonin reuptake inhibitor (various); TCA = tricyclic antidepressant (all clomipramine); No. Studies = number of studies directly comparing; NMD = net mean difference

For SSRI versus placebo the pooled NMD is −4.4 (95% CI −6.1 to −2.6) on the (C)Y-BOCS scale. This estimate is statistically significant and compatible with effects ranging from clinically important, to effects of uncertain clinical importance.

Treatment with the TCA clomipramine was more effective than placebo, with a NMD of −4.5 (95% CI −6.8 to −2.1). This estimate is statistically significant, and the confidence interval is compatible with a range of effects from clinically important, to effects of uncertain clinical importance.

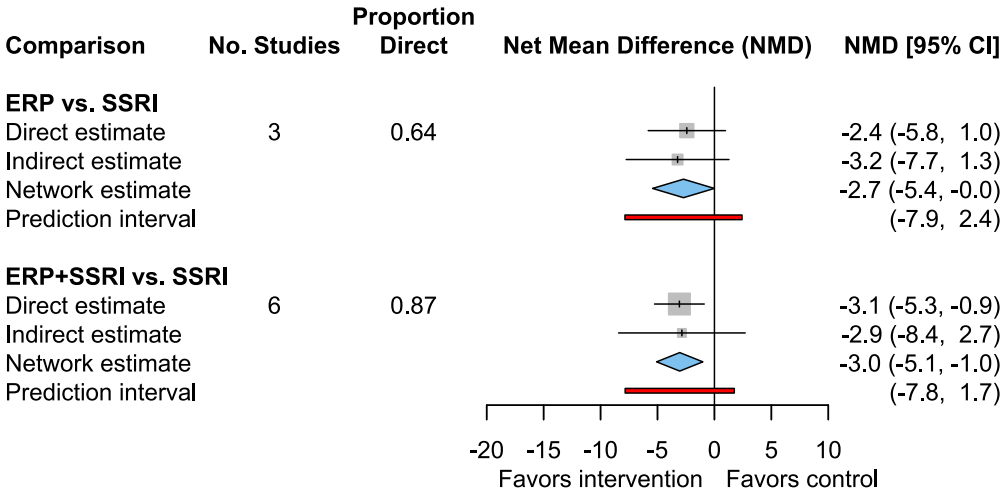
For SSRI versus TCA, the NMD in CY-BOCS was 0.1 (95% CI −1.9 to 2.1). This comparative effect estimate overlaps the null effect, and the confidence interval includes effects of uncertain clinical importance only.

3.4.3.1.2.3 Effects of Combinations of Behavioral and Pharmacological Interventions — (C)Y-BOCS

Figure 11 displays the relative effects for ERP versus SSRI and for ERP+SSRI versus SSRI.

3.4.3 Results, Key Question 2: Treatment Interventions, OCD Severity, Clinical Remission, Functional Impairment, and Family Accommodation, Network Meta-Analyses of RCTs

Figure 11. ERP versus SSRI, ERP+SSRI versus SSRI — CY-BOCS



P values for null hypothesis of local coherence: ERP vs. SSRI, P=0.778; ERP+SSRI vs. SSRI; P = 0.942.

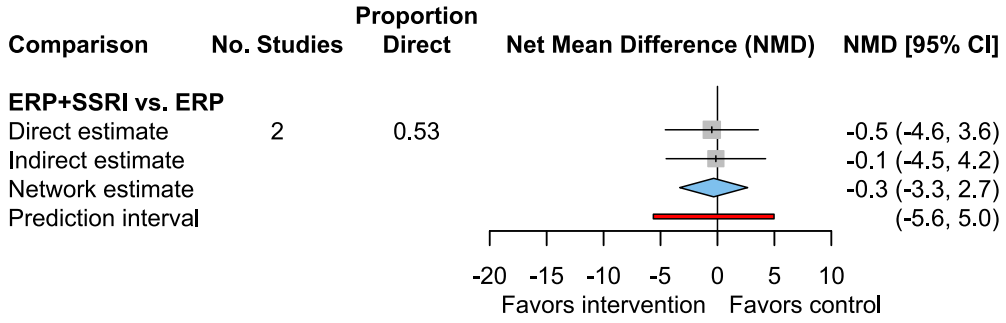
Abbreviations: CI = confidence interval; (C)Y-BOCS = (Children's)Yale-Brown Obsessive Compulsive Disorder Scale; ERP = CBT with Exposure and Response Prevention; SSRI = selective serotonin reuptake inhibitor (various); No. Studies = number of studies directly comparing; NMD = net mean difference; "+" = indicates a combination of interventions

For ERP versus SSRI, the pooled NMD is −2.7 (95% CI −5.4 to −0.0). There were 3 RCTs[91, 92, 130] with 179 participants that contributed direct evidence. This estimate is statistically significant, and the confidence interval is compatible with both clinically important effects, and with effects of uncertain clinical importance.

For ERP+SSRI versus SSRI, the pooled NMD is −3.0 (95% CI −5.1 to 1.0). There were 6 RCTs[83, 91, 105, 117, 120, 132]with 273 participants that contributed direct evidence. This estimate is statistically significant, and the confidence interval is compatible with both clinically important effects, and with effects of uncertain clinical importance.

Figure 12 displays the relative effects for ERP versus SSRI and for ERP+SSRI vs. SSRI.

Figure 12. ERP+SSRI versus ERP—CY-BOCS



P values for null hypothesis of local coherence: ERP+SSRI vs. ERP, P=0.907

Abbreviations: CI = confidence interval; (C)Y-BOCS = (Children's)Yale-Brown Obsessive Compulsive Disorder Scale; ERP = CBT with Exposure and Response Prevention; SSRI = selective serotonin reuptake inhibitor (various); No. Studies = number of studies directly comparing; NMD = net mean difference; "+" = indicates a combination of interventions

3.4.3 Results, Key Question 2: Treatment Interventions, OCD Severity, Clinical Remission, Functional Impairment, and Family Accommodation, Network Meta-Analyses of RCTs

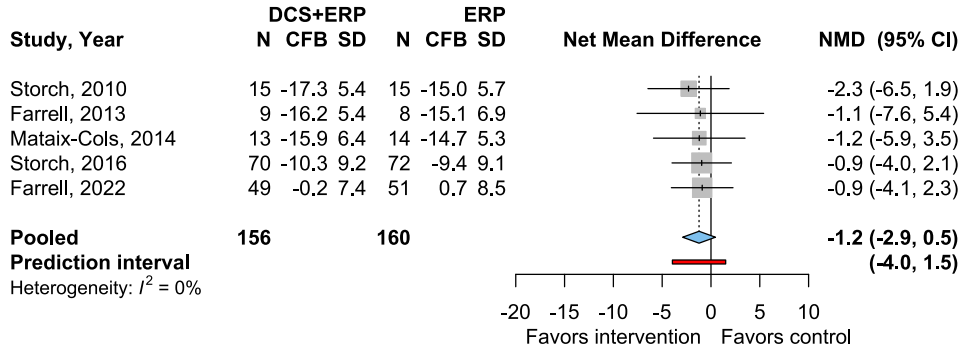
For ERP+SSRI versus ERP, the pooled NMD is −0.3 (95% CI −3.3 to 2.7). There were 2 RCTs[91, 113]with 103 participants that contributed direct evidence. This estimate overlaps the null effect, and the confidence interval is compatible with small effects of uncertain clinical importance only.

3.4.3.1.4 Pairwise Meta-Analyses

3.4.3.1.4.1 Augmentation of ERP With D-Cycloserine Versus ERP—CY-BOCS

Five studies with 316 participants evaluated whether D-cycloserine augments the effect of ERP on symptom severity as assessed by the total CY-BOCS score. The summary NMD was −1.2 (95% CI −2.9 to 0.5). This comparative effect estimate overlaps the null effect, and the confidence interval includes effects of uncertain clinical importance only. See Figure 13.

Figure 13. D-cycloserine with ERP versus ERP—CY-BOCS



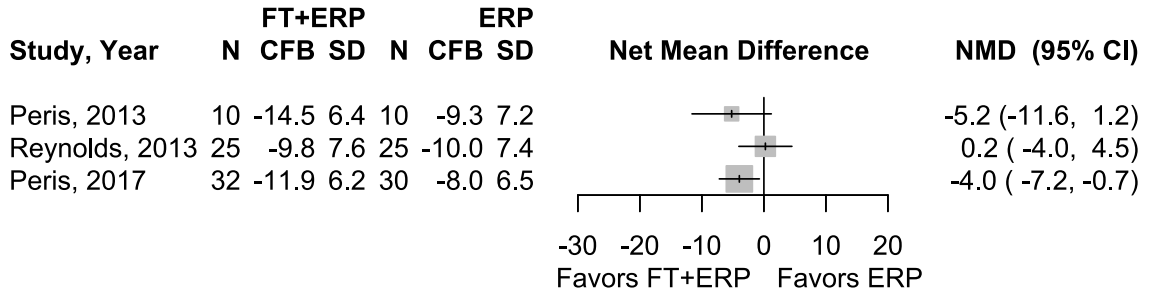
Abbreviations: CFB = change from baseline; CI = confidence interval; (C)Y-BOCS = (Children's)Yale-Brown Obsessive Compulsive Disorder Scale; DCS = D-cycloserine; ERP = exposure and response prevention; N = number of patients in arm; NMD = net mean difference; SD = sample standard deviation

3.4.3.1.4.2 Family Interventions Added to ERP Versus ERP—CY-BOCS

Three studies[110, 128] with 132 participants combined a supplemental family with ERP and compared to ERP alone (Figure 14). Two studies used Positive Family Interaction Therapy (PFIT) in addition to individual child CBT. Another trial, Reynolds 2013, evaluated the effect of parent-enhanced CBT, which emphasized parent and family factors, including accommodation.[111] Overall RoB was rated as low in 2 studies and moderate in one study. Given clinical and statistical heterogeneity, we do not report summary effect.

3.4.3 Results, Key Question 2: Treatment Interventions, OCD Severity, Clinical Remission, Functional Impairment, and Family Accommodation, Network Meta-Analyses of RCTs

Figure 14. Additional parent/family therapy with ERP versus ERP—CY-BOCS



Abbreviations: CFB = change from baseline; CI = confidence interval; Control = control condition (placebo, waitlist, behavioral intervention without ERP); (C)Y-BOCS = (Children's)Yale-Brown Obsessive Compulsive Disorder Scale; ERP = exposure and response prevention; FT = family therapy, N = number of patients in arm; NMD = net mean difference; SD = sample standard deviation

3.4.3.2 OCD Remission

There were 13 studies that reported the number of participants whose OCD remitted (by end of treatment in 11 to 17 weeks). Among these studies, remission was variably defined as subjective "clinical remission" or using CY-BOCS cutoffs ranging from ≤10 to ≤12.

3.4.3.2.1 Network Meta-Analyses — Remission

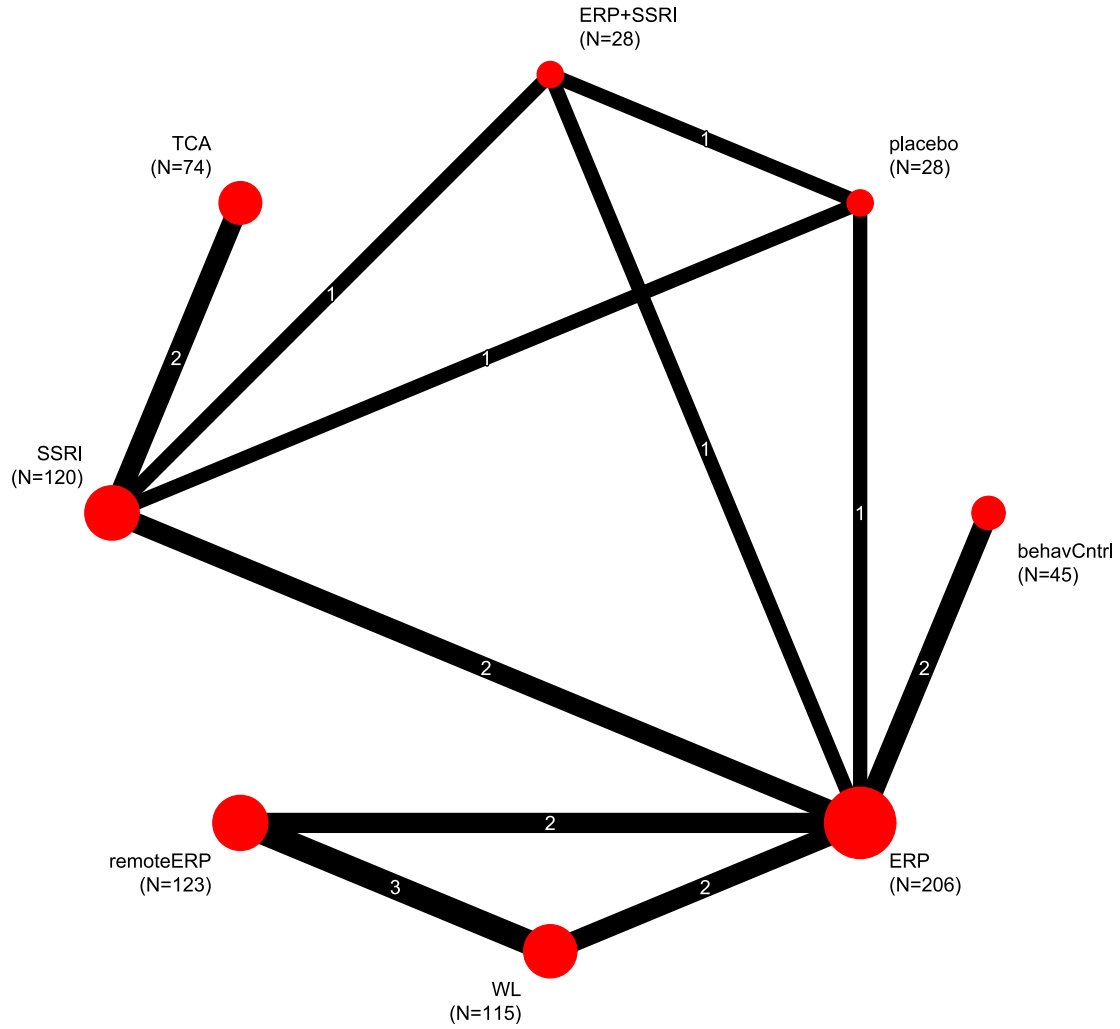
Figure 15 displays the network topology for the 13 RCTs included in the NMA that enrolled 739 participants, and provided direct evidence for 11 out of 27 possible pairwise comparisons between 5 interventions (ERP, remote ERP, SSRI, TCA, ERP+SSRI) and 3 separate control conditions—pill placebo (placebo), WL, and behavioral control groups (behavCntrl).

Among the 13 studies included in the remission network, we deemed overall RoB to be low in 9, moderate in 2, and high in 2 studies.

The omnibus null hypothesis of consistency was not rejected (P = 0.126).

3.4.3 Results, Key Question 2: Treatment Interventions, OCD Severity, Clinical Remission, Functional Impairment, and Family Accommodation, Network Meta-Analyses of RCTs

Figure 15. Network of comparators—Remission



The network presents all intervention categories (represented by circles/nodes) that were compared with one or more other intervention categories across studies. The diameter of the circles is proportional to the number of patients who received the intervention of interest. The lines connecting nodes (edges) represent the direct comparisons between pairs of interventions made by eligible studies. The width of the edges are proportional to the number (shown in white text on each line/edge) of studies that directly compared each pair of treatments.

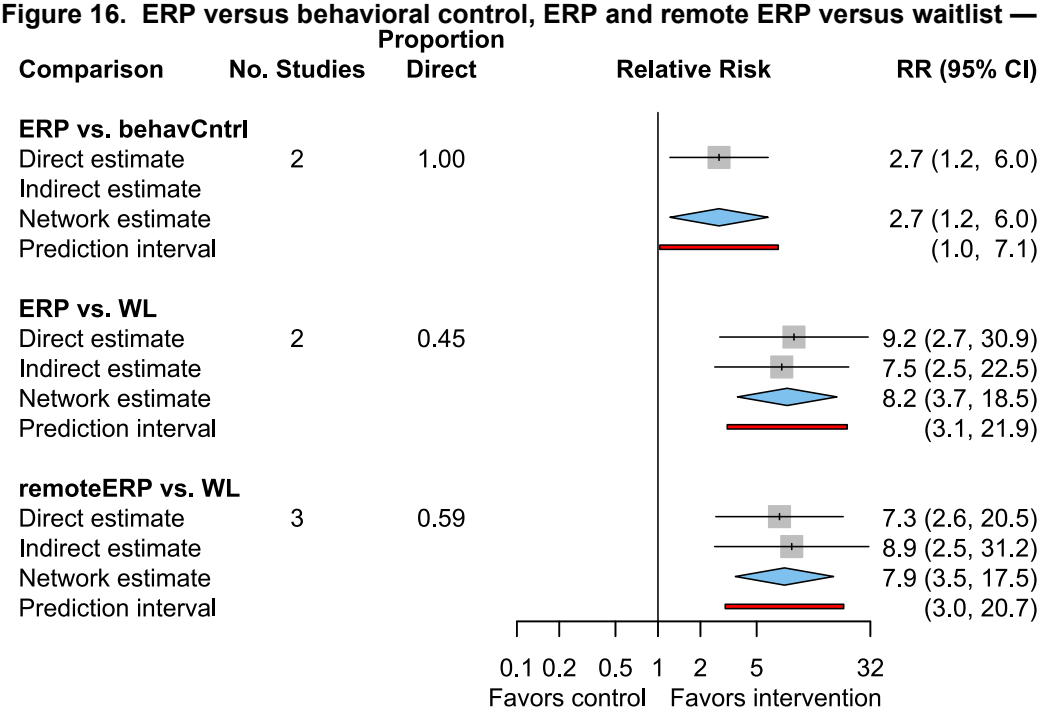
Abbreviations: behavControl = behavioral control; ERP = CBT with exposure and response prevention; placebo = pill placebo; '+' = combined interventions; remoteERP = remote synchronous or asynchronous ERP; SSRI = selective serotonin reuptake inhibitors (various); TCA = tricyclic antidepressant (clomipramine); WL = wait list

3.4.3.2.2 ERP and Remote ERP Versus Control—Remission

Figure 16 displays the relative rate of remission for comparisons informed by direct evidence from at least two studies — ERP versus behavioral control, ERP versus wait list and remote ERP versus wait list.

3.4.3 Results, Key Question 2: Treatment Interventions, OCD Severity, Clinical Remission, Functional Impairment, and Family Accommodation, Network Meta-Analyses of RCTs

Figure 16. ERP versus behavioral control, ERP and remote ERP versus waitlist — Remission



A P value for the null hypothesis of local coherence for ERP vs. behavControl cannot be calculated due to absence of indirect evidence. P values for null hypothesis of local coherence: ERP vs. WL, P = 0.810; remoteERP vs. WL, P = 0.810

Abbreviations: CI = confidence interval; behavCntrl = behavioral control; ERP = CBT with Exposure and Response Prevention; SSRI = selective serotonin reuptake inhibitors (various); RR = relative rate; No. = number of; remoteERP = remote synchronous or asynchronous ERP; vs. = versus; WL = wait list

The relative rate (RR) of remission for ERP versus behavioral control was significantly higher, with a RR of 2.7 (95% CI 1.2 to 6.0).

The RR of remission with ERP versus wait list was significantly higher, RR 8.2 (95% CI 3.7 to 18.5).

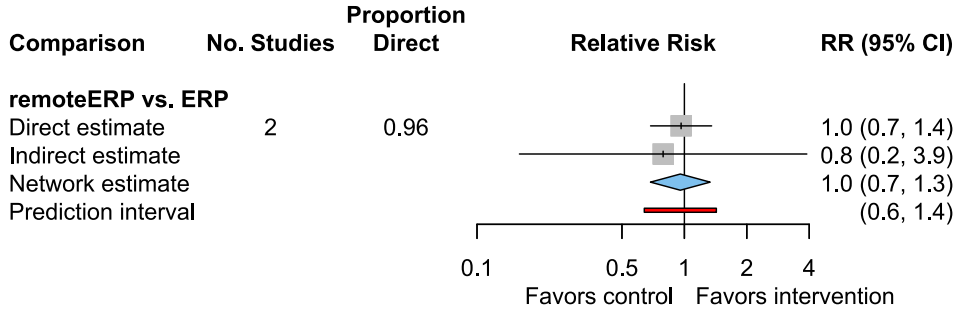
In participants receiving ERP remotely versus wait list, the rate of remission was significantly greater, RR 7.9 (95% CI 3.5 to 17.5).

3.4.3.2.3 Remote ERP Versus ERP and ERP Versus SSRI—Remission

Figure 17 displays the relative effects for comparisons informed by direct evidence from two studies— remote ERP versus ERP.

3.4.3 Results, Key Question 2: Treatment Interventions, OCD Severity, Clinical Remission, Functional Impairment, and Family Accommodation, Network Meta-Analyses of RCTs

Figure 17. Remote ERP vs. ERP—Remission



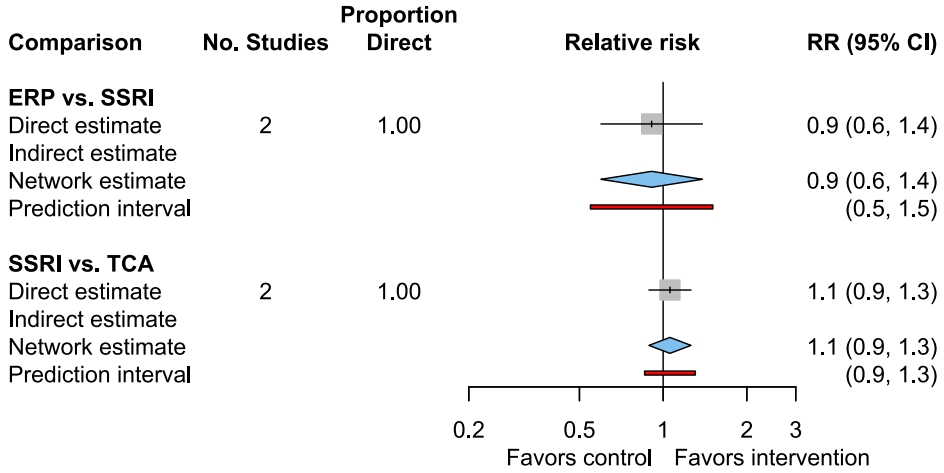
P values for null hypothesis of local coherence: remoteERP vs. ERP, P = 0.810

Abbreviations: CI = confidence interval; ERP = CBT with Exposure and Response Prevention; SSRI = selective serotonin reuptake inhibitors (various); RR = relative rate; No. = number of; remoteERP = remote synchronous or asynchronous ERP; vs. = versus

In participants receiving remoteERP versus ERP, the rate of remission was similar, RR 1.0 (95% CI 0.7 to 1.3).

Figure 18 displays the relative effects for comparisons informed by direct evidence from two studies— remote ERP versus ERP.

Figure 18. ERP versus SSRI and TCA versus SSRI — Remission



P values for the null hypothesis of local coherence cannot be calculated due to absence of indirect evidence.

Abbreviations: CI = confidence interval; ERP = CBT with Exposure and Response Prevention; No. = number of; SSRI = selective serotonin reuptake inhibitors (various); RR = relative rate; remoteERP = remote synchronous or asynchronous ERP; TCA = tricyclic antidepressant (clomipramine); vs. = versus

In participants receiving ERP versus SSRI, the rates of remission were similar, RR 1.1 (95% CI 0.9 to 1.3).

Those receiving SSRI versus TCA had a similar remission rate, RR 0.9 (95% CI 0.9 to 1.3).

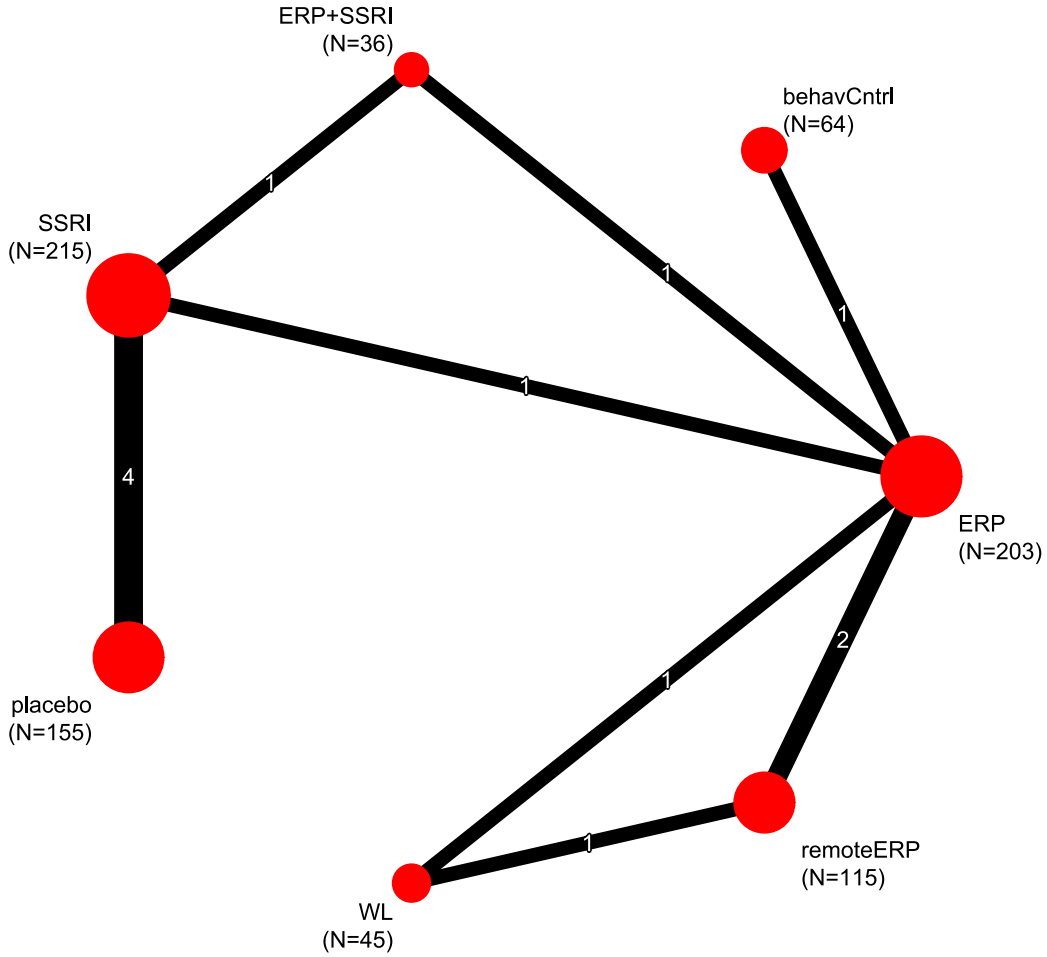
3.4.3.3 OCD Symptom Severity—CGI-S

CGI-S is a global assessment of overall OCD illness severity, with 7 severity categories: 1 = normal, 2 = borderline, 3 = mild, 4 = moderate, 5 = marked, 6 = severe, and 7 = extremely severe.[193]

3.4.3 Results, Key Question 2: Treatment Interventions, OCD Severity, Clinical Remission, Functional Impairment, and Family Accommodation, Network Meta-Analyses of RCTs

Figure 19 displays the network topology for the 12 RCTs included in the NMA that enrolled 833 participants, that provided direct evidence for 8 out of 12 possible pairwise comparisons between 5 interventions (ERP, remoteERP, ERP+SSRI, SSRI) and control conditions (waitlist, placebo and behavioral control). Among the 12 studies included in the GGI-S network, the overall RoB was low in 8, moderate in 2, and high in 2 studies. The omnibus null hypothesis of consistency was not rejected (P = 0.826).

Figure 19. Network of comparators—CGI-S



The network presents all intervention categories (represented by circles/nodes) that were compared with one or more other intervention categories across studies. The diameter of the circles is proportional to the number of patients who received the intervention of interest. The lines connecting nodes (edges) represent the direct comparisons between pairs of interventions made by eligible studies. The widths of the edges are proportional to the number (shown in white text on each line/edge) of studies that directly compared each pair of treatments.

Abbreviations: behavCntrl = behavioral control; CGI-S = Clinical Global Impressions Scale-Severity; ERP = CBT with Exposure and Response Prevention; '+' = combined interventions; placebo = pill placebo; remoteERP = remote synchronous or asynchronous ERP; SSRI = selective serotonin reuptake inhibitors (various); WL = wait list

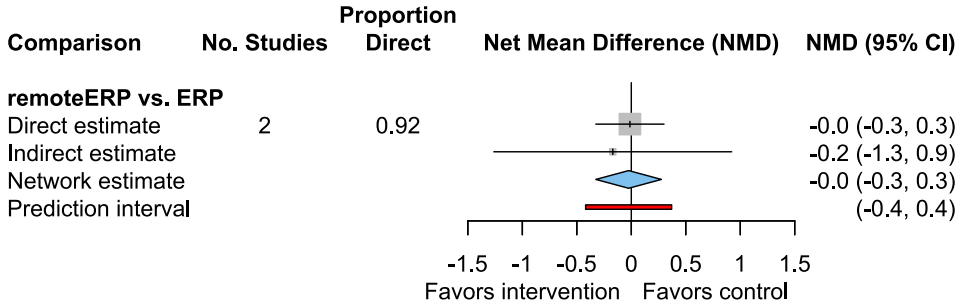
3.4.3.3.1 Network Meta-Analysis CGI-S

Figure 20 displays the comparisons informed by direct evidence from at least two studies—Remote ERP vs. ERP

3.4.3 Results, Key Question 2: Treatment Interventions, OCD Severity, Clinical Remission, Functional Impairment, and Family Accommodation, Network Meta-Analyses of RCTs

The pooled estimate for remote ERP versus in-person ERP is a NMD in CGI-S score of −0.0 (95% CI −0.3 to 0.3).

Figure 20. Remote ERP versus ERP — CGI-S



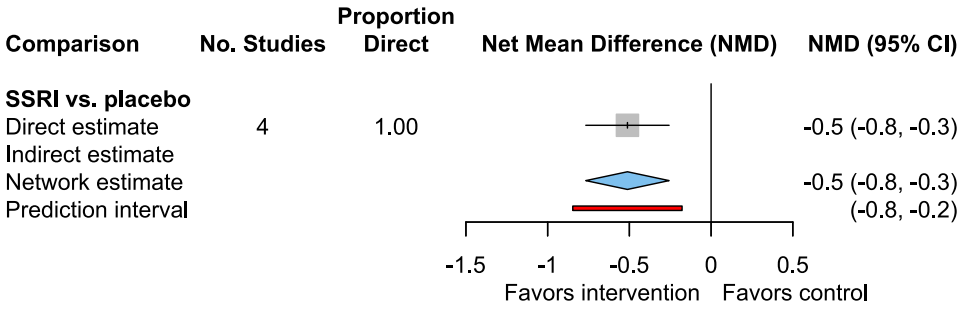
P values for null hypothesis of local coherence: remoteERP vs. ERP, P=0.786

Abbreviations: CGI-S = Clinical Global Impressions Scale-Severity; CI = confidence interval; ERP = CBT with Exposure and Response Prevention; No. = number of; NMD = net mean difference; SSRI = selective serotonin reuptake inhibitor (various); vs. = versus

Figure 21 displays the comparisons informed by direct evidence from four studies — SSRI versus pill placebo.

The pooled estimate for the remote ERP versus ERP comparison is a NMD in CGI-S score of −0.5 (95% CI −0.8 to −0.2).

Figure 21. SSRI versus pill placebo — CGI-S



P values for the null hypothesis of local coherence cannot be calculated due to absence of indirect evidence.

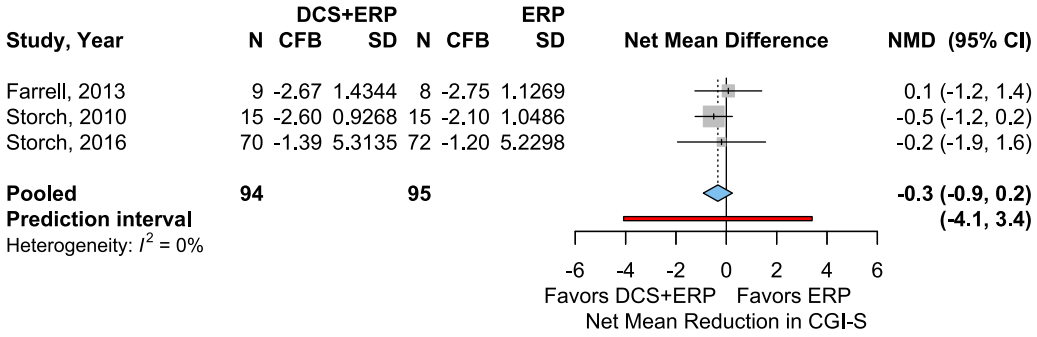
Abbreviations: CGI-S = Clinical Global Impressions Scale-Severity; CI = confidence interval; ERP = CBT with Exposure and Response Prevention; No. = number of; NMD = net mean difference; placebo = pill placebo; SSRI = selective serotonin reuptake inhibitor (various); vs. = versus

3.4.3.3.2 Pairwise Meta-Analyses: Augmentation of ERP with D-Cycloserine Versus ERP — CGI-S

Figure 22 presents the pairwise MA for the 3 trials that enrolled 189 participants[102, 109, 123] that compared augmentation of ERP with D-cycloserine and reported a CGI-S outcome. The summary NMD in CGI-S is −0.3 (95% CI −0.9 to 0.2). The prediction interval is very wide.

3.4.3 Results, Key Question 2: Treatment Interventions, OCD Severity, Clinical Remission, Functional Impairment, and Family Accommodation, Network Meta-Analyses of RCTs

Figure 22. D-cycloserine augmented ERP versus ERP—CGI-S



Abbreviations: CI = confidence interval; CGI-S = clinical global impression of severity; DCS = D-cycloserine; ERP = CBT with Exposure and Response Prevention; No. = number of; NMD = net mean difference; remoteERP = remote synchronous or asynchronous ERP; SD = standard deviation; SSRI = selective serotonin reuptake inhibitor (various); vs. = versus

3.4.3. Results, Key Question 2: Treatment Interventions, OCD Severity, Clinical Remission, Functional Impairment, and Family Accommodation

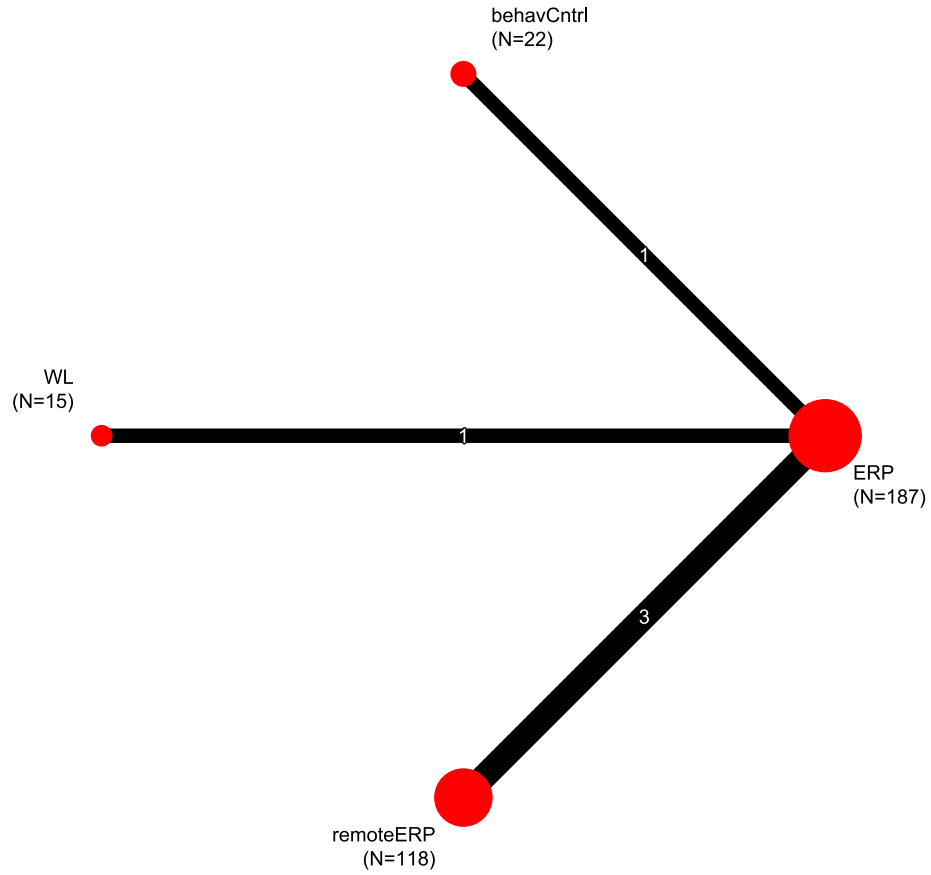
3.4.3.4 Family Accommodation—FAS

The FAS is a 12-item clinician-rated semi-structured interview designed to assess the family's accommodation to the child's OCD symptoms.[194] Accommodation is a change in the family's behavior with the goal of reducing distress in children with OCD. Greater family accommodation is associated with more severe OCD symptoms[195] and may decrease in response to treatment.[196, 197]

Five studies with 342 participants reported FAS outcomes that directed compared 3 of 5 possible pairwise comparisons of 2 interventions (ERP, remoteERP) and 2 control comparators (waitlist and behavioral control).[106, 107, 125, 127, 137]

Among the 5 studies included in the FAS network, the overall RoB was low in 4 studies, and high in 1 study. The network topology is shown in Figure 23.

Figure 23. Network of comparators—FAS



The network presents all intervention categories (represented by circles/nodes) that were compared with one or more other intervention categories across studies. The diameter of the circles is proportional to the number of patients who received the intervention of interest. The lines connecting nodes (edges) represent the direct comparisons between pairs of interventions made by eligible studies. The widths of the edges are proportional to the number (shown in white text on each line/edge) of studies that directly compared each pair of treatments.

Abbreviations: behavCntrl = behavioral control; ERP = Cognitive behavioral therapy with exposure and response prevention; FAS = Family Accommodation Scale; remoteERP = remote synchronous or asynchronous ERP; WL = wait list

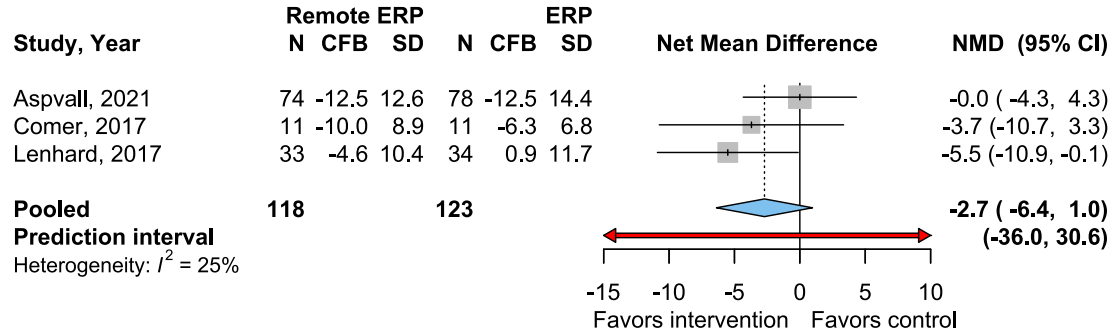
3.4.3. Results, Key Question 2: Treatment Interventions, OCD Severity, Clinical Remission, Functional Impairment, and Family Accommodation

3.4.3.4.1 Pairwise Meta-Analyses: Remote ERP Versus ERP —FAS

Figure 24 is a forest plot the shows the individual study effects and the summary estimate of the effect of remote versus in-person ERP on family accommodation, as measured by FAS.

For this comparison, family accommodation is reduced, with a pooled NMD −2.7 (95% CI −6.4 to 1.0).

Figure 24. Pairwise meta-analysis: Remote ERP versus ERP — FAS



Abbreviations: CI = confidence interval; CFB = change from baseline; Control = combined control group; ERP = CBT with Exposure and Response Prevention; FAS = Family Accommodation Scale; N = number of participants in each arm; NMD = net mean difference; SD = standard deviation

3.4.4 Other Outcomes

Other outcome domains include functional impairment, quality of life, satisfaction, and adverse events. These were more sparsely reported, used different scales, were assessed by variable respondents (i.e., child versus parent), and were reported across different comparators, precluding meta-analysis and graded conclusions. We summarize studies reporting these outcomes and the scales used briefly below and in detail in Appendix E.

3.4.4.1 Functional Impairment—Child Obsessive Compulsive Impact Scale (COIS)

Twelve studies, all RCTs,[86, 94, 104, 106, 107, 113, 114, 123, 128, 138, 140, 141] enrolling a total of 844 participants, assessed functional impairment using the COIS. The COIS is a 56-item, parent- or child-report measuring the degree to which the child experiences OCD-related impairment across several domains of functioning: school, social, and home/family activities.[107] The COIS-R (the revised version) is a 33-item of the scale, where responses are rated from 0 (not at all) to 3 (very much).[106]

Eight studies assessed the comparative effectiveness of ERP alone or as a combination, and 4 studies assessed a medication as a primary intervention or in combination. Studies which delivered ERP alone differed in setting (remote versus in-person, home versus hospital), and intensity (daily versus weekly). Seven studies compared **ERP with Control**, or another form of ERP.[94, 104, 106, 107, 114, 138, 141] In all studies, the net mean difference favored ERP over control, with the difference reaching statistical significance in all but one (Appendix Tables E-KQ2-14, E-KQ2-17). Two studies reported nonsignificant differences between **home- and clinic-based ERP and intensive versus non-intensive ERP** (Appendix Table E-KQ2-16). One study reported a statistically significant improvement with an **family intervention plus ERP versus ERP** alone[128] (Appendix Table E-KQ2-17); one study reported a statistically significant improvement with **SSRI versus placebo** (Appendix Table E-KQ2-20).[86] Three studies compared of **pharmacological agents (e.g., D-cycloserine, SSRI) plus ERP to placebo** plus ERP and reported no significant differences
(Appendix Tables E-KQ2-18, E-KQ2-19, E-KQ2-20).[113, 123, 140]

3.4.4.2 Quality of Life

Six RCTs[104, 114, 126, 127, 137, 138] and one NRCS,[185] enrolling a total of 1642 participants, measured quality of life using a variety of instruments; Child Health Utility 9D (CHU9D), Manchester Short Assessment of Quality of Life (MANSA), Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire (PQ-LES-Q), Pediatric Quality of life Inventory (PEDSQL) and the EuroQol 5 Dimension (EQ-5D_.

CHU9D is a self-reported measure of quality of life with 9 items rated from 1 to 5, yielding a total score of 9-45, with higher scores indicating greater quality of life.[137] MANSA is a brief and modified version of LQLP (Lancashire Quality of Life Profile). As in the LQLP, satisfaction is rated on 7-point rating scales (1 = negative extreme, 7 = positive extreme); PQ-LES-Q is a 15-item rating scale with items scored from 1 (very poor) to (very good); the first 14 items are summed based on the original Q-LES-Q, with higher scores reflecting greater enjoyment and satisfaction.[185, 198] The Pediatric Quality of Life Inventory™ (PedsQL™) 4.0 Generic Core Scales with two subscales, physical functioning, and emotional and social functioning. Higher scores reflect lower domain specific quality of life. The EQ-5D is a widely used measure in health economic evaluations and consists of five dimensions measuring health-related functioning and quality of life—pain/discomfort, anxiety/depression, self-care, mobility, and

usual activities. It also consists of a 0–100 visual analogue scale (VAS) used to measure subjective ratings of health. Results are in Appendix Tables E-KQ2-24 to E-KQ2-30. Across scales and comparisons (ERP vs. control, ERP vs. remote ERP, N-Acetylcysteine vs. SSRI), only a single study reported a statistically significant difference: Ghanizadeh 2017 reported that in 29 children, those taking N-Acetylcysteine plus a SSRI had a statistically significant net mean improvement on the PedsQL (Table E-KQ2-31).[126]

3.4.4.3 Parent Satisfaction With Services

Three RCTs[110, 125, 137]enrolling a total of 192 participants measured parent satisfaction with services using The Client Satisfaction Questionnaire (CSQ-8) or the 7-Item inventory at the end of intervention. CSQ-8 is an 8-item scale that is used to measure satisfaction with the treatment, each item is rated from 1 to 4, yielding a total score of 9-36 where higher scores indicate greater satisfaction.[137] The 7-item inventory includes items such as, “To what extent has this program met your needs?” and “If a friend's child were in similar need, would you recommend the program?” Items were rated on a 4-point Likert scale with 0=not at all and 4=very much (maximum score= 28).[110] Across scales and comparisons (ERP vs. remote ERP, ERP vs. ERP+Family focused intervention), no study reported a statistically significant difference. Results are in Appendix Tables E-KQ2-31 to E-KQ2-34.

3.4.4.4 Adverse Events

3.4.4.4.1 Serious or Leading to Withdrawal or Discontinuation

Seven studies reported on adverse events leading to withdrawal or discontinuation.[77, 81, 88, 90-92, 105] Three studies compared clomipramine with placebo,[81, 88, 90] 2 studies compared ERP with SSRI,[91, 105] one study compared different TCAs,[77] and one compared ERP with clomipramine.[92]

Among these, 2 RCTs reported a significantly greater risk of adverse events leading to withdrawal—3.6-fold greater in a placebo controlled study of paroxetine,[90] and 4.1-fold higher for a similar study comparing sertraline with placebo.[81] Full results in Appendix Table E-KQ2-35.

Four studies reported on serious/severe adverse events.[88, 105, 113, 123] One study reported on the comparison of TCA versus Placebo,[88] one on NMDA versus CBT,[123] one on CBT versus SSRI,[105] and one on standard dosing versus slowly titrated SSRI.[113] No significant differences in risk of serious/severe adverse events were reported (Appendix Table E-KQ2-36).

3.4.4.4.2 Adverse Events—Total

Ten studies reported on total adverse events (Appendix Table E-KQ2-37).[84, 93, 100, 102, 105, 108, 118, 129, 137, 199] One study reported on the comparison of different TCAs,[93] two on NMDA versus placebo,[102, 118] one on cognitive bias modification-interpretation (CBM-I) versus waitlist,[199] one on TCA versus placebo,[129] one on antipsychotic drug versus TCA,[108] one on SSRI versus placebo,[84] one on SSRI versus CBT,[105] one on internet CBT versus in-person CBT,[137] and one on SSRI versus TCA.[100]

One study reported a reduced risk of total adverse events using fluvoxamine versus clomipramine (RR 0.48, 95% CI 0.27-0.83).[93] Another study comparing SSRI and TCA reported that participants treated with sertraline reported fewer adverse events than those treated with clomipramine (RR 0.42, 95% CI 0.24-0.72).[100]

3.4.4.4.3 Adverse Events—Suicidal Thoughts and Behavior

One study reported on suicidal thoughts and behavior using a questionnaire developed by the researchers.[90] No cases were reported in both regular sertraline plus CBT and slow sertraline plus CBT groups (Appendix Table E-KQ2-38).

3.4.4.4.4 Withdrawals/Discontinuation

Eleven studies reported on withdrawals and discontinuation not only due to adverse events.[61, 81, 84, 88, 90, 105, 113, 115, 122, 123, 127] One study reported on the comparison of CBT versus SSRI,[105] one on different TCAs,[88] two on TCA versus placebo,[81, 90] one on Internet-delivered cognitive-behavioral therapy (iCBT) versus placebo,[127] one on CBT versus TCA,[122] one on acceptance and Commitment therapy (ACT) versus CBT,[61] one on SSRI versus placebo,[84] and one on different SSRIs.[113] No study reported a significant effect of any intervention on the risk of withdrawal or discontinuation (Appendix Table E-KQ2-39).

3.4.5 Nonrandomized Comparative Studies

Two NRCSs that adjusted for potential confounders (and were, thus, eligible) evaluated the comparative effectiveness of treatments for OCD.

Franklin 2024[185] reported outcomes from 1,286 youth, ages 7 to 17, who received intensive CBT with exposure and response therapy in intensive outpatient and partial hospitalization settings. This study evaluated the comparative effectiveness of CBT delivered via telehealth during the COVID-19 pandemic with a propensity-matched sample of patients treated in-person prior to the pandemic. At discharge, patients treated in-person had significantly lower CY-BOCS-SR (self-report) scores, corresponding to an effect size (Cohen's d, P=0.0004) interpreted as a small comparative benefit for in-person CBT. The authors reported no significant difference in quality of life, assessed using the PQ-LES-Q, or in treatment response (defined as a reduction of 35% in CY-BOCS-SR). In the in-person group, 218 of 643 patients (33.9%) achieved remission (defined as CY-BOCS-SR ≤12) compared to 187 of 643 (29.1%) in the telehealth group. This corresponded to a risk difference of 0.048 (95% CI −0.002 to 0.099, P = 0.062) and a risk ratio of 1.17 (95% CI 0.99, 1.37, P = 0.063).

Schuberth 2023[186] evaluated the comparative effectiveness of group parent management training (PMT) in addition to ERP, compared to ERP alone. Inverse probability of treatment weighting (IPTW) was used to account for differences in measured confounders. The adjusted 95 percent confidence intervals for the post-treatment between-group means for the following scales: CY-BOCS, the Coercive Disruptive Behavior Scale (CD-POC), COIS-R, OCD Family Functioning Scale (OFF), and FAS—all overlapping the null—providing no evidence that PMT+ERP improved OCD severity or family functioning.

3.4.6 Randomized, Phase II Trials Following Single Arm Phase I Interventions

Geller 2003[88] enrolled 335 participants in a phase I (open label) trial of paroxetine. They reported that 238 of 335 patients evaluated in phase I achieved a reduction of ≥25 percent in baseline CY-BOCS and a Clinical Global Impressions scale-improvement (CGI-I) score of 1 or 2 ("very much improved or much improved"). In phase II, 193 of the patients who were responsive to paroxetine were randomized to continued paroxetine versus placebo. Relapse was defined as any of the following: an increase in CGI-I of 2 or more points between two visits or 5 points

("much worse") compared to baseline. In the paroxetine group, 33/95 (34.7%) experienced relapse compared to 43/98 (43.9%) in the placebo group [unadjusted risk ratio 0.79, 95% CI 0.56 to 1.12, P=0.197].

The NordLOTS enrolled 269 participants in a phase I (single arm) trial of ERP delivered in community outpatient mental clinics.[200] Among 66 step I completers who were did not respond to ERP, defined as CY-BOCS <16 after ERP, 54 were randomized to continued ERP or sertraline for 16 weeks. The authors reported no significant between group difference in CY-BOCS total score or the proportion of responders, suggesting that continued ERP and adding sertraline have similar effectiveness.[122]

3.4.7. Results, Key Question 2: Treatment Interventions, Predictors of Treatment Response

3.4.7 Predictors of Treatment Response

There were 21 papers (2 secondary analyses of included RCTs[150, 167] and 19 single-arm studies[199, 201-218]). representing 15 cohorts, that reported multivariable analyses of predictors of treatment response for CBT or a comparison of CBT with medication that was included in a multivariable model. The RCTs included two studies that reported on three outcomes. The RCTs were generally at low RoB across all domains, and none were industry funded. Both had CBT with Psychoeducation, Cognitive Restructuring, and ERP in both arms. The 19 single-arm articles represented 13 unique cohorts. In no instance did two different articles report the same outcome and predictor combination for the same cohort at the same time point. Most articles evaluated outcomes immediately post-treatment, but two also had evaluations at 6 months after treatment,[213, 218] and one reported an interim analysis at 7 weeks.[201] All studies evaluated predictors of treatment success with CBT; in 17 articles CBT included ERP, while in two the CBT type was not specified and may or may not have included ERP. Study sizes ranged from 63 to 573 children.

We concluded that regressions were adequate in 12 articles and not adequate in the other 7. Details of interventions, regression quality, baseline data, and summaries of each study's predictors by outcome are in Appendix Tables E-KQ2-40 and E-KQ2-41; full data are in Appendix H.

OCD treatment (i.e., CBT) response and final CY-BOCS score were the only outcomes assessed by more than one study. Across studies, the strongest predictor of both CBT response (Table 4) and final CY-BOCS score (Table 5) was baseline CY-BOCS score. Higher baseline scores mostly predicted higher post-treatment CY-BOCS scores (i.e., positive correlation between baseline and final scores), but also greater reduction in CY-BOCS scores. However, four of the six studies that evaluated treatment effect (change in score) found a nonsignificant association, and one study (of 63 children in a hospital cohort in Norway) found a nonsignificant association with CY-BOCS score at the end of treatment but a statistically significant negative association after 6 months (higher baseline scores were associated with lower 6-month scores), after controlling for baseline functional impairment.

One of three analyses found a significant association between comorbid ASD and a poorer treatment response to CBT. Jassi 2023 reported that having comorbid ASD predicted less reduction in CY-BOCS score.[217] A mediator analysis of this association found that it was partially explained by the higher functional impairment of children with ASD and their being on prescribed medication for OCD, primarily SSRIs.

Age, sex, baseline COIS, baseline family accommodation, and other comorbidities, including anxiety, depression, and tics, were not predictors of CBT response across studies.

3.4.7. Results, Key Question 2: Treatment Interventions, Predictors of Treatment Response

Table 4. Predictors of treatment response to ERP (net change, remission, or response) in two or more studies

Predictor	Comparison	+ Association N (n)	– Association N (n)	NS Association N (n)	Total Studies N (n)	Consistency	Association
Age	Younger vs. older	1 (573) cohort§[201, 215]	0	5 (699) cohorts[199, 202, 206, 214, 218] 2 (219) RCTs[150, 167]	5 (1272) cohorts 2 (219) RCTs	Consistent	No association found
Sex	Male vs. female	0	0	5 (905) cohorts[199, 201, 202, 206, 212, 214] 1 (142) RCT[167]	6 (968) cohorts* 1 (142) RCT	Consistent	No association found
Baseline COIS score	Higher vs. lower score	0	0	2 (347) cohorts[201, 206, 212]	2 (347) cohorts	Consistent	No association found
Baseline CY-BOCS score	Higher vs. lower score	2 (758) cohorts‡[202, 215] 1 (77) RCT‡[150]	0	4 (536) cohorts[199, 206, 211, 214]	6 (1294) cohorts 1 (77) RCT	Inconsistent	Variable association
Baseline FAS	Higher vs. lower score	0	0	2 (413) cohorts[201, 205, 212]	2 (413) cohorts	Consistent	No association found
Comorbid ASD	ASD vs. no ASD	0	1 (323) cohort†[217]	2 (248) cohort[201, 205, 214]	3 (571) cohorts	Consistent	No association found
Comorbid tics	Tics vs. no tics	0	0	2 (248) cohorts[201, 205, 214] 1 (142) RCT[167]	2 (248) cohorts 1 (142) RCT	Consistent	No association found

Cell coloring applied for visual emphasis only; it does not provide unique information.
Abbreviations: +, positive association (first comparator, e.g., younger, is associated with larger treatment response/improvement); – negative association; ASD = autism spectrum disorder; COIS = Child Obsessive Compulsive Impact Scale; CY-BOCS = Children's Yale-Brown Obsessive Compulsive Scale; ERP = exposure and response prevention; FAS = Family Accommodation Scale; N, studies; n, participants; NS, no significant association; RCT, randomized controlled trial

* Includes one study that reported a significant predictor but did not specify direction.
† Significant predictor in logistic regression but mediation analysis noted this was partially explained by the higher functional impairment of children with ASD and their being on prescribed medication.
‡ Higher baseline CY−BOCS score may predict greater response to ERP.
§ Based on two analyses of the same cohort, one at 7 weeks and one at the end of treatment

3.4.7. Results, Key Question 2: Treatment Interventions, Predictors of Treatment Response

Table 5. Predictors of final CY-BOCS score after ERP treatment in two or more studies

Predictor	Comparison	+ Association N (n)	– Association N (n)	NS Association N (n)	Total Studies N (n)	Consistency	Association
Age	younger vs older	1 (269)[209]	0	3 (490) cohorts[206, 207, 214] 2 (219) RCTs[150, 167]	4 (759) cohorts 2 (219) RCTs	Consistent	No association found
Age at onset	younger vs older	0	0	2 (378)[204, 209]	2 (378)	Consistent	No association found
Sex	Male vs Female	0	0	4 (770) cohorts[204, 207, 209, 214] 1 (142) RCT[167]	4 (770) cohorts 1 (142) RCT	Consistent	No association found
Baseline Functioning	higher vs lower score	0	0	2 (141) cohorts[206, 213]	2 (141) cohorts	Consistent	No association found
Baseline CY-BOCS score	higher vs lower score	1 (63) cohort‡[213]	4 (599) cohorts[204, 206, 207, 214]		5 (662) cohorts	Inconsistent	Variable association
Baseline FAS	higher vs lower score	0	0	3 (410) cohorts[206, 209, 213]	3 (410) cohorts	Consistent	No association found
Comorbid Tics	Tics vs no Tics	0	0	2 (378) cohorts[204, 209] 1 (142) RCT[167]	2 (378) cohorts 1 (142) RCT	Consistent	No association found

+ Assn. Positive Association, N studies (n participants); – Assn. Negative Association, N studies (n participants); NS Assn. No Significant Association, single arm + RCT, N studies (n participants); SPE = Strength of evidence for association; ASD = Autism Spectrum Disorder; FAS = family accommodation scale; ERP = exposure and response prevention; CY-BOCS = Children's Yale-Brown Obsessive Compulsive Scale; RCT = randomized controlled trial

* Includes 1 study that gave a significant p value, but did not report direction; ‡ at end of treatment, no significant association found, but after 6 months lower baseline CY-BOCS predicted higher CY-BOCS

3.4.8 Evidence Profile for Key Question 2

Table 6 gives the evidence profile for treatment of OCD by intervention comparison and outcome.

Table 6. Evidence profile for Key Question 2, treatment of OCD

Comparison: Overall Conclusion	Outcomes	Control	N Studies (Participants)	RoB L/M/H	Consistency	Precision	Directness	Other	SoE	Conclusions
ERP vs. control: **ERP is more effective than control**	CY-BOCS	Waitlist	6 (237)	3/3/0	Consistent	Precise	Direct (NMA)	None	High	CY-BOCS NMD **−10.5 (−12.6, −8.4)**
	CY-BOCS	Behavioral	3 (240)	3/0/0	Consistent	Imprecise	Direct (NMA)	None	Moderate	CY-BOCS NMD **−5.3 (−8.0, −2.7)**
	Remission	Waitlist	2 (84)	2/0/0	Consistent	Precise	Direct (NMA)	None	High	Remission RR **8.2 (3.7, 18.5)**
	Remission	Behavioral	2 (115)	2/0/0	Consistent	Precise	Direct (NMA)	None	Moderate	Remission RR **2.7 (1.2, 6.0)**
	CGI-S	Waitlist	1 (31)	0/0/1	NA	Precise	Direct (NMA)	Sparse	Insufficient	No conclusion
	CGI-S	Behavioral	1 (126)	1/0/0	NA	Precise	Direct (NMA)	Sparse	Insufficient	No conclusion
	FAS	Behavioral	1 (70)	1/0/0	NA	Imprecise	Direct (NMA)	Sparse	Insufficient	No conclusion
	FAS	Waitlist	1 (31)	0/0/1	NA	Imprecise	Direct (NMA)	Sparse	Insufficient	No conclusion
Remote ERP vs. control: **Remote ERP is more effective than control**	CY-BOCS	Waitlist	3 (158)	2/0/1	Consistent	Precise	Direct (NMA)	None	High	CY-BOCS NMD **−9.4 (−11.9, −7.0)**
	Remission	Waitlist	3 (145)	2/0/1	Consistent	Precise	Direct (NMA)	None	High	Remission RR **7.9 (3.5, 17.5)**
	CGI-S	Waitlist	1 (60)	1/0/0	NA	Imprecise	Direct (no MA)	Sparse	Insufficient	No conclusion
	FAS	NA	0 (NA)	NA	NA	Imprecise	NA	Sparse	Insufficient	No evidence
Remote ERP vs. ERP: **Remote ERP is as effective as in-person ERP**	CY-BOCS	NA	3 (246)	3/0/0	Consistent	Precise	Direct	None	High	CY-BOCS NMD 1.1 (−1.3, 3.5)
	Remission	NA	2 (88)	2/0/0	Consistent	Precise	Direct (NMA)	Sparse	High	Remission RR 1.0 (0.7, 1.3)
	CGI-S	NA	2 (174)	2/0/0	Consistent	Precise	Direct (NMA)	Sparse	Moderate	CGI-S NMD −0.0 (−0.3, 0.3)
	FAS	NA	3 (241)	3/0/0	Inconsistent	Imprecise	Direct (NMA)	None	Low	FAS NMD −2.7 (−6.4, 1.0)
SSRI vs. control: **SSRI is more effective than control**	CY-BOCS	Placebo	8 (762)	5/3/0	Consistent	Precise	Direct (NMA)	None	High	CY-BOCS NMD: **−4.4 (−6.1, −2.6)**
	Remission	Placebo	1 (56)	1/0/0	NA	Imprecise	Direct (no MA)	Sparse	Insufficient	No conclusion

3.4.8. Results, Key Question 2: Treatment Interventions, Evidence Profile

Comparison: Overall Conclusion	Outcomes	Control	N Studies (Participants)	RoB L/M/H	Consistency	Precision	Directness	Other	SoE	Conclusions
	CGI-S	Placebo	4 (346)	3/1/0	Consistent	Precise	Direct (NMA)	None	High	CGI-S NMD: **−0.5 (−0.8, −0.3)**
	FAS	NA	0 (NA)	NA	NA	NA	NA	NA	Insufficient	No evidence
TCA vs. control: **Treatment with TCA is more effective than placebo**	CY-BOCS	Placebo	2 (76)	1/1/0	Consistent	Imprecise	Direct (NMA)	Sparse	Moderate	NMD: **−4.5 (−6.8, −2.1)**
	Remission	NA	0 (NA)	NA	NA	NA	NA	NA	Insufficient	No evidence
	CGI-S	NA	0 (NA)	NA	NA	NA	NA	NA	Insufficient	No evidence
	FAS	NA	0 (NA)	NA	NA	NA	NA	NA	Insufficient	No evidence
ERP vs. SSRI: **ERP is more effective than SSRI**	CY-BOCS	NA	3 (179)	2/0/1	Consistent	Precise	Direct (NMA)	None	Moderate	CY-BOCS NMD: **−2.7 (−5.4, −0.0)**
	Remission	NA	2 (89)	1/0/1	NA	Imprecise	Direct (no MA)	Sparse	Moderate†	Remission RR: 0.9 (0.6, 1.4)
	CGI-S	NA	1 (39)	0/0/1	NA	Imprecise	Direct (no MA)	Sparse	Insufficient	No conclusion
	FAS	NA	0 (NA)	NA	NA	NA	NA	NA	Insufficient	No evidence
ERP+SSRI vs ERP: **ERP+SSRI is as effective as ERP alone**	CY-BOCS	NA	2 (103)	2/0/0	Consistent	Precise	Direct (NMA)	None	High	CY-BOCS NMD: −0.3 (−3.3, 2.7)
	Remission	NA	1 (56)	1/0/0	NA	Imprecise	Direct (no MA)	Sparse	Insufficient	No conclusion
	CGI-S	NA	1 (47)	1/0/0	NA	Imprecise	Direct (no MA)	Sparse	Insufficient	No conclusion
	FAS	NA	0(NA)	NA	NA	NA	NA	NA	Insufficient	No evidence
ERP+SSRI vs. SSRI: **ERP+SSRI is more effective than SSRI**	CY-BOCS	NA	6 (273)	2/3/1	Consistent	Imprecise	Direct (NMA)	None	Moderate	CY-BOCS NMD: **−3.0 (−5.1, −1.0)**
	Remission	NA	1 (56)	1/0/0	NA	Imprecise	Direct (no MA)	Sparse	Insufficient	No conclusion
	CGI-S	NA	1 (10)	0/1/0	NA	Imprecise	Direct (no MA)	Sparse	Insufficient	No conclusion
	FAS		0 (NA)	NA	NA	NA	NA	NA	Insufficient	No evidence
SSRI vs. TCA: **SSRI is as effective as TCA**	CY-BOCS	NA	6 (409)	0/5/1	Consistent	Precise	Direct (NMA)	None	High	CY-BOCS NMD 0.1 (−1.9, 2.1)
	Remission	NA	2 (149)	0/2/0	Consistent	Precise	Direct (NMA)	Sparse	High	Remission RR 1.1 (0.9, 1.3)
	CGI-S	NA	0 (NA)	NA	NA	NA	NA	NA	Insufficient	No evidence
	FAS	NA	0 (NA)	NA	NA	NA	NA	NA	Insufficient	No evidence

3.4.8. Results, Key Question 2: Treatment Interventions, Evidence Profile

Comparison: Overall Conclusion	Outcomes	Control	N Studies (Participants)	RoB L/M/H	Consistency	Precision	Directness	Other	SoE	Conclusions
DCS+ERP vs. ERP: **DCS+ERP is as effective as ERP**	CY-BOCS	NA	5 (316)	5/0/0	Consistent	Precise	Direct (pwMA)	None	High	CY-BOCS NMD: −1.2 (−2.9, 0.5)
	Remission	NA	2 (242)	2/0/0	Consistent	Highly Imprecise	Direct (no MA)	Sparse	Insufficient	No conclusion
	CGI-S	NA	3 (189)	3/0/0	Consistent	Precise	Direct (pwMA)	None	Moderate	CGI-S NMD: −0.3 (−0.9, 0.2)
	FAS	NA	0 (NA)	NA	NA	NA	NA	NA	Insufficient	No evidence

Prioritized outcomes with insufficient evidence across all listed comparisons are omitted. Cell coloring and bold font applied for visual emphasis only; it does not provide unique information. † Moderate SoE ERP is as effective (but not more effective) for remission outcome.

Abbreviations: Behavioral = behavioral control; CGI-S = Clinical Global Impressions Scale-Severity; Control = one of granular control groups , placebo or behavioral) or Combined (all control groups combined); CY-BOCS = Children's Yale-Brown Obsessive Compulsive Scale; DCS = D-cycloserine; ERP = CBT with exposure and response prevention; FAS = Family Accommodation Scale; L, M, H = low, medium and high strength of evidence; N = number of studies (number of participants); NMD = net mean difference; NMA = network meta-analysis; placebo = pill placebo; pwMA = pairwise meta-analysis; RoB = risk of bias (L= low, M=moderate, H=high); SOE = strength of evidence; SSRI = selective serotonin reuptake inhibitors; TCA = tricyclic antidepressant; Waitlist = wait list control.

4. Discussion

4.1 Findings in Relation to the Decisional Dilemmas

4.2.1 Key Question (KQ) 1: Diagnosis of Obsessive Compulsive Disorder

Brief assessment tools. Brief assessment tools can be used to determine whether a child should be further evaluated for obsessive compulsive disorder (OCD). Across 22 studies, 9 different scales were evaluated for multiple cutoffs. For only one tool was there evidence from a sufficient number of studies to draw any conclusions across studies. There is moderate strength of evidence (SoE) that the 8-question version of the Child Behavior Checklist-Obsessive Compulsive subscale (CBCL-OCS) is sufficiently sensitive and specific (summary area under the curve of 0.84, 95% CI 0.74 to 0.91) to prompt specialist referral for additional diagnostic assessment. Overall, the current evidence is insufficient to justify broad conclusions about the performance of the other 8 brief assessment tools. However, assessment tools need not have perfect diagnostic accuracy, only acceptable sensitivity and specificity as screens to prompt referral or further inquiry. Based on the current evidence the CBCL-OCS has good enough performance for use, and more studies should be done on the other eight scales to verify their usefulness in this way.

4.2.2 KQ2: Treatment of Obsessive Compulsive Disorder

CBT with exposure and response prevention (ERP) is consistently effective for the treatment of OCD across multiple outcomes, including symptoms, remission, global severity, and reduction in family accommodation. Large effects are consistently reported in studies that compare ERP with a waitlist control. In a pooled estimate from 4 recent randomized controlled trials (RCTs) that compare ERP with active control interventions (e.g., psychoeducation and relaxation therapy, but not ERP), the magnitude of the ERP effect is somewhat attenuated.

ERP delivered via telehealth is more effective than waitlist control, with effects similar to those seen with in-person ERP, supporting consideration of telehealth as a means to increase access to care, particularly in rural areas, and in locations with a shortage trained ERP providers.

Pharmacological treatment and combination of ERP and medication. Selective serotonin reuptake inhibitors (SSRI) and clomipramine (a tricyclic antidepressant [TCA]) are both more effective than pill placebo. ERP is probably more effective than SSRI, and the combination of ERP and an SSRI are probably more effective than SSRI alone. These conclusions argue for early referral for ERP, and treatment with medications in patients who have more severe illness, are not able to engage in ERP whether because of degree of distress/impairment or logistical/access barriers, have an incomplete response to ERP, or have been referred but are not yet receiving ERP. Our review found very sparse evidence to inform recommendations relating to how to treat individuals who fail to respond to ERP alone, or combined treatment with ERP and an SSRI or TCA. In the patients enrolled in clinical trials, augmentation of ERP with the glutamate inhibitor D-cycloserine is not more effective than ERP alone.

4.2 Strengths and Limitations

4.2.1 Strengths and Limitations of the Evidence Base

KQ 1: Strengths— Multiple scales (with multiple informants) have been developed which have face validity as brief assessment tools, providing an opportunity for future research.

KQ 1: Limitations—While we found 22 studies that evaluated the diagnostic accuracy of brief assessment tools, almost all used a case-control design or had other critical methodologic limitations, including inclusion of only patients with OCD and inclusion of nonclinical controls, potentially overestimating both sensitivity and specificity due to the spectrum effect (or bias).[219] Few tools were assessed by more than 2 or 3 studies, and we found no studies designed to evaluate potential clinical effects, such as resource use or time to treatment, or potential effect modifiers, such as race or comorbidity status.

KQ 2: Strengths—The evidence base was large (71RCTs and nonrandomized comparative studies). Meta-analysis was facilitated by the near universal use of a common outcome metric, (Children's) Yale-Brown Obsessive Compulsive Scale [(C)Y-BOCS] to assess changes in overall clinical severity.

KQ 2: Limitations—Many RCTs enrolled a small number of participants, and conclusions may be influenced by "small-study effects", a term for observation that small studies sometimes show different, often larger, treatment effects than large studies.[220] Reporting of outcome measures was variable, and effects were often reported in the form of regression parameters with significance tests, or as standardized effects (i.e., Cohen's d rather than mean within- and between-group mean and standard deviation of total CY-BOCS score). Across studies, there was a lack of consistent definitions regarding what constituted clinical remission or relapse. Trials often reported last observation carried forward analyses to account for missing data due to dropouts, potentially increasing bias and resulting in overly precise estimates. Treatment durations were relatively short, and somewhat variable, and durability of treatment effects remains unclear. Across all interventions, inclusion and exclusion criteria varied, as did treatment intensity. Providers and participants in trials of behavioral interventions cannot be masked, thus the potential for investigator bias is more easily controlled in pharmacological trials.

Few individual studies were adequately powered to evaluate predictors and moderators of intervention effectiveness.

Given the small sample size of included RCTs and the inconsistent reporting of medication side effects, there was insufficient evidence for graded conclusions regarding the harms and comparative harms of pharmacological treatments. However, based on evidence from other sources, the side effects of these drugs in children and adolescents are well known.[221] None of the included studies systematically collected or reported potential adverse events related to psychotherapy.

We found no studies that identified participants with OCD who had concurrent features of pediatric acute-onset neuropsychiatric syndrome or pediatric autoimmune neuropsychiatric disorder associated with streptococcal infections (PANS/PANDAS), precluding any direct conclusions about intervention effects in this subgroup.

All included RCTs enrolled adolescents younger than 18 years of age, precluding conclusions specific to treatment of OCD in youth aged 18 to 20 years inclusive.

4.2.2 Strengths and Limitations of the Systematic Review Process

Visualization of the network of treatment comparisons provides a visual overview of the available intervention comparisons. For the CY-BOCS outcome in particular, this resulted in a robust connected network, allowing for pooled effect estimates to include both direct and indirect information for most intervention comparisons, and opportunities to assess for local consistency. Our findings were, thus, more robust than conclusions we could have made from pairwise (direct) comparisons only.

In our network meta-analyses of CY-BOCS and remission outcomes, pooled treatment effects were smaller when ERP was compared to behavioral controls compared to waitlist. Therefore, rather than pooling different control conditions, we retained wait list, behavioral controls and pill placebo as separate comparators across all outcomes.

Given the large number of intervention comparisons with limited direct evidence, we report combined effects (indirect and direct evidence) from the network meta-analyses where two or more study arms contributed direct evidence. Effect estimates for comparisons with fewer than two (or no) direct comparisons (particularly for small studies) are much less likely to be robust.

Given the relatively sparse evidence within comparator-outcome categories, we did not perform subgroup analyses or meta-regression of potential predictors and moderators of treatment effects. Potential predictors and moderators are described narratively.

We followed contemporary standards for conducting systematic reviews, including engaging multiple stakeholders in KQ development and refinement and careful adherence to recommended methods for literature searching, screening, data extraction, risk of bias assessment, qualitative synthesis, quantitative synthesis, and SoE assessment. During protocol development, we prioritized interventions in consultation with panels of Key Informants and Technical Experts. However, due to the multiple comparisons reported across studies, small sample size, many of the potential comparison-outcome combinations were reported in an insufficient number of studies to allow conclusions (or to support either pairwise or network meta-analyses).

4.3 Applicability

Studies of brief assessment tools primarily relied on case-control designs, and therefore may not be representative of symptomatic patients in primary settings for whom OCD is a consideration. Thus, existing studies may overestimate both sensitivity and specificity, limiting the applicability of recommended thresholds for diagnostic referral.

Across both KQs, studies performed in the United States enrolled primarily White, middle class, socially advantaged participants (more than about 90% of study participants were White, about two-thirds their parents were living together, and about two-thirds of their parents were college educated), with a major underrepresentation of marginalized or socially disadvantaged youth. For both behavioral and pharmacological interventions, prior experiences of stigmatization and discrimination may contribute to negative perceptions of diagnostic assessments and treatment. The majority of RCTs evaluating the efficacy of ERP are done specialty care settings by therapists providing provide high fidelity, within-session CBT with ERP. This may not translate into all clinical settings.[222] A poor fit with providers may impede treatment quality by reducing engagement and retention. Clinical outcomes may be attenuated if families feel misunderstood or not believed, or if clinicians fail to adapt to the cultural context (e.g., by not involving community members such as faith leaders or extended family). Inequities in access to CBT with ERP may contribute to overuse of psychotropic medications.[223] In those

receiving ERP, exposure quality and clinical outcomes may be attenuated for such reasons as families feeling misunderstood or not believing in the treatment, or if clinicians fail to adapt for cultural context.[6, 224, 225]

4.4 Implications for Clinical Practice

KQ 1: Across the 9 brief assessment tools, only the CBCL-OCS 8-question version was evaluated by a sufficient number of studies to draw conclusions, and probably has sufficiently diagnostic accuracy to help identify symptomatic patients for specialist referral and comprehensive diagnostic evaluation of OCD.

KQ 2: There is strong evidence that CBT with ERP is effective, and probably more effective than SSRIs alone. Remote ERP appears to have similar efficacy compared to in-person ERP.

These findings support widespread dissemination of CBT with ERP as a first-line treatment in children and adolescents with OCD. Provision of ERP via telehealth may facilitate wider dissemination. The evidence suggests that treatment with an SSRI cannot replace ERP, though pharmacological treatments could be useful in selected patients to facilitate engagement in ERP, or when ERP is not available.

Only a minority of youth with OCD receive minimally acceptable care,[222] and average wait times exceed 6 to 12 months. Even when able to access CBT, these youth rarely receive ERP,[226] due in part to low rates of exposure training and comfort among providers.[227] Marginalized youth face even greater barriers to accessing high-quality care. Barriers to access include limited availability of services, transportation difficulties, being less aware of the illness and/or treatment options, and experiences of stigmatization and discrimination. Health equity initiatives to increase access and quality must focus on settings that serve a majority of marginalized youth and promote culturally responsive interventions.[225, 228]

4.5 Implications for Research

KQ 1: All of the brief assessment tools should be evaluated in further studies to assess their sensitivity and specificity. These studies should ideally be prospective cohorts, enrolling a consecutive sample of patients for whom there is clinical concern for OCD. Comparative accuracy is best assessed by directly comparing two or more index tests in the same study, rather than across studies.[229] In addition, future studies should evaluate diagnostic accuracy across important effect modifiers, such as race and comorbidity status.

The same reference standard should be applied to all patients, ideally using a Longitudinal Expert All Data (LEAD) process that incorporates an expert clinical assessment, semi-structured interviews (e.g., Kiddie Schedule for Affective Disorders and Schizophrenia [K-SADS], Anxiety Disorders Interview Schedule for Children [ADIS-C]), multiple informants, assessment of level of impairment (e.g., CY-BOCS, CY-BOCS-II), and longitudinal response to treatment.[64, 230] Diagnostic evaluations should include assessment for common comorbid diagnoses (e.g., autism spectrum disorders, tic disorders, and presentations that raise concern for PANS/PANDAS). Once reliable tools are developed and validated, trials that evaluate the impact diagnostic strategies on clinical outcomes, such as time to treatment and improved functional outcomes, should be performed.

KQ 2: SSRIs are widely used in pharmacotherapy for children and adolescents with anxiety and depressive disorders.[221] A recent meta-analysis[231] of placebo controlled trials of pediatric patients with OCD and other anxiety disorders (generalized, separation or social anxiety

disorders) concluded that SSRIs are associated with distinct adverse events (AE), including activation, abdominal pain, and drowsiness. They found higher rates of AE-related discontinuation compared to placebo, but no association with suicidality. Future studies should assess for a standardized set of potential side-effects and assess the potential role of pharmacogenetic testing.

Future studies should evaluate interventions for which we have found no evidence, or insufficient evidence, including, neuromodulation, identification of patients for whom SSRI+ERP improves outcomes compared to ERP, and interventions in patients resistant to standard therapy (i.e., atypical antipsychotic mediations, and novel therapies based on advances in the understanding of the underlying pathophysiology of OCD. None of the included studies provide direct evidence for the magnitude of the placebo effect. Assuming participants in waitlist are otherwise similar to participants receiving pill placebo, an estimate (based on indirect evidence only) for the placebo effect[232] (placebo versus waitlist comparison) is a net mean difference in CY-BOCS of −3.1 with a 95 percent confidence interval ranging from −7.1 to 0.3. Future pharmacological studies should consider assigning patients to active intervention and both waitlist and placebo arms.

Given the overall strong evidence for efficacy, future studies should prioritize the evaluation of treatment strategies tailored to OCD and co-occurring mental health disorders. Implementation trials are needed to evaluate what works best for whom, and to inform shared decision-making about treatment between patients, families and providers. Studies should address the comparative benefits alternative settings (e.g., remote, home, clinic, partial hospitalization), and intensities. Predictors studies should be adequately powered to detect effect modifiers and should more fully report the model specifications and results. Individual participant data meta-analysis of existing trials may also be useful to evaluate predictors and moderators.[233]

There has been a longstanding failure to include youth who have been historically underrepresented (e.g., based on race, ethnicity, or income) in pediatric OCD treatment studies.[224] Past studies often under recruit marginalized youth, in part because the settings (academic settings) and treatment models (once weekly in an office) perpetuate barriers to equitable access and acceptability. Consequently, there is a resounding call from patients, families, clinicians, researchers, and advocacy groups to prioritize the inclusion of youth who have been historically underrepresented in clinical science and underserved in clinical practice. This is imperative for research that addresses tailoring treatment to better address barriers to access, quality, and clinical improvement for these groups.[234]

KQ 2 Research planned or in progress. We surveyed ongoing studies registered in ClinicalTrials.gov and found 8 trials (see Appendix Table C-2.1.3) whose design would meet the inclusion criteria for KQ 2. Of these, one is an effectiveness trial (Treatment Effects of Family Based Cognitive Therapy in Children and Adolescents with Obsessive Compulsive Disorder [TECTO]) comparing family based cognitive behavioral therapy with psychoeducation/relaxation training. The TECTO trial plans to gather qualitative and quantitative information related to potential adverse events associated with ERP.[235] Other ongoing trial addresses the comparative effectiveness of different delivery methods and styles of CBT, comparing patient-centered home-based CBT versus patient-centered-telehealth versus traditional office-based CBT; three registered trials will evaluate transcranial magnetic stimulation; two trials evaluate pharmacological strategies, including a trial of celecoxib as an adjunct to treatment as usual,[236] and a trial enrolling both adolescents and adults, comparing

fluvoxamine and sertraline versus aripiprazole and sertraline. Finally, a two-phase trial is seeking to determine whether participants who benefit from CBT augmentation of their SSRI treatment can successfully discontinue SSRI treatment without relapse.

4.6 Conclusions

The diagnosis of OCD relies on expert clinical evaluation, often augmented by semi-structured interviews. Brief assessment tools have been proposed to be used by primary care providers evaluating youth with symptoms of OCD to facilitate early identification and specialty referral for a comprehensive diagnostic evaluation and early initiation of treatment. The CBCL-OCS may be sufficiently accurate to indicate which youth should be further evaluated for OCD, but the available evidence is insufficient for other brief assessment tools.

We found evidence supporting the efficacy of ERP, delivered in-person or remotely, and for both SSRIs and clomipramine compared to placebo. ERP alone, or ERP in combination with an SSRI, is more effective than treatment with an SSRI alone.

The side effects of SSRIs and clomipramine were inconsistently reported in the included RCTs, precluding graded conclusions. However, based on evidence from other sources, the side effects of these drugs in children and adolescents are well known.[221] No study collected or reported potential harms of behavioral interventions.

Treatment with D-cycloserine to augment ERP is not more effective than ERP alone in reducing OCD symptom severity and is probably not more effective in reducing global OCD severity.

Future research efforts should focus on: 1) inclusion of study participants who are representative of all youth affected by OCD, including non-white, low socioeconomic status children, and of sufficient size to allow subgroup analyses to determine what works for whom; 2) increased transparency in study reporting around dose of exposure, as well as therapist training and quality monitoring; 3) implementation research around the when/where/who/how of OCD treatment to be sure it is reaching everyone who needs it; and 4) development and evaluation of both pharmacologic and behavioral augmentation to ERP and novel interventions (e.g., neuromodulation)

3.3.3 Results, Key Question 1: Brief Assessment Tools, Evidence Profile for Key Question 1

References

1. Practice parameter for the assessment and treatment of children and adolescents with obsessive-compulsive disorder. J Am Acad Child Adolesc Psychiatry. 2012 Jan;51(1):98-113. doi: 10.1016/j.jaac.2011.09.019. PMID: 22176943.
2. Dell'Osso B, Benatti B, Hollander E, et al. Childhood, adolescent and adult age at onset and related clinical correlates in obsessive-compulsive disorder: a report from the International College of Obsessive-Compulsive Spectrum Disorders (ICOCS). Int J Psychiatry Clin Pract. 2016 Nov;20(4):210-7. doi: 10.1080/13651501.2016.1207087. PMID: 27433835.
3. Katz JA, Rufino KA, Werner C, et al. OCD in Ethnic Minorities. Clinical and Experimental Psychology. 2020;6(1):1-6.
4. Wang JJ, Lin S, Best JR, et al. Race and ethnicity in pediatric OCD: An exploratory study of a clinical North American sample. Ann Clin Psychiatry. 2021 Feb;33(1):4-17. doi: 10.12788/acp.0007. PMID: 33125453.
5. Wetterneck CT, Little TE, Rinehart KL, et al. Latinos with obsessive-compulsive disorder: Mental healthcare utilization and inclusion in clinical trials. J Obsessive Compuls Relat Disord. 2012 Apr;1(2):85-97. doi: 10.1016/j.jocrd.2011.12.001. PMID: 29057210.
6. Williams MT, Sawyer, B., Ellsworth, M., Singh, S., Tellawi, G.,. Obsessive-Compulsive and Related Disorders in Ethnoracial Minorities: Attitudes, Stigma, and Barriers to Treatment. In: J. Abramowitz DM, E. Storch,, ed The Wiley Handbook of Obsessive Compulsive Disorders. Wiley; 2017.
7. Zhang AY, Snowden LR. Ethnic characteristics of mental disorders in five U.S. communities. Cultur Divers Ethnic Minor Psychol. 1999 May;5(2):134-46. doi: 10.1037/1099-9809.5.2.134. PMID: 15605683.
8. Himle JA, Muroff JR, Taylor RJ, et al. Obsessive-compulsive disorder among African Americans and blacks of Caribbean descent: results from the National Survey of American Life. Depress Anxiety. 2008;25(12):993-1005. doi: 10.1002/da.20434. PMID: 18833577.
9. Kessler RC, Berglund P, Demler O, et al. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry. 2005 Jun;62(6):593-602. doi: 10.1001/archpsyc.62.6.593. PMID: 15939837.
10. Piacentini J, Bergman RL. Obsessive-compulsive disorder in children. Psychiatr Clin North Am. 2000 Sep;23(3):519-33. doi: 10.1016/s0193-953x(05)70178-7. PMID: 10986725.
11. Piacentini J, Bergman RL, Keller M, et al. Functional impairment in children and adolescents with obsessive-compulsive disorder. J Child Adolesc Psychopharmacol. 2003;13 Suppl 1:S61-9. doi: 10.1089/104454603322126359. PMID: 12880501.
12. Storch EA, Milsom VA, Merlo LJ, et al. Insight in pediatric obsessive-compulsive disorder: associations with clinical presentation. Psychiatry Res. 2008 Aug 15;160(2):212-20. doi: 10.1016/j.psychres.2007.07.005. PMID: 18556071.
13. Ezpeleta L, Keeler G, Erkanli A, et al. Epidemiology of psychiatric disability in childhood and adolescence. J Child Psychol Psychiatry. 2001 Oct;42(7):901-14. doi: 10.1111/1469-7610.00786. PMID: 11693585.
14. Flament MF, Whitaker A, Rapoport JL, et al. Obsessive compulsive disorder in adolescence: an epidemiological study. J Am Acad Child Adolesc Psychiatry. 1988 Nov;27(6):764-71. doi: 10.1097/00004583-198811000-00018. PMID: 3264280.
15. Thomsen PH, Mikkelsen HU. Course of obsessive-compulsive disorder in children and adolescents: a prospective follow-up study of 23 Danish cases. J Am Acad Child Adolesc Psychiatry. 1995 Nov;34(11):1432-40. doi: 10.1097/00004583-199511000-00009. PMID: 8543510.
16. Krebs G, Heyman I. Obsessive-compulsive disorder in children and adolescents. Arch Dis Child. 2015 May;100(5):495-9. doi: 10.1136/archdischild-2014-306934. PMID: 25398447.

17. Boileau B. A review of obsessive-compulsive disorder in children and adolescents. Dialogues Clin Neurosci. 2011;13(4):401-11. doi: 10.31887/DCNS.2011.13.4/bboileau. PMID: 22275846.

18. Sharma E, Sharma LP, Balachander S, et al. Comorbidities in Obsessive-Compulsive Disorder Across the Lifespan: A Systematic Review and Meta-Analysis. Front Psychiatry. 2021;12:703701. doi: 10.3389/fpsyt.2021.703701. PMID: 34858219.

19. Silverman WK, Nelles WB. The Anxiety Disorders Interview Schedule for Children. J Am Acad Child Adolesc Psychiatry. 1988 Nov;27(6):772-8. doi: 10.1097/00004583-198811000-00019. PMID: 3198566.

20. Hudziak JJ, Althoff RR, Stanger C, et al. The Obsessive Compulsive Scale of the Child Behavior Checklist predicts obsessive-compulsive disorder: a receiver operating characteristic curve analysis. J Child Psychol Psychiatry. 2006 Feb;47(2):160-6. doi: 10.1111/j.1469-7610.2005.01465.x. PMID: 16423147.

21. Deeks JJ, Bossuyt P, Leeflang MM, et al. Cochrane handbook for systematic reviews of diagnostic test accuracy. Hoboken, NJ

22. Abramovitch A, Abramowitz JS, McKay D, et al. The OCI-CV-R: A Revision of the Obsessive-Compulsive Inventory - Child Version. J Anxiety Disord. 2022 Mar;86:102532. doi: 10.1016/j.janxdis.2022.102532. PMID: 35091252.

23. Nelson EC, Hanna GL, Hudziak JJ, et al. Obsessive-compulsive scale of the child behavior checklist: specificity, sensitivity, and predictive power. Pediatrics. 2001 Jul;108(1):E14. doi: 10.1542/peds.108.1.e14. PMID: 11433093.

24. Shephard E, Batistuzzo MC, Hoexter MQ, et al. Neurocircuit models of obsessive-compulsive disorder: limitations and future directions for research. Braz J Psychiatry. 2022 Mar-Abr;44(2):187-200. doi: 10.1590/1516-4446-2020-1709. PMID: 35617698.

25. Endres D, Pollak TA, Bechter K, et al. Immunological causes of obsessive-compulsive disorder: is it time for the concept of an "autoimmune OCD" subtype? Transl Psychiatry. 2022 Jan 10;12(1):5. doi: 10.1038/s41398-021-01700-4. PMID: 35013105.

26. Susan E. Swedo, James F. Leckman, Rose NR. From Research Subgroup to Clinical Syndrome: Modifying the PANDAS Criteria to Describe PANS (Pediatric Acute-onset Neuropsychiatric Syndrome). Pediatr Therapeut. 2012;2(2). doi: 10.4172/2161-0665.1000113.

27. Jaspers-Fayer F, Han SHJ, Chan E, et al. Prevalence of Acute-Onset Subtypes in Pediatric Obsessive-Compulsive Disorder. J Child Adolesc Psychopharmacol. 2017 May;27(4):332-41. doi: 10.1089/cap.2016.0031. PMID: 28121463.

28. Berkman ND, Lohr KN, Ansari M, et al. Grading the Strength of a Body of Evidence When Assessing Health Care Interventions for the Effective Health Care Program of the Agency for Healthcare Research and Quality: An Update. Methods Guide for Comparative Effectiveness Reviews (Prepared by the RTI-UNC Evidence-based Practice Center under Contract No. 290-2007-10056-I). AHRQ Publication No. 13(14)-EHC130-EF. 2013.

29. Berkman ND, Lohr KN, Ansari M, et al. Grading the Strength of a Body of Evidence When Assessing Health Care Interventions for the Effective Health Care Program of the Agency for Healthcare Research and Quality: An Update. Methods Guide for Effectiveness and Comparative Effectiveness Reviews. Rockville (MD); 2008.

30. Higgins JP, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. Bmj. 2011 Oct 18;343:d5928. doi: 10.1136/bmj.d5928. PMID: 22008217.

31. Sterne JA, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. Bmj. 2016 Oct 12;355:i4919. doi: 10.1136/bmj.i4919. PMID: 27733354.

32. Whiting P, Rutjes AW, Dinnes J, et al. Development and validation of methods for assessing the quality of diagnostic accuracy studies. Health Technol Assess. 2004 Jun;8(25):iii, 1-234. doi: 10.3310/hta8250. PMID: 15193208.

33. Whiting P, Rutjes AW, Reitsma JB, et al. The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. BMC Med Res Methodol. 2003 Nov 10;3:25. doi: 10.1186/1471-2288-3-25. PMID: 14606960.

34. Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med. 2011 Oct 18;155(8):529-36. doi: 10.7326/0003-4819-155-8-201110180-00009. PMID: 22007046.

35. Steinhauser S, Schumacher M, Rücker G. Modelling multiple thresholds in meta-analysis of diagnostic test accuracy studies. BMC medical research methodology. 2016;16(1):1-15.

36. R Core Team. R: A Language and Environment for Statistical Computing. Vienna, Austria: R Foundation for Statistical Computing; 2021.

37. Balduzzi S, Rücker G, Nikolakopoulou A, et al. netmeta: An R Package for Network Meta-Analysis Using Frequentist Methods. Journal of Statistical Software. 2023;106(2):1-40. doi: 10.18637/jss.v106.i02.

38. Dias S, Welton NJ, Caldwell DM, et al. Checking consistency in mixed treatment comparison meta-analysis. Stat Med. 2010 Mar 30;29(7-8):932-44. doi: 10.1002/sim.3767. PMID: 20213715.

39. IntHout J, Ioannidis JP, Rovers MM, et al. Plea for routinely presenting prediction intervals in meta-analysis. BMJ Open. 2016 Jul 12;6(7):e010247. doi: 10.1136/bmjopen-2015-010247. PMID: 27406637.

40. Balduzzi S, Rucker G, Schwarzer G. How to perform a meta-analysis with R: a practical tutorial. Evid Based Ment Health. 2019 Nov;22(4):153-60. doi: 10.1136/ebmental-2019-300117. PMID: 31563865.

41. Guyatt GH, Oxman AD, Kunz R, et al. Going from evidence to recommendations. BMJ. 2008 May 10;336(7652):1049-51. doi: 10.1136/bmj.39493.646875.AE. PMID: 18467413.

42. Gerrity M, Fiordalisi C, Pillay J, et al. Roadmap for Narratively Describing Effects of Interventions in Systematic Reviews. Rockville (MD); 2020.

43. Murad MH, Fiordalisi C, Pillay J, et al. Making Narrative Statements to Describe Treatment Effects. J Gen Intern Med. 2021 Jan;36(1):196-9. doi: 10.1007/s11606-020-06330-y. PMID: 33111244.

44. Abramovitch A, Abramowitz JS, McKay D, et al. An ultra-brief screening scale for pediatric obsessive-compulsive disorder: The OCI-CV-5. J Affect Disord. 2022 Sep 1;312:208-16. doi: 10.1016/j.jad.2022.06.009. PMID: 35697331.

45. Adamowska S, Adamowski T, Frydecka D, et al. Diagnostic validity Polish language version of the questionnaire MINI-KID (Mini International Neuropsychiatry Interview for Children and Adolescent). Compr Psychiatry. 2014 Oct;55(7):1744-50. doi: 10.1016/j.comppsych.2014.05.019. PMID: 25023384.

46. Andersen PA, Bilenberg N. Comparison of Child Behavior Checklist subscales in screening for obsessive-compulsive disorder. Dan Med J. 2012 Nov;59(11):A4523. PMID: 23171745.

47. Bamber D, Tamplin A, Park RJ, et al. Development of a short leyton obsessional inventory for children and adolescents. J Am Acad Child Adolesc Psychiatry. 2002 Oct;41(10):1246-52. doi: 10.1097/00004583-200210000-00015. PMID: 12364847.

48. Batlle S, Duñó L, Camprodon E, et al. Subescala OCS-CBCL de Nelson para la evaluación del trastorno obsesivo-compulsivo infanto-juvenil: Análisis de validez en una muestra Española = Nelson's OCS-CBCL subscale for the assessment of obsessive-compulsive disorder (OCD) in children and adolescents: Validity analysis in a Spanish sample. Revista de Psicopatología y Psicología Clínica. 2013;18(1):81-92. doi: 10.5944/rppc.vol.18.num.1.2013.12765. PMID: 2013-15434-007.

49. Fisher PW, Shaffer D, Piacentini JC, et al. Sensitivity of the Diagnostic Interview Schedule for Children, 2nd edition (DISC-2.1) for specific diagnoses of children and adolescents. J Am Acad Child Adolesc Psychiatry. 1993 May;32(3):666-73. doi: 10.1097/00004583-199305000-00026. PMID: 8496131.

50. Geller DA, Doyle R, Shaw D, et al. A quick and reliable screening measure for OCD in youth: reliability and validity of the obsessive compulsive scale of the Child Behavior Checklist. Compr Psychiatry. 2006 May-Jun;47(3):234-40. doi: 10.1016/j.comppsych.2005.08.005. PMID: 16635654.

51. Högberg C, Billstedt E, Björck C, et al. Diagnostic validity of the MINI-KID disorder classifications in specialized child and adolescent psychiatric outpatient clinics in Sweden. BMC Psychiatry. 2019 May 9;19(1):142. doi: 10.1186/s12888-019-2121-8. PMID: 31072319.

52. Ivarsson T, Larsson B. The Obsessive-Compulsive Symptom (OCS) scale of the Child Behavior Checklist: a comparison between Swedish children with Obsessive-Compulsive Disorder from a specialized unit, regular outpatients and a school sample. J Anxiety Disord. 2008 Oct;22(7):1172-9. doi: 10.1016/j.janxdis.2007.12.004. PMID: 18280696.

53. Krebs G, Liang H, Hilton K, et al. Computer-assisted assessment of obsessive-compulsive disorder in young people: A preliminary evaluation of the development and well-being assessment. Child and Adolescent Mental Health. 2012;17(4):246-51. doi: 10.1111/j.1475-3588.2012.00651.x. PMID: 2012-28430-008.

54. Lambe LJ, Burton CL, Anagnostou E, et al. Clinical validation of the parent-report Toronto Obsessive-Compulsive Scale (TOCS): A pediatric open-source rating scale. JCPP Adv. 2021 Dec;1(4):e12056. doi: 10.1002/jcv2.12056. PMID: 37431399.

55. Novara C, Pardini S, Cardona F, et al. Comparing Models of the Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS) in an Italian Clinical Sample. Front Psychiatry. 2020;11:615. doi: 10.3389/fpsyt.2020.00615. PMID: 32848897.

56. Piqueras JA, Rodríguez-Jiménez T, Ortiz AG, et al. Validation of the Short Obsessive-Compulsive Disorder Screener (SOCS) in children and adolescents. BJPsych Open. 2015 Jun;1(1):21-6. doi: 10.1192/bjpo.bp.115.000695. PMID: 27703719.

57. Piqueras JA, Rodríguez-Jiménez T, Ortiz AG, et al. Factor Structure, Reliability, and Validity of the Spanish Version of the Children's Florida Obsessive Compulsive Inventory (C-FOCI). Child Psychiatry Hum Dev. 2017 Feb;48(1):166-79. doi: 10.1007/s10578-016-0661-4. PMID: 27283942.

58. Rough HE, Hanna BS, Gillett CB, et al. Screening for Pediatric Obsessive-Compulsive Disorder Using the Obsessive-Compulsive Inventory-Child Version. Child Psychiatry Hum Dev. 2020 Dec;51(6):888-99. doi: 10.1007/s10578-020-00966-x. PMID: 32030629.

59. Saad LO, do Rosario MC, Cesar RC, et al. The Child Behavior Checklist-Obsessive-Compulsive Subscale Detects Severe Psychopathology and Behavioral Problems Among School-Aged Children. J Child Adolesc Psychopharmacol. 2017 May;27(4):342-8. doi: 10.1089/cap.2016.0125. PMID: 28151703.

60. Sattler AF, Whiteside SPH, Bentley JP, et al. Development and validation of a brief screening procedure for pediatric obsessive-compulsive disorder derived from the Spence Children's Anxiety Scale. Journal of Obsessive-Compulsive and Related Disorders. 2018;16:29-35. doi: 10.1016/j.jocrd.2017.12.004. PMID: 2019-05127-008.

61. Shabani MJ, Mohsenabadi H, Zanjani Z, et al. Psychometric evaluation of the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS) in Iranian clinical and non-clinical samples. Journal of Obsessive-Compulsive and Related Disorders. 2019;22. doi: 10.1016/j.jocrd.2019.100450. PMID: 2019-80248-001.

62. Shafran R, Frampton I, Heyman I, et al. The preliminary development of a new self-report measure for OCD in young people. J Adolesc. 2003 Feb;26(1):137-42. doi: 10.1016/s0140-1971(02)00083-0. PMID: 12550826.

63. Sheehan DV, Sheehan KH, Shytle RD, et al. Reliability and validity of the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID). J Clin Psychiatry. 2010 Mar;71(3):313-26. doi: 10.4088/JCP.09m05305whi. PMID: 20331933.

64. Skarphedinsson G, Jarbin H, Andersson M, et al. Diagnostic efficiency and validity of the DSM-oriented Child Behavior Checklist and Youth Self-Report scales in a clinical sample of Swedish youth. PLoS One. 2021;16(7):e0254953. doi: 10.1371/journal.pone.0254953. PMID: 34293000.

65. Stewart SE, Ceranoglu TA, O'Hanley T, et al. Performance of clinician versus self-report measures to identify obsessive-compulsive disorder in children and adolescents. J Child Adolesc Psychopharmacol. 2005 Dec;15(6):956-63. doi: 10.1089/cap.2005.15.956. PMID: 16379516.

66. Storch EA, Murphy TK, Bagner DM, et al. Reliability and validity of the Child Behavior Checklist Obsessive-Compulsive Scale. J Anxiety Disord. 2006;20(4):473-85. doi: 10.1016/j.janxdis.2005.06.002. PMID: 16046257.

67. Storch EA, Park JM, Lewin AB, et al. The Leyton Obsessional Inventory-Child Version Survey Form does not demonstrate adequate psychometric properties in American youth with pediatric obsessive-compulsive disorder. J Anxiety Disord. 2011 May;25(4):574-8. doi: 10.1016/j.janxdis.2011.01.005. PMID: 21353458.

68. Uher R, Heyman I, Mortimore C, et al. Screening young people for obsessive–compulsive disorder. The British Journal of Psychiatry. 2007;191(4):353-4. doi: 10.1192/bjp.bp.106.034967. PMID: 2012-20796-014.

69. Whiteside SP, Gryczkowski MR, Biggs BK, et al. Validation of the Spence Children's Anxiety Scale's obsessive compulsive subscale in a clinical and community sample. J Anxiety Disord. 2012 Jan;26(1):111-6. doi: 10.1016/j.janxdis.2011.10.002. PMID: 22078243.

70. Zemestani M, Isanejad O, Valiei Z, et al. Psychometric Properties of the Obsessive Compulsive Inventory-Child Version in Iranian Clinical and Community Samples. Child Psychiatry Hum Dev. 2022 Feb;53(1):156-64. doi: 10.1007/s10578-020-01108-z. PMID: 33409771.

71. Zemestani M, Valiei Z, Isanejad O, et al. Factor structure, reliability, and validity of a Persian version of the Children's Florida Obsessive Compulsive Inventory (C-FOCI). Journal of Psychopathology and Behavioral Assessment. 2021;43(4):937-45. doi: 10.1007/s10862-021-09896-x. PMID: 2021-61128-001.

72. Storch EA, Kaufman DA, Bagner D, et al. Florida Obsessive-Compulsive Inventory: development, reliability, and validity. J Clin Psychol. 2007 Sep;63(9):851-9. doi: 10.1002/jclp.20382. PMID: 17674398.

73. Berg CZ, Whitaker A, Davies M, et al. The survey form of the Leyton Obsessional Inventory-Child Version: norms from an epidemiological study. J Am Acad Child Adolesc Psychiatry. 1988 Nov;27(6):759-63. doi: 10.1097/00004583-198811000-00017. PMID: 3198565.

74. Foa EB, Coles M, Huppert JD, et al. Development and validation of a child version of the obsessive compulsive inventory. Behav Ther. 2010 Mar;41(1):121-32. doi: 10.1016/j.beth.2009.02.001. PMID: 20171333.

75. Uher R, Heyman I, Turner CM, et al. Self-, parent-report and interview measures of obsessive–compulsive disorder in children and adolescents. Journal of anxiety disorders. 2008;22(6):979-90.

76. Flament MF, Rapoport JL, Berg CJ, et al. Clomipramine treatment of childhood obsessive-compulsive disorder. A double-blind controlled study. Arch Gen Psychiatry. 1985 Oct;42(10):977-83. doi: 10.1001/archpsyc.1985.01790330057007. PMID: 3899048.

77. Leonard HL, Swedo SE, Rapoport JL, et al. Treatment of obsessive-compulsive disorder with clomipramine and desipramine in children and adolescents. A double-blind crossover comparison. Arch Gen Psychiatry. 1989 Dec;46(12):1088-92. doi: 10.1001/archpsyc.1989.01810120030006. PMID: 2686576.

78. March JS, Johnston H, Jefferson JW, et al. Do subtle neurological impairments predict treatment resistance to clomipramine in children and adolescents with obsessive-compulsive disorder? J Child Adolesc Psychopharmacol. 1990 Fall;1(2):133-40. doi: 10.1089/cap.1990.1.133. PMID: 19630661.

79. DeVeaugh-Geiss J, Moroz G, Biederman J, et al. Clomipramine hydrochloride in childhood and adolescent obsessive-compulsive disorder--a multicenter trial. J Am Acad Child Adolesc Psychiatry. 1992 Jan;31(1):45-9. doi: 10.1097/00004583-199201000-00008. PMID: 1537780.

80. Riddle MA, Scahill L, King RA, et al. Double-blind, crossover trial of fluoxetine and placebo in children and adolescents with obsessive-compulsive disorder. J Am Acad Child Adolesc Psychiatry. 1992 Nov;31(6):1062-9. doi: 10.1097/00004583-199211000-00011. PMID: 1429406.

81. March JS, Biederman J, Wolkow R, et al. Sertraline in children and adolescents with obsessive-compulsive disorder: a multicenter randomized controlled trial. Jama. 1998 Nov 25;280(20):1752-6. doi: 10.1001/jama.280.20.1752. PMID: 9842950.

82. de Haan E, Hoogduin KA, Buitelaar JK, et al. Behavior therapy versus clomipramine for the treatment of obsessive-compulsive disorder in children and adolescents. J Am Acad Child Adolesc Psychiatry. 1998 Oct;37(10):1022-9. doi: 10.1097/00004583-199810000-00011. PMID: 9785713.

83. Neziroglu F, Yaryura-Tobias JA, Walz J, et al. The effect of fluvoxamine and behavior therapy on children and adolescents with obsessive-compulsive disorder. J Child Adolesc Psychopharmacol. 2000 Winter;10(4):295-306. doi: 10.1089/cap.2000.10.295. PMID: 11191690.

84. Geller DA, Hoog SL, Heiligenstein JH, et al. Fluoxetine treatment for obsessive-compulsive disorder in children and adolescents: a placebo-controlled clinical trial. J Am Acad Child Adolesc Psychiatry. 2001 Jul;40(7):773-9. doi: 10.1097/00004583-200107000-00011. PMID: 11437015.

85. Riddle MA, Reeve EA, Yaryura-Tobias JA, et al. Fluvoxamine for children and adolescents with obsessive-compulsive disorder: a randomized, controlled, multicenter trial. J Am Acad Child Adolesc Psychiatry. 2001 Feb;40(2):222-9. doi: 10.1097/00004583-200102000-00017. PMID: 11211371.

86. Liebowitz MR, Turner SM, Piacentini J, et al. Fluoxetine in children and adolescents with OCD: a placebo-controlled trial. J Am Acad Child Adolesc Psychiatry. 2002 Dec;41(12):1431-8. doi: 10.1097/00004583-200212000-00014. PMID: 12447029.

87. Barrett P, Healy L, March JS. Behavioral avoidance test for childhood obsessive-compulsive disorder: a home-based observation. Am J Psychother. 2003;57(1):80-100. doi: 10.1176/appi.psychotherapy.2003.57.1.80. PMID: 12647571.

88. Geller DA, Biederman J, Stewart SE, et al. Impact of comorbidity on treatment response to paroxetine in pediatric obsessive-compulsive disorder: is the use of exclusion criteria empirically supported in randomized clinical trials? J Child Adolesc Psychopharmacol. 2003;13 Suppl 1:S19-29. doi: 10.1089/104454603322126313. PMID: 12880497.

89. Barrett P, Healy-Farrell L, March JS. Cognitive-behavioral family treatment of childhood obsessive-compulsive disorder: a controlled trial. J Am Acad Child Adolesc Psychiatry. 2004 Jan;43(1):46-62. doi: 10.1097/00004583-200401000-00014. PMID: 14691360.

90. Geller DA, Wagner KD, Emslie G, et al. Paroxetine treatment in children and adolescents with obsessive-compulsive disorder: a randomized, multicenter, double-blind, placebo-controlled trial. J Am Acad Child Adolesc Psychiatry. 2004 Nov;43(11):1387-96. doi: 10.1097/01.chi.0000138356.29099.f1. PMID: 15502598.

91. POTS Team. Cognitive-behavior therapy, sertraline, and their combination for children and adolescents with obsessive-compulsive disorder: the Pediatric OCD Treatment Study (POTS) randomized controlled trial. Jama. 2004 Oct 27;292(16):1969-76. doi: 10.1001/jama.292.16.1969. PMID: 15507582.

92. Asbahr FR, Castillo AR, Ito LM, et al. Group cognitive-behavioral therapy versus sertraline for the treatment of children and adolescents with obsessive-compulsive disorder. J Am Acad Child Adolesc Psychiatry. 2005 Nov;44(11):1128-36. doi: 10.1097/01.chi.0000177324.40005.6f. PMID: 16239861.

93. He Y. Control Study of Fluvoxamine and Chlormipramine in Treatment of Child-Adolescence Obsession. Medical Journal of Chinese People's Health. 2007;19(6):438-40. PMID: He-2007_SR-35121274.

94. Storch EA, Geffken GR, Merlo LJ, et al. Family-based cognitive-behavioral therapy for pediatric obsessive-compulsive disorder: comparison of intensive and weekly approaches. J Am Acad Child Adolesc Psychiatry. 2007 Apr;46(4):469-78. doi: 10.1097/chi.0b013e31803062e7. PMID: 17420681.

95. Bolton D, Perrin S. Evaluation of exposure with response-prevention for obsessive compulsive disorder in childhood and adolescence. J Behav Ther Exp Psychiatry. 2008 Mar;39(1):11-22. doi: 10.1016/j.jbtep.2006.11.002. PMID: 17207457.

96. Freeman JB, Garcia AM, Coyne L, et al. Early childhood OCD: preliminary findings from a family-based cognitive-behavioral approach. J Am Acad Child Adolesc Psychiatry. 2008 May;47(5):593-602. doi: 10.1097/CHI.0b013e31816765f9. PMID: 18356758.

97. Guo F. A comparative study of sertraline and clomipramine in the treatment of children obsessive-compulsive disorder. China Journal of Health Psychology. 2008;16(3):314-5. PMID: Guo-2008_SR-35121274.

98. Zhu J. A comparative study of Sertraline and Clomipramine in the treatment of Child obsessive-compulsive disorder. Medical Journal of Chinese People's Health. 208;20(23). PMID: Zhu-2008_SR-35121274.

99. Alaghband-Rad J, Hakimshooshtary M. A randomized controlled clinical trial of citalopram versus fluoxetine in children and adolescents with obsessive-compulsive disorder (OCD). Eur Child Adolesc Psychiatry. 2009 Mar;18(3):131-5. doi: 10.1007/s00787-007-0634-z. PMID: 19190958.

100. Nai X. A comparative study of sertraline and clomipramine in the treatment of children obsessive-compulsive disorder. Chinese Journal of Practical Nervous Diseases 2009;12(20):10-1. PMID: Nai-2009_SR-35121274.

101. Merlo LJ, Storch EA, Lehmkuhl HD, et al. Cognitive behavioral therapy plus motivational interviewing improves outcome for pediatric obsessive-compulsive disorder: a preliminary study. Cogn Behav Ther. 2010;39(1):24-7. doi: 10.1080/16506070902831773. PMID: 19675960.

102. Storch EA, Murphy TK, Goodman WK, et al. A preliminary study of D-cycloserine augmentation of cognitive-behavioral therapy in pediatric obsessive-compulsive disorder. Biol Psychiatry. 2010 Dec 1;68(11):1073-6. doi: 10.1016/j.biopsych.2010.07.015. PMID: 20817153.

103. Williams TI, Salkovskis PM, Forrester L, et al. A randomised controlled trial of cognitive behavioural treatment for obsessive compulsive disorder in children and adolescents. Eur Child Adolesc Psychiatry. 2010 May;19(5):449-56. doi: 10.1007/s00787-009-0077-9. PMID: 19921305.

104. Bolton D, Williams T, Perrin S, et al. Randomized controlled trial of full and brief cognitive-behaviour therapy and wait-list for paediatric obsessive-compulsive disorder. J Child Psychol Psychiatry. 2011 Dec;52(12):1269-78. doi: 10.1111/j.1469-7610.2011.02419.x. PMID: 21644984.

105. Franklin ME, Sapyta J, Freeman JB, et al. Cognitive behavior therapy augmentation of pharmacotherapy in pediatric obsessive-compulsive disorder: the Pediatric OCD Treatment Study II (POTS II) randomized controlled trial. Jama. 2011 Sep 21;306(11):1224-32. doi: 10.1001/jama.2011.1344. PMID: 21934055.

106. Piacentini J, Bergman RL, Chang S, et al. Controlled comparison of family cognitive behavioral therapy and psychoeducation/relaxation training for child obsessive-compulsive disorder. J Am Acad Child Adolesc Psychiatry. 2011 Nov;50(11):1149-61. doi: 10.1016/j.jaac.2011.08.003. PMID: 22024003.

107. Storch EA, Caporino NE, Morgan JR, et al. Preliminary investigation of web-camera delivered cognitive-behavioral therapy for youth with obsessive-compulsive disorder. Psychiatry Res. 2011 Oct 30;189(3):407-12. doi: 10.1016/j.psychres.2011.05.047. PMID: 21684018.

108. Liu Y. Randomized controlled trial of fluvoxoxamine combining with risperidonein the treatment of children and adolescents with obsessive-compulsive disorder. China Journal of Health Psychology. 2012;20(10):1460-1. PMID: Liu-2012_SR-37347947.

109. Farrell LJ, Waters AM, Boschen MJ, et al. Difficult-to-treat pediatric obsessive-compulsive disorder: feasibility and preliminary results of a randomized pilot trial of D-cycloserine-augmented behavior therapy. Depress Anxiety. 2013 Aug;30(8):723-31. doi: 10.1002/da.22132. PMID: 23722990.

110. Peris TS, Piacentini J. Optimizing treatment for complex cases of childhood obsessive compulsive disorder: a preliminary trial. J Clin Child Adolesc Psychol. 2013;42(1):1-8. doi: 10.1080/15374416.2012.673162. PMID: 22548378.

111. Reynolds SA, Clark S, Smith H, et al. Randomized controlled trial of parent-enhanced CBT compared with individual CBT for obsessive-compulsive disorder in young people. J Consult Clin Psychol. 2013 Dec;81(6):1021-6. doi: 10.1037/a0034429. PMID: 24060194.

112. Rezvan S, Bahrami F, Abedi M, et al. A Preliminary Study on the Effects of Attachment-based Intervention on Pediatric Obsessive-Compulsive Disorder. Int J Prev Med. 2013 Jan;4(1):78-87. PMID: 23413047.

113. Storch EA, Bussing R, Small BJ, et al. Randomized, placebo-controlled trial of cognitive-behavioral therapy alone or combined with sertraline in the treatment of pediatric obsessive-compulsive disorder. Behav Res Ther. 2013 Dec;51(12):823-9. doi: 10.1016/j.brat.2013.09.007. PMID: 24184429.

114. Freeman J, Sapyta J, Garcia A, et al. Family-based treatment of early childhood obsessive-compulsive disorder: the Pediatric Obsessive-Compulsive Disorder Treatment Study for Young Children (POTS Jr)--a randomized clinical trial. JAMA Psychiatry. 2014 Jun;71(6):689-98. doi: 10.1001/jamapsychiatry.2014.170. PMID: 24759852.

115. Grant PJ, Joseph LA, Farmer CA, et al. 12-week, placebo-controlled trial of add-on riluzole in the treatment of childhood-onset obsessive-compulsive disorder. Neuropsychopharmacology. 2014 May;39(6):1453-9. doi: 10.1038/npp.2013.343. PMID: 24356715.

116. Lewin AB, Park JM, Jones AM, et al. Family-based exposure and response prevention therapy for preschool-aged children with obsessive-compulsive disorder: a pilot randomized controlled trial. Behav Res Ther. 2014 May;56:30-8. doi: 10.1016/j.brat.2014.02.001. PMID: 24657310.

117. Ma Y. Sertraline combined with behavioral therapy in the treatment of children obsessive-compulsive disorder. Medical Journal of Chinese People's Health. 2014;26(18):61-2. PMID: Ma-2014_SR-35121274.

118. Mataix-Cols D, Turner C, Monzani B, et al. Cognitive-behavioural therapy with post-session D-cycloserine augmentation for paediatric obsessive-compulsive disorder: pilot randomised controlled trial. Br J Psychiatry. 2014 Jan;204(1):77-8. doi: 10.1192/bjp.bp.113.126284. PMID: 24262813.

119. Turner CM, Mataix-Cols D, Lovell K, et al. Telephone cognitive-behavioral therapy for adolescents with obsessive-compulsive disorder: a randomized controlled non-inferiority trial. J Am Acad Child Adolesc Psychiatry. 2014 Dec;53(12):1298-307.e2. doi: 10.1016/j.jaac.2014.09.012. PMID: 25457928.

120. Zhang L. Efficacy and safety of cognitive behavioral therapy combined with sertraline in treatment of adolescent obsessive - compulsive disorder. J Medical Forum 2014;35(12):83–7. PMID: Zhang-2014_SR-35121274.

121. Salemink E, Wolters L, de Haan E. Augmentation of Treatment As Usual with online Cognitive Bias Modification of Interpretation training in adolescents with Obsessive Compulsive Disorder: A pilot study. J Behav Ther Exp Psychiatry. 2015 Dec;49(Pt A):112-9. doi: 10.1016/j.jbtep.2015.02.003. PMID: 25724385.

122. Skarphedinsson G, Weidle B, Thomsen PH, et al. Continued cognitive-behavior therapy versus sertraline for children and adolescents with obsessive-compulsive disorder that were non-responders to cognitive-behavior therapy: a randomized controlled trial. Eur Child Adolesc Psychiatry. 2015 May;24(5):591-602. doi: 10.1007/s00787-014-0613-0. PMID: 25239489.

123. Storch EA, Wilhelm S, Sprich S, et al. Efficacy of Augmentation of Cognitive Behavior Therapy With Weight-Adjusted d-Cycloserine vs Placebo in Pediatric Obsessive-Compulsive Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2016 Aug 1;73(8):779-88. doi: 10.1001/jamapsychiatry.2016.1128. PMID: 27367832.

124. Wolters LH, de Haan E, Hogendoorn SM, et al. Severe pediatric obsessive compulsive disorder and co-morbid autistic symptoms: effectiveness of cognitive behavioral therapy. Journal of obsessive-compulsive and related disorders. 2016;10:69-77. doi: 10.1016/j.jocrd.2016.06.002. PMID: CN-01166610.

125. Comer JS, Furr JM, Kerns CE, et al. Internet-delivered, family-based treatment for early-onset OCD: A pilot randomized trial. J Consult Clin Psychol. 2017 Feb;85(2):178-86. doi: 10.1037/ccp0000155. PMID: 27869451.

126. Ghanizadeh A, Mohammadi MR, Bahraini S, et al. Efficacy of N-Acetylcysteine Augmentation on Obsessive Compulsive Disorder: A Multicenter Randomized Double Blind Placebo Controlled Clinical Trial. Iran J Psychiatry. 2017 Apr;12(2):134-41. PMID: 28659986.

127. Lenhard F, Andersson E, Mataix-Cols D, et al. Therapist-Guided, Internet-Delivered Cognitive-Behavioral Therapy for Adolescents With Obsessive-Compulsive Disorder: A Randomized Controlled Trial. J Am Acad Child Adolesc Psychiatry. 2017 Jan;56(1):10-9.e2. doi: 10.1016/j.jaac.2016.09.515. PMID: 27993223.

128. Peris TS, Rozenman MS, Sugar CA, et al. Targeted Family Intervention for Complex Cases of Pediatric Obsessive-Compulsive Disorder: A Randomized Controlled Trial. J Am Acad Child Adolesc Psychiatry. 2017 Dec;56(12):1034-42.e1. doi: 10.1016/j.jaac.2017.10.008. PMID: 29173737.

129. Sponsor: AbbVie. A Phase 3 Study of Fluvoxamine (SME3110) in Pediatric/ Adolescent Patients With Obsessive Compulsive Disorder. National Library of Medicine, ClinicalTrials.gov; 2017. https://clinicaltrials.gov/study/NCT01933919.

130. Fatori D, de Braganca Pereira CA, Asbahr FR, et al. Adaptive treatment strategies for children and adolescents with Obsessive-Compulsive Disorder: A sequential multiple assignment randomized trial. J Anxiety Disord. 2018 Aug;58:42-50. doi: 10.1016/j.janxdis.2018.07.002. PMID: 30025255.

131. Rosa-Alcázar Á, Rosa-Alcázar AI, Olivares-Olivares PJ, et al. Family involvement and treatment for young children with Obsessive-Compulsive Disorder: Randomized control study. Int J Clin Health Psychol. 2019 Sep;19(3):218-27. doi: 10.1016/j.ijchp.2019.06.001. PMID: 31516500.

132. Shabani MJ, Mohsenabadi H, Omidi A, et al. An Iranian study of group acceptance and commitment therapy versus group cognitive behavioral therapy for adolescents with obsessive-compulsive disorder on an optimal dose of selective serotonin reuptake inhibitors. Journal of obsessive-compulsive and related disorders. 2019;22. doi: 10.1016/j.jocrd.2019.04.003. PMID: CN-02003764.

133. Li F, Welling MC, Johnson JA, et al. N-Acetylcysteine for Pediatric Obsessive-Compulsive Disorder: A Small Pilot Study. J Child Adolesc Psychopharmacol. 2020 Feb;30(1):32-7. doi: 10.1089/cap.2019.0041. PMID: 31800306.

134. Nasiry S, Ameli Z, Pezeshki P. Online cognitive bias modification of interpretation for children with obsessive-compulsive disorder. Journal of Practice in Clinical Psychology. 2020 Aut 2020;8(4):325-34. doi: 10.32598/jpcp.8.4.739.1. PMID: 2021-41311-008.

135. Shen J. Effect of escitalopram in treatment of adolescent obsessive-compulsive disorder and its influence on behavioral thinking change. J Med Theor & Prac. 2020;30(16):2654–5. PMID: Shen-2020_SR-35121274.

136. Xie K. Efficacy and safety analysis of escitalopram in children and adolescents with obsessive compulsive disorder. J Med Theor & Prac. 2020;33(10):1609–11. PMID: Xie-2020_SR-35121274.

137. Aspvall K, Andersson E, Melin K, et al. Effect of an Internet-Delivered Stepped-Care Program vs In-Person Cognitive Behavioral Therapy on Obsessive-Compulsive Disorder Symptoms in Children and Adolescents: A Randomized Clinical Trial. Jama. 2021 May 11;325(18):1863-73. doi: 10.1001/jama.2021.3839. PMID: 33974020.

138. Selles RR, Naqqash Z, Best JR, et al. Effects of Treatment Setting on Outcomes of Flexibly-Dosed Intensive Cognitive Behavioral Therapy for Pediatric OCD: A Randomized Controlled Pilot Trial. Front Psychiatry. 2021;12:669494. doi: 10.3389/fpsyt.2021.669494. PMID: 34079488.

139. Wolters LH, Hagen A, Beek VOD, et al. Effectiveness of an online interpretation training as a pre-treatment for cognitive behavioral therapy for obsessive-compulsive disorder in youth: a randomized controlled trial. Journal of obsessive-compulsive and related disorders. 2021;29. doi: 10.1016/j.jocrd.2021.100636. PMID: CN-02248290.

140. Farrell LJ, Waters AM, Tiralongo E, et al. Efficacy of D-cycloserine augmented brief intensive cognitive-behavioural therapy for paediatric obsessive-compulsive disorder: A randomised clinical trial. Depress Anxiety. 2022 Jun;39(6):461-73. doi: 10.1002/da.23242. PMID: 35084071.

141. Hollmann K, Hohnecker CS, Haigis A, et al. Internet-based cognitive behavioral therapy in children and adolescents with obsessive-compulsive disorder: A randomized controlled trial. Front Psychiatry. 2022;13:989550. doi: 10.3389/fpsyt.2022.989550. PMID: 36329915.

142. Noras MR, Soltanifar A, Salari R, et al. Comparing the Effects of a Herbal Drug based on Echium Amoenum With Fluvoxamine in the Treatment of Adolescents with Obsessive-compulsive Disorder. Curr Drug Discov Technol. 2022;19(5):e240622206368. doi: 10.2174/1570163819666220624093416. PMID: 35748547.

143. Rempel S, Backhausen LL, McDonald M, et al. App-Based Mindfulness Meditation Training and an Audiobook Intervention Reduce Symptom Severity but Do Not Modify Backward Inhibition in Adolescent Obsessive-Compulsive Disorder: Evidence from an EEG Study. J Clin Med. 2023 Mar 24;12(7). doi: 10.3390/jcm12072486. PMID: 37048570.

144. Agrawal A, Agarwal V, Kumar Kar S, et al. Transcranial direct current stimulation as early augmentation in adolescent obsessive compulsive disorder: A pilot proof-of-concept randomized control trial. World Journal of Clinical Pediatrics,. 2024;13(2). doi: 10.5409/wjcp.v13.i2.93138. PMID: CN-02530420.

145. Himle JA, Grogan-Kaylor A, Hiller MA, et al. Exposure and response prevention versus stress management training for adults and adolescents with obsessive compulsive disorder: A randomized clinical trial. Behav Res Ther. 2024 Jan;172:104458. doi: 10.1016/j.brat.2023.104458. PMID: 38103359.

146. Tuerk PW, McGuire JF, Piacentini J. A Randomized Controlled Trial of OC-Go for Childhood Obsessive–Compulsive Disorder: Augmenting Homework Compliance in Exposure With Response Prevention Treatment. Behavior Therapy. 2023. PMID: 38418042.

147. Leonard HL, Swedo SE, Lenane MC, et al. A double-blind desipramine substitution during long-term clomipramine treatment in children and adolescents with obsessive-compulsive disorder. Arch Gen Psychiatry. 1991 Oct;48(10):922-7. doi: 10.1001/archpsyc.1991.01810340054007. PMID: 1929762.

148. GlaxoSmithKline. A 38-Week, Two Phase, Multicenter Study to Investigate the Safety and Effectiveness of Paroxetine (10-60 mg/day) in the Treatment of Children and Adolescent Outpatients with Obsessive-Compulsive Disorder. GSK - clinical study register [wwwgsk-clinicalstudyregistercom]. 1998. PMID: CN-00763268.

149. GlaxoSmithKline. A Randomized, Multicenter, 10-Week, Double-Blind, Placebo-Controlled, Flexible-Dose Study to Evaluate the Efficacy and Safety of Paroxetine in Children and Adolescents with Obsessive-Compulsive Disorder (OCD) (29060/704). GSK - clinical study register [wwwgsk-clinicalstudyregistercom]. 2001. PMID: CN-00763844.

150. Barrett P, Farrell L, Dadds M, et al. Cognitive-behavioral family treatment of childhood obsessive-compulsive disorder: long-term follow-up and predictors of outcome. J Am Acad Child Adolesc Psychiatry. 2005 Oct;44(10):1005-14. doi: 10.1097/01.chi.0000172555.26349.94. PMID: 16175105.

151. March JS, Franklin ME, Leonard H, et al. Tics moderate treatment outcome with sertraline but not cognitive-behavior therapy in pediatric obsessive-compulsive disorder. Biol Psychiatry. 2007 Feb 1;61(3):344-7. doi: 10.1016/j.biopsych.2006.09.035. PMID: 17241830.

152. Freeman JB, Choate-Summers ML, Garcia AM, et al. The Pediatric Obsessive-Compulsive Disorder Treatment Study II: rationale, design and methods. Child Adolesc Psychiatry Ment Health. 2009 Jan 30;3(1):4. doi: 10.1186/1753-2000-3-4. PMID: 19183470.

153. O'Leary EM, Barrett P, Fjermestad KW. Cognitive-behavioral family treatment for childhood obsessive-compulsive disorder: a 7-year follow-up study. J Anxiety Disord. 2009 Oct;23(7):973-8. doi: 10.1016/j.janxdis.2009.06.009. PMID: 19640677.

154. Garcia AM, Sapyta JJ, Moore PS, et al. Predictors and moderators of treatment outcome in the Pediatric Obsessive Compulsive Treatment Study (POTS I). J Am Acad Child Adolesc Psychiatry. 2010 Oct;49(10):1024-33; quiz 86. doi: 10.1016/j.jaac.2010.06.013. PMID: 20855047.

155. Freeman J, Sapyta J, Garcia A, et al. Still Struggling: characteristics of youth with OCD who are partial responders to medication treatment. Child Psychiatry Hum Dev. 2011 Aug;42(4):424-41. doi: 10.1007/s10578-011-0227-4. PMID: 21484416.

156. Peris TS, Yadegar M, Asarnow JR, et al. Pediatric obsessive compulsive disorder: family climate as a predictor of treatment outcome. Journal of obsessive-compulsive and related disorders. 2012;1(4):267-73. doi: 10.1016/j.jocrd.2012.07.003. PMID: CN-01733862.

157. Conelea CA, Walther MR, Freeman JB, et al. Tic-related obsessive-compulsive disorder (OCD): phenomenology and treatment outcome in the Pediatric OCD Treatment Study II. J Am Acad Child Adolesc Psychiatry. 2014 Dec;53(12):1308-16. doi: 10.1016/j.jaac.2014.09.014. PMID: 25457929.

158. Bussing R, Reid AM, McNamara JP, et al. A pilot study of actigraphy as an objective measure of SSRI activation symptoms: results from a randomized placebo controlled psychopharmacological treatment study. Psychiatry Res. 2015 Feb 28;225(3):440-5. doi: 10.1016/j.psychres.2014.11.070. PMID: 25535011.

159. Gorenstein G, Gorenstein C, de Oliveira MC, et al. Child-focused treatment of pediatric OCD affects parental behavior and family environment. Psychiatry Res. 2015 Sep 30;229(1-2):161-6. doi: 10.1016/j.psychres.2015.07.050. PMID: 26216164.

160. Olatunji BO, Rosenfield D, Monzani B, et al. Effects of homework compliance on cognitive-behavioral therapy with d-cycloserine augmentation for children with obsessive compulsive disorder. Depress Anxiety. 2015 Dec;32(12):935-43. doi: 10.1002/da.22423. PMID: 26372401.

161. Reid AM, McNamara JP, Murphy TK, et al. Side-effects of SSRIs disrupt multimodal treatment for pediatric OCD in a randomized-controlled trial. J Psychiatr Res. 2015 Dec;71:140-7. doi: 10.1016/j.jpsychires.2015.10.006. PMID: 26495770.

162. Skarphedinsson G, Compton S, Thomsen PH, et al. Tics Moderate Sertraline, but Not Cognitive-Behavior Therapy Response in Pediatric Obsessive-Compulsive Disorder Patients Who Do Not Respond to Cognitive-Behavior Therapy. J Child Adolesc Psychopharmacol. 2015 Jun;25(5):432-9. doi: 10.1089/cap.2014.0167. PMID: 26091197.

163. Skriner LC, Freeman J, Garcia A, et al. Characteristics of Young Children with Obsessive-Compulsive Disorder: Baseline Features from the POTS Jr. Sample. Child Psychiatry Hum Dev. 2016 Feb;47(1):83-93. doi: 10.1007/s10578-015-0546-y. PMID: 25820921.

164. Conelea CA, Selles RR, Benito KG, et al. Secondary outcomes from the pediatric obsessive compulsive disorder treatment study II. J Psychiatr Res. 2017 Sep;92:94-100. doi: 10.1016/j.jpsychires.2017.04.001. PMID: 28412602.

165. Lenhard F, Ssegonja R, Andersson E, et al. Cost-effectiveness of therapist-guided internet-delivered cognitive behaviour therapy for paediatric obsessive-compulsive disorder: results from a randomised controlled trial. BMJ Open. 2017 May 17;7(5):e015246. doi: 10.1136/bmjopen-2016-015246. PMID: 28515196.

166. Cancilliere MK, Freeman J, Garcia A, et al. Assessing Acute Secondary Treatment Outcomes in Early-Onset Obsessive-Compulsive Disorder. Child Psychiatry Hum Dev. 2018 Oct;49(5):718-29. doi: 10.1007/s10578-018-0786-8. PMID: 29435695.

167. Wilhelm S, Berman N, Small BJ, et al. D-Cycloserine augmentation of cognitive behavior therapy for pediatric OCD: Predictors and moderators of outcome. J Affect Disord. 2018 Dec 1;241:454-60. doi: 10.1016/j.jad.2018.07.042. PMID: 30149332.

168. Nair A, Turner C, Heyman I, et al. Moderators and predictors of outcomes in telephone delivered compared to face-to-face cognitive behaviour therapy for paediatric obsessive-compulsive disorder: preliminary evidence from a non-inferiority RCT. Cogn Behav Ther. 2019 Sep;48(5):353-68. doi: 10.1080/16506073.2018.1513555. PMID: 30221589.

169. Tie H, Krebs G, Lang K, et al. Cost-effectiveness analysis of telephone cognitive-behaviour therapy for adolescents with obsessive-compulsive disorder. BJPsych Open. 2019 Jan;5(1):e7. doi: 10.1192/bjo.2018.73. PMID: 30762502.

170. Fatori D, Polanczyk GV, de Morais R, et al. Long-term outcome of children and adolescents with obsessive-compulsive disorder: a 7-9-year follow-up of a randomized clinical trial. Eur Child Adolesc Psychiatry. 2020 Nov;29(11):1613-6. doi: 10.1007/s00787-019-01457-8. PMID: 31858264.

171. Peris TS, Rozenman MS, Bai S, et al. Ethnicity moderates outcome in family focused treatment for pediatric obsessive compulsive disorder. J Anxiety Disord. 2020 Jun;73:102229. doi: 10.1016/j.janxdis.2020.102229. PMID: 32361032.

172. Aspvall K, Sampaio F, Lenhard F, et al. Cost-effectiveness of Internet-Delivered vs In-Person Cognitive Behavioral Therapy for Children and Adolescents With Obsessive-Compulsive Disorder. JAMA Netw Open. 2021 Jul 1;4(7):e2118516. doi: 10.1001/jamanetworkopen.2021.18516. PMID: 34328501.

173. Kim SK, McKay D, Murphy TK, et al. Age moderated-anxiety mediation for multimodal treatment outcome among children with obsessive-compulsive disorder: An evaluation with correspondence analysis. J Affect Disord. 2021 Mar 1;282:766-75. doi: 10.1016/j.jad.2020.12.198. PMID: 33601717.

174. Lauri KO, Andersson E, Mataix-Cols D, et al. Long-term effect of stepped-care vs in-person cognitive behavioral therapy for pediatric obsessive-compulsive disorder. Internet Interv. 2023 Apr;32:100613. doi: 10.1016/j.invent.2023.100613. PMID: 37033903.

175. O'Connor EE, Carper MM, Schiavone E, et al. Trajectory of Change in Parental Accommodation and Its Relation to Symptom Severity and Impairment in Pediatric OCD. Child Psychiatry Hum Dev. 2023 Feb;54(1):232-40. doi: 10.1007/s10578-021-01240-4. PMID: 34519945.

176. Becker HC, Beltz AM, Himle JA, et al. Changes in Brain Network Connections After Exposure and Response Prevention Therapy for Obsessive-Compulsive Disorder in Adolescents and Adults. Biol Psychiatry Cogn Neurosci Neuroimaging. 2024 Jan;9(1):70-9. doi: 10.1016/j.bpsc.2023.09.009. PMID: 37820789.

177. Sponsor: Duke University. Treatment of Obsessive Compulsive Disorder in Children. National Library of Medicine, ClinicalTrials.gov; 2014. https://clinicaltrials.gov/study/NCT00074815.

178. Sponsor: University of South Florida. D-Cycloserine Augmentation of Therapy for Pediatric Obsessive-Compulsive Disorder. National Library of Medicine, ClinicalTrials.gov; 2012. https://clinicaltrials.gov/study/NCT00864123.

179. Sponsor: University of South Florida. Videophone Administered Cognitive-Behavioral Therapy for Pediatric Obsessive-Compulsive Disorder. National Library of Medicine, ClinicalTrials.gov; 2015. https://clinicaltrials.gov/study/NCT00881465.

180. Sponsor: University of South Florida. Effectiveness of Sertraline and Cognitive Behavioral Therapy in Treating Pediatric Obsessive-Compulsive Disorder. National Library of Medicine, ClinicalTrials.gov; 2013. https://clinicaltrials.gov/study/NCT00382291.

181. Sponsor: National Institute of Mental Health (NIMH). Riluzole to Treat Child and Adolescent Obsessive-Compulsive Disorder With or Without Autism Spectrum Disorders. 2014. https://clinicaltrials.gov/study/NCT00251303.

182. Sponsor: Massachusetts General Hospital. 2/2 D-Cycloserine Augmentation of CBT for Pediatric OCD. 2017. https://clinicaltrials.gov/study/NCT01404208.

183. Sponsor: University of South Florida. D-cycloserine Augmentation of Cognitive Behavioral Therapy (CBT) for Pediatric Obsessive-compulsive Disorder (OCD). National Library of Medicine, ClinicalTrials.gov; 2018. https://clinicaltrials.gov/study/NCT01411774.

184. Sponsor: Yale University. N-acetylcysteine (NAC) for Pediatric Obsessive-Compulsive Disorder. National Library of Medicine; 2019. https://clinicaltrials.gov/study/NCT01172275.

185. Franklin ME, Engelmann JM, Bulkes NZ, et al. Intensive Cognitive-Behavioral Therapy Telehealth for Pediatric Obsessive-Compulsive Disorder During the COVID-19 Pandemic: Comparison With a Matched Sample Treated in Person. JAACAP Open. 2023. doi: 10.1016/j.jaacop.2023.09.007. PMID: Franklin-2023_adhoc_TEP.

186. Schuberth DA, McMahon RJ, Best JR, et al. Parent Management Training Augmentation to Address Coercive and Disruptive Behavior in Cognitive-Behavioral Therapy for Pediatric Obsessive-Compulsive Disorder. Child Psychiatry Hum Dev. 2023 May 20. doi: 10.1007/s10578-023-01543-8. PMID: 37209194.

187. Scahill L, Riddle MA, McSwiggin-Hardin M, et al. Children's Yale-Brown Obsessive Compulsive Scale: reliability and validity. J Am Acad Child Adolesc Psychiatry. 1997 Jun;36(6):844-52. doi: 10.1097/00004583-199706000-00023. PMID: 9183141.

188. Goodman WK, Price LH, Rasmussen SA, et al. The Yale-Brown Obsessive Compulsive Scale. I. Development, use, and reliability. Arch Gen Psychiatry. 1989 Nov;46(11):1006-11. doi: 10.1001/archpsyc.1989.01810110048007. PMID: 2684084.

189. Goodman WK, Price LH, Rasmussen SA, et al. The Yale-Brown Obsessive Compulsive Scale. II. Validity. Arch Gen Psychiatry. 1989 Nov;46(11):1012-6. doi: 10.1001/archpsyc.1989.01810110054008. PMID: 2510699.

190. Storch EA, McGuire JF, Wu MS, et al. Development and Psychometric Evaluation of the Children's Yale-Brown Obsessive-Compulsive Scale Second Edition. J Am Acad Child Adolesc Psychiatry. 2019 Jan;58(1):92-8. doi: 10.1016/j.jaac.2018.05.029. PMID: 30577944.

191. Lovell K, Cox D, Haddock G, et al. Telephone administered cognitive behaviour therapy for treatment of obsessive compulsive disorder: randomised controlled non-inferiority trial. BMJ. 2006 Oct 28;333(7574):883. doi: 10.1136/bmj.38940.355602.80. PMID: 16935946.

192. Salanti G, Nikolakopoulou A, Efthimiou O, et al. Introducing the Treatment Hierarchy Question in Network Meta-Analysis. Am J Epidemiol. 2022 Mar 24;191(5):930-8. doi: 10.1093/aje/kwab278. PMID: 35146500.

193. Lewin AB, Piacentini J, De Nadai AS, et al. Defining clinical severity in pediatric obsessive-compulsive disorder. Psychol Assess. 2014 Jun;26(2):679-84. doi: 10.1037/a0035174. PMID: 24320764.

194. Calvocoressi L, Mazure CM, Kasl SV, et al. Family accommodation of obsessive-compulsive symptoms: instrument development and assessment of family behavior. J Nerv Ment Dis. 1999 Oct;187(10):636-42. doi: 10.1097/00005053-199910000-00008. PMID: 10535658.

195. Skarphedinsson G, Torp NC, Weidle B, et al. Family Accommodation in Pediatric Obsessive-Compulsive Disorder: Investigating Prevalence and Clinical Correlates in the NordLOTS Study. Child Psychiatry Hum Dev. 2023 Sep 8. doi: 10.1007/s10578-023-01602-0. PMID: 37684419.

196. Lebowitz ER. Treatment of extreme family accommodation in a youth with obsessive-compulsive disorder. Clinical handbook of obsessive-compulsive and related disorders: A case-based approach to treating pediatric and adult populations. 2016:321-35.

197. Hermida-Barros L, Prime-Tous M, Garcia-Delgar B, et al. Family accommodation in obsessive-compulsive disorder: An updated systematic review and meta-analysis. Neurosci Biobehav Rev. 2024 Apr 14;161:105678. doi: 10.1016/j.neubiorev.2024.105678. PMID: 38621516.

198. Freeman J, Garcia A, Frank H, et al. Evidence base update for psychosocial treatments for pediatric obsessive-compulsive disorder. J Clin Child Adolesc Psychol. 2014;43(1):7-26. doi: 10.1080/15374416.2013.804386. PMID: 23746138.

199. Wolters LH, Ball J, Brezinka V, et al. Brief intensive cognitive behavioral therapy for children and adolescents with OCD: Two international pilot studies. Journal of Obsessive-Compulsive and Related Disorders. 2021;29:1-7. doi: 10.1016/j.jocrd.2021.100645. PMID: 2022-96874-001.

200. Torp NC, Dahl K, Skarphedinsson G, et al. Effectiveness of cognitive behavior treatment for pediatric obsessive-compulsive disorder: acute outcomes from the Nordic Long-term OCD Treatment Study (NordLOTS). Behav Res Ther. 2015 Jan;64:15-23. doi: 10.1016/j.brat.2014.11.005. PMID: 25463245.

201. Torp NC, Weidle B, Thomsen PH, et al. Is it time to rethink standard dosage of exposure-based cognitive behavioral therapy for pediatric obsessive-compulsive disorder? Psychiatry Res. 2019 Nov;281:112600. doi: 10.1016/j.psychres.2019.112600. PMID: 31622874.

202. Garcia AM, Case B, Freeman JB, et al. Predictors of Treatment Outcome and Length of Stay in a Partial Hospital Program for Pediatric Obsessive-Compulsive Disorder. Evidence-Based Practice in Child and Adolescent Mental Health. 2023:1-14. PMID: Garcia-2023_adhoc.

203. Storch EA, Merlo LJ, Larson MJ, et al. Symptom dimensions and cognitive-behavioural therapy outcome for pediatric obsessive-compulsive disorder. Acta Psychiatr Scand. 2008 Jan;117(1):67-75. doi: 10.1111/j.1600-0447.2007.01113.x. PMID: 17986317.

204. Nakatani E, Krebs G, Micali N, et al. Children with very early onset obsessive-compulsive disorder: clinical features and treatment outcome. J Child Psychol Psychiatry. 2011 Dec;52(12):1261-8. doi: 10.1111/j.1469-7610.2011.02434.x. PMID: 21726224.

205. McGuire JF, Small BJ, Lewin AB, et al. Dysregulation in pediatric obsessive compulsive disorder. Psychiatry Res. 2013 Oct 30;209(3):589-95. doi: 10.1016/j.psychres.2013.04.003. PMID: 23623154.

206. Rudy BM, Lewin AB, Geffken GR, et al. Predictors of treatment response to intensive cognitive-behavioral therapy for pediatric obsessive-compulsive disorder. Psychiatry Res. 2014 Dec 15;220(1-2):433-40. doi: 10.1016/j.psychres.2014.08.002. PMID: 25193378.

207. Brown HM, Lester KJ, Jassi A, et al. Paediatric Obsessive-Compulsive Disorder and Depressive Symptoms: Clinical Correlates and CBT Treatment Outcomes. J Abnorm Child Psychol. 2015 Jul;43(5):933-42. doi: 10.1007/s10802-014-9943-0. PMID: 25301176.

208. Weidle B, Ivarsson T, Thomsen PH, et al. Quality of life in children with OCD before and after treatment. Eur Child Adolesc Psychiatry. 2015 Sep;24(9):1061-74. doi: 10.1007/s00787-014-0659-z. PMID: 25527002.

209. Torp NC, Dahl K, Skarphedinsson G, et al. Predictors associated with improved cognitive-behavioral therapy outcome in pediatric obsessive-compulsive disorder. J Am Acad Child Adolesc Psychiatry. 2015 Mar;54(3):200-7.e1. doi: 10.1016/j.jaac.2014.12.007. PMID: 25721185.

210. Hybel KA, Mortensen EL, Lambek R, et al. Executive function predicts cognitive-behavioral therapy response in childhood obsessive-compulsive disorder. Behav Res Ther. 2017 Dec;99:11-8. doi: 10.1016/j.brat.2017.08.009. PMID: 28881220.

211. Selles RR, Belschner L, Negreiros J, et al. Group family-based cognitive behavioral therapy for pediatric obsessive compulsive disorder: Global outcomes and predictors of improvement. Psychiatry Res. 2018 Feb;260:116-22. doi: 10.1016/j.psychres.2017.11.041. PMID: 29179016.

212. Højgaard D, Skarphedinsson G, Ivarsson T, et al. Hoarding in children and adolescents with obsessive-compulsive disorder: prevalence, clinical correlates, and cognitive behavioral therapy outcome. Eur Child Adolesc Psychiatry. 2019 Aug;28(8):1097-106. doi: 10.1007/s00787-019-01276-x. PMID: 30656432.

213. Riise EN, Kvale G, Öst LG, et al. Does Family Accommodation Predict Outcome of Concentrated Exposure and Response Prevention for Adolescents? Child Psychiatry Hum Dev. 2019 Dec;50(6):975-86. doi: 10.1007/s10578-019-00898-1. PMID: 31134420.

214. Højgaard D, Schneider SC, La Buissonnière-Ariza V, et al. Predictors of treatment outcome for youth receiving intensive residential treatment for obsessive-compulsive disorder (OCD). Cogn Behav Ther. 2020 Jul;49(4):294-306. doi: 10.1080/16506073.2019.1614977. PMID: 31203735.

215. Selles RR, Højgaard D, Ivarsson T, et al. Avoidance, Insight, Impairment Recognition Concordance, and Cognitive-Behavioral Therapy Outcomes in Pediatric Obsessive-Compulsive Disorder. J Am Acad Child Adolesc Psychiatry. 2020 May;59(5):650-9.e2. doi: 10.1016/j.jaac.2019.05.030. PMID: 31228561.

216. Duholm CS, Højgaard D, Skarphedinsson G, et al. Health anxiety symptoms in pediatric obsessive-compulsive disorder: patient characteristics and effect on treatment outcome. Eur Child Adolesc Psychiatry. 2022 Aug;31(8):1317-28. doi: 10.1007/s00787-021-01774-x. PMID: 33861384.

217. Jassi AD, Vidal-Ribas P, Krebs G, et al. Examining clinical correlates, treatment outcomes and mediators in young people with comorbid obsessive-compulsive disorder and autism spectrum disorder. Eur Child Adolesc Psychiatry. 2023 Jul;32(7):1201-10. doi: 10.1007/s00787-021-01921-4. PMID: 34914003.

218. Farrell LJ, Lavell C, Baras E, et al. Clinical expression and treatment response among children with comorbid obsessive compulsive disorder and attention-deficit/hyperactivity disorder. J Affect Disord. 2020 Apr 1;266:585-94. doi: 10.1016/j.jad.2020.01.144. PMID: 32056931.

219. Usher-Smith JA, Sharp SJ, Griffin SJ. The spectrum effect in tests for risk prediction, screening, and diagnosis. BMJ. 2016 Jun 22;353:i3139. doi: 10.1136/bmj.i3139. PMID: 27334281.

220. Schwarzer G, Carpenter, J.R., Rücker, G.,. Small Sample Effects in Meta-Analysis. Meta-Analysis with R. Springer; 2015:107-41.

221. Strawn JR, Mills JA, Poweleit EA, et al. Adverse Effects of Antidepressant Medications and their Management in Children and Adolescents. Pharmacotherapy. 2023 Jul;43(7):675-90. doi: 10.1002/phar.2767. PMID: 36651686.

222. Farrell LJ, Waters AM, Storch EA, et al. Closing the Gap for Children with OCD: A Staged-Care Model of Cognitive Behavioural Therapy with Exposure and Response Prevention. Clin Child Fam Psychol Rev. 2023 Sep;26(3):642-64. doi: 10.1007/s10567-023-00439-2. PMID: 37405675.

223. Drake RE. Overmedicating vulnerable children in the U.S. Epidemiol Psychiatr Sci. 2019 Aug;28(4):358-9. doi: 10.1017/S2045796018000689. PMID: 30474575.

224. Williams MT, Domanico J, Marques L, et al. Barriers to treatment among African Americans with obsessive-compulsive disorder. J Anxiety Disord. 2012 May;26(4):555-63. doi: 10.1016/j.janxdis.2012.02.009. PMID: 22410094.

225. Williams MT, Rouleau TM, La Torre JT, et al. Cultural competency in the treatment of obsessive-compulsive disorder: practitioner guidelines. The Cognitive Behaviour Therapist. 2020;13:e48.

226. Whiteside SP, Deacon BJ, Benito K, et al. Factors associated with practitioners' use of exposure therapy for childhood anxiety disorders. J Anxiety Disord. 2016 May;40:29-36. doi: 10.1016/j.janxdis.2016.04.001. PMID: 27085463.

227. Schneider SC, Knott L, Cepeda SL, et al. Serious negative consequences associated with exposure and response prevention for obsessive-compulsive disorder: A survey of therapist attitudes and experiences. Depress Anxiety. 2020 May;37(5):418-28. doi: 10.1002/da.23000. PMID: 32048376.

228. Thurston IB, Alegria M, Hood KB, et al. How psychologists can help achieve equity in health care-advancing innovative partnerships and models of care delivery: Introduction to the special issue. Am Psychol. 2023 Feb-Mar;78(2):73-81. doi: 10.1037/amp0001153. PMID: 37011160.

229. Takwoingi Y, Leeflang MM, Deeks JJ. Empirical evidence of the importance of comparative studies of diagnostic test accuracy. Ann Intern Med. 2013 Apr 2;158(7):544-54. doi: 10.7326/0003-4819-158-7-201304020-00006. PMID: 23546566.

230. Kranzler HR, Kadden RM, Babor TF, et al. Longitudinal, expert, all data procedure for psychiatric diagnosis in patients with psychoactive substance use disorders. J Nerv Ment Dis. 1994 May;182(5):277-83. doi: 10.1097/00005053-199405000-00005. PMID: 10678309.

231. Mills JA, Strawn JR. Antidepressant Tolerability in Pediatric Anxiety and Obsessive-Compulsive Disorders: A Bayesian Hierarchical Modeling Meta-analysis. J Am Acad Child Adolesc Psychiatry. 2020 Nov;59(11):1240-51. doi: 10.1016/j.jaac.2019.10.013. PMID: 31682918.

232. Nikolakopoulou A, Chaimani A, Furukawa TA, et al. When does the placebo effect have an impact on network meta-analysis results? BMJ Evid Based Med. 2024 Mar 21;29(2):127-34. doi: 10.1136/bmjebm-2022-112197. PMID: 37385716.

233. Kemp J, Barker D, Benito K, et al. Moderators of Psychosocial Treatment for Pediatric Obsessive-Compulsive Disorder: Summary and Recommendations for Future Directions. J Clin Child Adolesc Psychol. 2021 Jul-Aug;50(4):478-85. doi: 10.1080/15374416.2020.1790378. PMID: 32706265.

234. Buchanan NT, Perez M, Prinstein MJ, et al. Upending racism in psychological science: Strategies to change how science is conducted, reported, reviewed, and disseminated. Am Psychol. 2021 Oct;76(7):1097-112. doi: 10.1037/amp0000905. PMID: 34990171.

235. Pretzmann L, Christensen SH, Bryde Christensen A, et al. Adverse events in cognitive behavioral therapy and relaxation training for children and adolescents with obsessive-compulsive disorder: A mixed methods study and analysis plan for the TECTO trial. Contemp Clin Trials Commun. 2023 Aug;34:101173. doi: 10.1016/j.conctc.2023.101173. PMID: 37497354.

236. Westwell-Roper C, Best JR, Elbe D, et al. Celecoxib versus placebo as an adjunct to treatment-as-usual in children and youth with obsessive-compulsive disorder: protocol for a single-site randomised quadruple-blind phase II study. BMJ Open. 2022 Jan 31;12(1):e054296. doi: 10.1136/bmjopen-2021-054296. PMID: 35105633.

3.3.3 Results, Key Question 1: Brief Assessment Tools, Evidence Profile for Key Question 1

Abbreviations and Acronyms

AACAP	American Academy of Child and Adolescent Psychiatry
ACT	Acceptance and commitment therapy
ADIS-C	Anxiety Disorders Interview Scale-Child Version
AHRQ	Agency for Healthcare Research and Quality
ANOVA	analysis of variance
ASD	Autism spectrum disorder
AUC ROC	Area Under the receiver operating characteristics curve
briefERP	Brief duration exposure and response therapy
CBCL-OCS	Child Behavior Checklist-Obsessive Compulsive subscale
CBT	Cognitive Behavioral Therapy
CD-POC	Coercive Disruptive Behavior Scale
CFB	Change from baseline
C-FOCI	Children's Florida Obsessive Compulsive Inventory
CGI-S	Clinical Global Impressions-Severity Severity
CHOCI	Obsessional Compulsive Inventory-Child
CMB-I	Cognitive bias modification-interpretation
COIS, COIS-R	Child Obsessive Compulsive Impact Scale-Revised
CY-BOCS	Children’s Yale-Brown Obsessive Compulsive Scale
CI	confidence interval
CINAHL	Cumulative Index to Nursing and Allied Health Literature
Cohen’s d	a standardized effect size
COI	conflicts of interest
COIS	Child Obsessive Compulsive Impact Scale
DABWA	The Development and Well-Being Assessment
DISC-2.1	Sensitivity of the Diagnostic Interview Schedule for Children, 2nd edition
DSM	Diagnostic and Statistical Manual of Mental Disorders
DCS	D-cycloserine
EPC	Evidence-based Practice Center
ERP	Cognitive behavioral therapy with exposure and response prevention
FAS	Family Accommodation Scale
FI	Family Intervention
GRADE	Grading of Recommendations, Assessment, Development, and Evaluations
I^2	Percent of total variability that is due to between-study variability
intensiveERP	Intensive delivery of exposure and response prevention
IPTW	Inverse probability of treatment weighting

K-SADS-PL	Kiddie Schedule for Affective Disorders and Schizophrenia, Present and Lifetime version
KI	Key Informant
KQ	Key Question
LEAD	Longitudinal Expert All Data
LOI-CV	Leyton Obsessional Inventory – Child Version
MD	mean difference
MINI-KID	Mini International Neuropsychiatric Interview for Children and Adolescents
N, n	number of (studies, participants)
MA	meta-analysis
N/A	not applicable
NMA	network meta-analysis
NMD	Net Mean Difference
NordLOTS	Nordic long-term OCD treatment study
NR	not reported
NRCS	nonrandomized comparative study
NS	not significant, defined as $P < 0.05$
OCI-CV	Obsessive Compulsive Inventory – Child Version
OCD	Obsessive-Compulsive Disorder
OFF	OCD Family Functioning Scale
OR	odds ratio
aOR	adjusted odds ratio
PANDAS	Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal infections
PANS	Pediatric Acute-onset Neuropsychiatric Syndrome
PCORI	Patient-Centered Outcomes Research Institute
PFIT	Positive Family Interaction Therapy
PMT	Parent Management Training
PQ-LES-Q	Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire
PROSPERO	International Prospective register of systematic reviews
pwMA	pairwise meta-analysis
QoL	Quality of Life
QUADAS-2	Quality Assessment of Diagnostic Accuracy Studies 2
RCT	randomized controlled trial
RD	risk difference
REML	restricted maximum likelihood
RoB	risk of bias
ROBINS-I	Risk of Bias in Nonrandomized Studies of Interventions

RR	relative risk
aRR	adjusted relative risk
remoteERP	Remotely delivered ERP
rTMS	repetitive transcranial magnetic stimulation
SD	sample standard deviation
SoE	strength of evidence
SCAS-OCD	Spence Children's Anxiety Scale – OCD subscale
SOCS	Short Obsessive-Compulsive Disorder Screener
SPE	Strength of evidence for association
SR	systematic review
SROC	Summary receiver operating characteristics
SRDR+	Systematic Review Data Repository Plus
SSRI	Selective Serotonin Reuptake Inhibitor
TAU	Treatment As Usual
TCA	Tricyclic antidepressant
TEP	Technical Expert Panel
TOCS	Toronto Obsessive–Compulsive Scale
TOO	Task Order Officer
U.S.	United States
U.K.	United Kingdom
vs	versus
Y-BOCS	Yale-Brown Obsessive Compulsive Scale
CY-BOCS-SR	Children’s Yale-Brown Obsessive Compulsive Scale -Self Report
YSR OCD	Youth Self-Report OCD subscale

Contents

Tables

Appendix A. Methods

Details of Study Selection

Search Strategy (Details)

We searched for studies and existing systematic reviews in MEDLINE (via PubMed), the Cochrane Register of Clinical Trials, the Cochrane Database of Systematic Reviews, Embase, CINAHL and PsycINFO and Education Resources Information Center (ERIC) databases on July 6, 2023, with an update search on May 15, 2024. We searched using index terms, along with free-text words, for concepts related to OCD and pediatric and adolescent populations. Duplicate citations were removed prior to screening. We did not apply language, date, or country restrictions. Search strategies included filters to remove nonhuman studies and articles that are not primary studies or systematic reviews. The full search strategies for all databases are detailed below.

Additional searches were conducted on September 1, 2023 in the ClinicalTrials.gov registry for ongoing and unpublished studies with study results. The reference lists of relevant existing systematic reviews were screened for additional eligible studies. A Supplemental Evidence And Data for Systematic review (SEADS) portal and Federal Register Notice was e available for this review. Additional articles suggested to us from any source, including through the SEADS portal, were screened with the same eligibility criteria as the studies identified in the database searches.

Per our EPC's standard processes, we took advantage of the machine learning capacities of Abstrackr (http://abstrackr.cebm.brown.edu/) to limit resources spent on abstract screening. We trained the machine learning algorithm as follows: (1) We reviewed the reference lists from known existing systematic reviews and clinical practice guidelines to identify potentially relevant studies for each KQ. (2) We confirmed this set of potentially relevant citations was successfully captured by our database searched. (3) Based on recently published work by Sampson et. al.,[1] we selected the top 500 articles from our search using PubMed's best-match algorithm. (4) The articles from steps (1) and (3) were entered into Abstrackr and screened by all team members, with resolution of all conflicts in conference. (5) Subsequently, citations found by the full literature searches were added to the already-screened citations in Abstrackr, and abstract screening continued in duplicate, with conflicts adjudicated in conference or by a third screener. (6) We stopped double screening when the predicted likelihood of the remaining unscreened papers was below 0.40 (this threshold is based on experience with several dozen screening projects and an analysis in preparation for publication) and we had rejected at least 400 consecutive citations.

Potentially relevant citations were retrieved in full text. Non-English language articles were screened, and data extracted from full text, either by readers of the relevant languages or after translation via Google Translate (https://translate.google.com/), if possible. The search strategies for all databases were peer reviewed by another experienced systematic review librarian. Searches will be updated during the draft report's public posting period.

PubMed Search

(("Obsessive-Compulsive Disorder"[Mesh] OR (Obsessive Compulsive AND (Disorder* OR Neuros*)) OR Anankastic Personalit*[tiab] OR "OCD"[tiab]) AND ("child"[Mesh] OR "adolescent"[Mesh] OR toddler*[tiab] OR nursery[tiab] OR preschool[tiab] OR pre-school[tiab] OR child*[tiab] OR childhood[tiab] OR children[tiab] OR girl[tiab] OR girls[tiab] OR boy[tiab] OR boys[tiab] OR pediatri*[tiab] OR paediatri*[tiab] OR adolesc*[tiab] OR pubescen*[tiab] OR school-age*[tiab] OR student*[tiab] OR preteen*[tiab] OR pre-teen*[tiab] OR teen*[tiab] OR juvenile[tiab] OR juveniles[tiab] OR young* adult*[tiab] OR youth[tiab] OR youths[tiab] OR minors[tiab] OR college[tiab] OR university[tiab] OR student[tiab]) AND ("Cohort Studies"[Mesh] OR cohort OR "Clinical Trial"[Publication Type] OR follow-up OR followup OR "different models" OR longitudinal OR "Placebos"[Mesh] OR placebo* OR "Research Design"[Mesh] OR "Evaluation Study" [Publication Type] OR "Comparative Study"[Publication Type] OR ((comparative OR Intervention) AND study) OR pretest* OR posttest* OR prepost* OR "before and after" OR interrupted time* OR time serie* OR intervention* OR ((quasi-experiment* OR quasiexperiment* OR quasi OR experimental) AND (method OR study OR trial OR design*)) OR "real world" OR "real-world" OR "Case-Control Studies"[Mesh] OR case control OR "Random Allocation"[Mesh] OR "Clinical Trial"[Publication Type] OR "Double-Blind Method"[Mesh] OR "Single-Blind Method"[Mesh] OR random* OR "Placebos"[Mesh] OR placebo OR ((clinical OR controlled) AND trial*) OR ((singl* OR doubl* OR trebl* OR tripl*) AND (blind* OR mask*)) OR crossover OR cross-over OR cross-over OR "treatment switching" OR "Treatment Switching"[Mesh] OR RCT OR "Randomized Controlled Trial"[Publication Type] OR systematic[sb] OR reliability OR validity OR sensitivity OR specificity OR area under the curve OR AUC)) NOT ("addresses" OR "autobiography"[pt] OR "bibliography"[pt] OR "biography"[pt] OR "case reports" OR "comment"[pt] OR "congresses" OR "dictionary"[pt] OR "directory"[pt] OR "festschrift"[pt] OR "government publications" OR "historical article"[pt] OR "interview"[pt] OR "lectures" OR "legal cases" OR "legislation"[pt] OR "news"[pt] OR "newspaper article"[pt] OR "patient education handout"[pt] OR "periodical index"[pt] OR "comment on" OR ("Animals"[Mesh] NOT "Humans"[Mesh]) OR rats[tw] OR cow[tw] OR cows[tw] OR chicken*[tw] OR horse[tw] OR horses[tw] OR mice[tw] OR mouse[tw] OR bovine[tw] OR sheep OR ovine OR murinae OR "animal model")

Embase Search

No. Query

#15 #13 NOT #14

#14 #10 AND #11 AND ([article]/lim OR [article in press]/lim OR [erratum]/lim OR [letter]/lim) AND [medline]/lim

#13 #10 AND #11 AND ([article]/lim OR [article in press]/lim OR [erratum]/lim OR [letter]/lim)

#11 'cohort studies'/exp OR longitudinal OR ((comparative OR intervention) AND study) OR prepost* OR 'before and after' OR 'interrupted time*' OR 'time serie*' OR intervention* OR (('quasi experiment*' OR quasiexperiment* OR quasi OR experimental) AND (method OR study OR trial OR design*)) OR 'real world' OR 'random allocation'/exp OR 'double-blind method'/exp OR 'single-blind method'/exp OR random* OR ((clinical OR controlled) AND trial*)

#10 #3 AND #9

#9 #4 OR #5 OR #6 OR #7 OR #8

#8 toddler* OR nursery OR preschool OR 'pre school' OR child* OR childhood OR children OR girl OR girls OR boy OR boys OR pediatri* OR paediatri* OR adolesc* OR pubescen* OR 'school age*' OR student* OR preteen* OR 'pre teen*' OR teen* OR juvenile OR juveniles OR youth OR youths OR minors OR college OR university OR student
#7 'adolescent'/exp OR 'adolescent'
#6 'young adult'/exp OR 'young adult'
#5 'juvenile'/exp OR 'juvenile'
#4 'child'/exp OR 'child'
#3 #1 OR #2
#2 'ocd'
#1 'obsessive compulsive disorder'/exp OR 'obsessive compulsive disorder'

Cochrane Search

ID	Search	Hits
#1	MeSH descriptor: [Obsessive-Compulsive Disorder] explode all trees	1291
#2	Obsessive Compulsive or Obsessive-Compulsive	3773
#3	Disorder* OR Neuros*	225566
#4	#2 AND #3	3599
#5	"OCD"	1973
#6	#1 OR #4 OR #5	3910
#7	MeSH descriptor: [Child] explode all trees	77901
#8	MeSH descriptor: [Adolescent] explode all trees	125416
#9	toddler* OR nursery OR preschool OR pre-school OR child* OR childhood OR childrenOR girl OR girls OR boy OR boys OR pediatri* OR paediatri* OR adolesc* OR pubescen* OR school-age* OR student* OR preteen* OR pre-teen* OR teen* OR juvenile OR juveniles OR young* adult* OR youth OR youths OR minors OR college OR university OR student	812843
#10	#7 OR #8 OR #9	812843
#11	#6 AND #10	2228

CINAHL Search

(obsessive compulsive disorder or obsessive-compulsive disorder or ocd)
AND
Limits
Source Types
- Academic Journals

Age
- young adulthood (18-29 yr...
- adolescence (13-17 yrs)
- childhood (birth-12 yrs)
- school age (6-12 yrs)
- adolescent: 13-18 years
- child: 6-12 years
- preschool age (2-5 yrs)
- child, preschool: 2-5 yea...

Methodology
- empirical study
- quantitative study
- longitudinal study
- followup study
- clinical trial
- treatment outcome
- prospective study
- retrospective study
- meta analysis
- systematic review

ClinicalTrials.gov Search

Condition
Obsessive Compulsive Disorder OR OCD OR Anankastic Personality

Other terms
Pediatric OR child OR children OR adolescent OR teen OR college OR university OR kid

Inclusion and Exclusion Criteria (Details)

The specific eligibility criteria provided below (Table A-1) have been refined based on discussions with a panel of Key Informants (KIs) and a Technical Expert Panel (TEP). These stakeholders included perspectives from clinicians and researchers in child and adolescent psychiatry, child psychology, research funding, patient, and family advocacy.

Table A-1 Inclusion and exclusion criteria

PICOTS Element	Key Question 1 (Diagnosis of OCD)	Key Question 2 (Treatment of OCD)
Population	Children and adolescents (<21 years) • in whom there is clinical consideration of OCD • diagnosed with OCD and/or other conditions which may be either be comorbid with OCD or may present with similar symptoms *Include*: • Studies evaluating only children and adolescents with OCD (to estimate test sensitivity alone) *Exclude*: • Studies that include both adults and children that do not explicitly report a pediatric or adolescent subgroup in the abstract • Studies that perform population-based screening (among individuals without a clinical concern for OCD)	Children and adolescents (<21 years) with diagnosed OCD, including those with: • possible PANS/PANDAS (with OCD) • other comorbid conditions (e.g., autism) *Exclude:* • Children and adolescents diagnosed with other OCD-spectrum conditions (e.g., body dysmorphic disorder, body focused repetitive behaviors) without an OCD diagnosis • Subclinical OCD or obsessive or compulsive symptoms without an OCD diagnosis • Studies that include both adults and children that do not explicitly report a subgroup by age in the abstract

PICOTS Element	Key Question 1 (Diagnosis of OCD)	Key Question 2 (Treatment of OCD)
Interventions	Index Test(s) • Tools to diagnose OCD in symptomatic patients. For example, ○ Obsessive Compulsive Inventory-Child Version (OCI-CV-R) ○ Toronto Obsessive-Compulsive Scale (TOCS) ○ Short Obsessive-Compulsive Screener (SOCS) • Diagnostic prediction models • Must report use of specific cut-point(s) to classify an individual as having OCD or a prediction algorithm or model to predict the probability of OCD • Alternative administration (e.g., child versus parent versus teacher report, in-person versus telehealth) *Exclude*: • Specific individual symptoms, behaviors, or characteristics • Genetic studies • Biomarker studies	Psychological interventions for OCD, alone or in combination with pharmacological and/or other interventions, including: • Cognitive behavioral therapy (CBT) ○ Exposure and response prevention (ERP) ○ Psychoeducation ○ Coping skills ○ Cognitive therapy • Acceptance and commitment therapy (ACT) • Targeted family interventions • Other psychological interventions • Delivery method ○ Therapist led, e.g., scheduled, in-person, or via telephone, video conference ○ Self-guided, e.g., asynchronous, therapist serves as supportive coach Pharmacological interventions, alone or in combination with psychological interventions • Selective serotonin reuptake inhibitors (SSRIs) • Tricyclic antidepressants (TCA), including clomipramine • Serotonin and norepinephrine reuptake inhibitors (SNRIs) • Medication augmentation strategies ○ SSRI augmentation with clomipramine, and other medications, including neuroleptics, nonsteroidal anti-inflammatory drugs (NSAIDs) ○ Glutamate modulating agents (e.g., D—cycloserine, riluzole) • Other pharmacologic interventions, alone or in combination with psychological and/or other interventions, including dose escalation, longer treatment duration Neuromodulation interventions: • Transcranial magnetic stimulation (TMS), • Transcranial direct current stimulation (tDCS), • Transcranial alternating current stimulation (tACS), • Deep brain stimulation (DBS) Complementary/integrative therapies: • Naturopathic interventions • Mind-body practices (e.g., mindfulness, meditation, yoga) • Sensory integration (e.g., deep pressure) *Exclude*: • Specific treatments for PANS/PANDAS (e.g., antibiotics, immunomodulation, intravenous immunoglobulin)

PICOTS Element	Key Question 1 (Diagnosis of OCD)	Key Question 2 (Treatment of OCD)
Comparators	Reference standard(s) • Clinical interview • Validated diagnostic assessment instruments (others may be included) ○ Anxiety Disorders Interview Schedule for DSM-5 child version ○ (ADIS-C) ○ Kiddie Schedule for Affective Disorders and Schizophrenia, Present and Lifetime version (K-SADS-PL) for DSM-5 ○ Mini-International Neuropsychiatric Interview for Children and Adolescents (MINI-KID) ○ Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS) ○ Children's Yale-Brown Obsessive-Compulsive Scale Second Edition (CY-BOCS-II) • Different index tests (if also compared with reference standard) • Different reference standards (i.e., comparison of reference standards) • Different respondents (e.g., clinician, self, parent, educator) • Different methods to give test (e.g., in person vs. via tele-health) • Different populations (see effect modifiers below)	• No treatment (e.g., waitlist control) • Pill placebo or sham control • Another active intervention or co-intervention (e.g., relaxation therapy) • Alternative delivery methods

PICOTS Element	Key Question 1 (Diagnosis of OCD)	Key Question 2 (Treatment of OCD)
Outcomes (prioritized outcomes have an asterisk and are in bold font)	OCD diagnosis • **Sensitivity/Specificity*** • Positive and negative likelihood ratios • Accuracy • Area under the Receiver Operator Characteristic Curve (AUC ROC) • Predicted probability of OCD (model calibration/discrimination) • Time to initiation of treatment (cohort studies) *Exclude:* • Studies not reporting predictive validity that report other psychometric properties of scales: for example, reliability or validity (content, construct, convergent, discriminant, divergent, face)	OCD symptom severity • **Children's Yale-Brown Obsessive Compulsive Scale Total (CY-BOCS)*** • **Clinical Global Impression–Severity (CGI–S)*** Treatment response and remission • **Clinical remission (posttreatment CY-BOCS total score ≤ 12 as defined by Farhat et. al.[2], or as reported)*** • **Clinical Global Impression–Improvement (CGI–I)*** Functional impairment in school, social, and home/family domains • **The Child Obsessive Compulsive Impact Scale— Revised (COIS-R)*** ○ Raters: child (COIS-C), parent (COIS-P) Family accommodation • **Family Accommodation Scale (FAS)*** Family functioning • OCD Family Functioning Scale • Family Environment Scale (FES) • Parental Attitudes and Behaviors Scale (PABS) Patient/parent reported experience measures (PREMs) Patient reported outcome measure (PROMs) • Top Problems assessment (TPA) **Quality of Life (QoL) General and Health Related (HRQoL) (validated scales only)*** • Quality of Life Enjoyment and Satisfaction Questionnaire-Short Form (QLESQ) **Acceptability of treatment*** • Parental satisfaction with services • Withdrawals/discontinuation Sleep-related problems Suicidal thoughts and behavior • Columbia Suicide Severity Rating Scale Recent Self-Report Screener (C-SSRS) Anxiety and depression **Adverse events related to treatment*** *Exclude:* • Neuroimaging (e.g., functional MRI)

PICOTS Element	Key Question 1 (Diagnosis of OCD)	Key Question 2 (Treatment of OCD)
Potential Effect Modifiers/Subgroups of interest	• Patient, family, social, and other characteristics, including: ○ Race/Ethnicity (racial and ethnic discrimination is the effect modifier of interest but many/most studies will not contain that so we will use race/ethnicity as a marker for likelihood of experience with discrimination and would explicitly discuss this in the review) ○ Identity and Culture (e.g., spiritual and religious beliefs and practices, native language, gender identity, sexual orientation, physical/mental disability status) ○ Age ○ Age at symptom onset ○ Social determinants of health, including education level, socioeconomic status, immigration status, refugee status, and geography (e.g., urban vs. rural) ○ Diagnosis of PANS/PANDAS ○ OCD in first degree relatives ○ Level of family accommodation ○ Co-occurring disorders (e.g., major depressive disorder, anxiety disorders, attention-deficit hyperactivity disorder, conduct disorders, autism spectrum disorder, and Tourette syndrome, other tic disorders) ○ Diagnosis during COVID-19 pandemic (as defined by study authors) ○ Primary versus specialist care • Respondent type *<u>Exclude</u>:* • Neuroimaging, e.g., functional MRI	• Patient, family, social, and other characteristics, including: ○ Race/Ethnicity (racial and ethnic discrimination is the effect modifier of interest but many/most studies will not contain that so we will use race/ethnicity as a marker for likelihood of experience with discrimination and would explicitly discuss this in the review) ○ Identity and culture (e.g., spiritual, and religious beliefs and practices, native language, gender identity, sexual orientation, physical/mental disability status) ○ Age ○ Age at symptom onset ○ Social determinants of health, including education level, socioeconomic status, immigration status, refugee status, and geography (e.g., urban vs. rural) ○ Diagnosis of PANS/PANDAS ○ OCD in first degree relatives ○ Level of family accommodation ○ Co-occurring disorders (e.g., major depressive disorder, anxiety disorders, attention-deficit hyperactivity disorder, conduct disorders, autism spectrum disorder, and Tourette syndrome, other tic disorders) ○ Diagnosis during COVID-19 pandemic (as defined by study authors) ○ Duration of symptoms prior to treatment ○ Symptom severity ○ In-session exposure and response prevention ○ Medication dose ○ Care settings and care intensities ▪ Traditional outpatient ▪ Intensive outpatient • Day programs (e.g., partial hospitalization) • Residential ▪ Inpatient ▪ Other care settings, including school-based settings ▪ Telehealth (vs. in-person) ▪ Primary versus specialist care

PICOTS Element	Key Question 1 (Diagnosis of OCD)	Key Question 2 (Treatment of OCD)
Design	Cohort or cross-sectional studies • comparing an index test(s) to a reference standard • comparing an index test(s) in two or more subgroups of interest • comparing two or more diagnostic strategies Randomized controlled trials Nonrandomized comparative studies • prospective or retrospective with appropriate adjustment for confounding Systematic reviews (for reference lists only) *Exclude*: • Prevalence studies • Qualitative studies • Case reports and case series, • Unpublished studies, including conference abstracts (but include studies with reported results in the ClinicalTrials.gov database)	Comparative trials • Randomized controlled trials • Nonrandomized comparative studies o prospective or retrospective with appropriate adjustment for confounding Single arm studies, N ≥50 • with multivariable analyses of potential effect modifiers/subgroups of interest Systematic reviews (for reference lists only) *Exclude:* • Cross-sectional studies (no longitudinal follow-up) • Qualitative studies • Case reports and case series, • Unpublished studies, including conference abstracts (but include studies with reported results in the ClinicalTrials.gov database)
Timing	Any	Any
Setting	Any, including administration of test(s) in-person or via tele-health	Any

Abbreviations: OCD = obsessive compulsive disorder; N = number; PANDAS = pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection; PANS = pediatric acute-onset neuropsychiatric syndrome; PICOTS = population, interventions, outcomes, timing, setting

* Prioritized outcome

Data Extraction and Data Management (Details)

We extracted data from eligible primary studies into the Systematic Review Data Repository-Plus (https://srdrplus.ahrq.gov) and GSheets as appropriate. Data extracted in GSheets were imported into SRDR+ at the end of the project. For each study, one researcher extracted and entered data, which were confirmed by a second, independent researcher. In the instance where two studies, or separate subgroups were reported within a single article, outcomes for each study or relevant subgroup were extracted separately.

For each study, we extracted article-identifying information, study design features, funding source, population characteristics and sample sizes, intervention and comparator names and descriptions, and relevant outcomes and their definitions.

For priority outcomes, we extracted the number of participants, mean and standard deviation (SD), standard error (SE) or confidence interval (CI) for both arms at baseline and end-of-treatment. When available, we extracted mean, SD, SE, or CI for within group change from baseline. When the within group correlation was not reported, we imputed a correlation of 0.5 as described in an AHRQ Methods Research Report.[3] When necessary, we extracted data from figures using the Plot Digitizer program.[4]

Assessing Applicability

For each KQ, we assessed the applicability of the included studies primarily based on the studies' eligibility criteria and their included participants, specifically related to such factors as age, race/ethnicity, and comorbidities.

Peer Review and Public Commentary

Experts in OCD, including clinicians and researchers in child and adolescent psychiatry and child psychology are being invited to provide external peer review of this SR. The Agency for Healthcare Research and Quality (AHRQ) and an Associate Editor from a fellow Evidence-based Practice Center also provide comments. The draft report were posted on the AHRQ Website to elicit public comment for a period of 45 days. All reviewer and public comments were addressed, revising the text as appropriate. A summary of peer review comments and a disposition of public comments table will be posted on the Effective Health Care website (https://effectivehealthcare.ahrq.gov).

Appendix B. List of Excluded Studies

The 282 excluded articles and records, along with reasons for exclusion, are summarized in Appendix Table B-1. Details on exclusion reasons and numbers are given in Figure C–1, the flow diagram for studies.

Table B-1. Excluded articles and records with reasons for exclusion

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
1	Adam	2019	31244891	Psychometric evaluation of a parent-rating and self-rating inventory for pediatric obsessive-compulsive disorder: German OCD Inventory for Children and Adolescents (OCD-CA)	*Child Adolesc Psychiatry Ment Health*	I: Index test not used for diagnosis
2	Adam	2022	36494821	Extended treatment of multimodal cognitive behavioral therapy in children and adolescents with obsessive,Äìcompulsive disorder improves symptom reduction: A within-subject design	*Child and Adolescent Psychiatry and Mental Health*	D: Single-arm study N≥50, unadjusted
3	Albert	2012	23023076	[Combined treatments in obsessive-compulsive disorder: current knowledge and future prospects]	*Riv Psichiatr*	D: Not a primary study
4	Alderman	2006	16553533	Drug concentration monitoring with tolerability and efficacy assessments during open-label, long-term sertraline treatment of children and adolescents	*J Child Adolesc Psychopharmacol*	D: Single-arm study N≥50, unadjusted
5	Anderson	2007	16540080	Group versus individual cognitive-behavioural treatment for obsessive-compulsive disorder: a controlled trial	*Behav Res Ther*	P: Not a population <21 years with OCD

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
6	Arnold	2014	2014-49981-008 (PsycINFO)	Does cognitive-behavioral therapy response in youth with obsessive-compulsive disorder differ if treatment ends during summer?	*Annals of Clinical Psychiatry*	D: Single-arm study N≥50, unadjusted
7	Aspvall	2018	29971153	Internet-delivered cognitive behavioural therapy for young children with obsessive-compulsive disorder: development and initial evaluation of the BIP OCD Junior programme	*BJPsych Open*	D: Single-arm study N≥50, unadjusted
8	Aspvall	2020	32013900	Validity and clinical utility of the obsessive compulsive inventory - child version: further evaluation in clinical samples	*BMC Psychiatry*	I: Index test not used for diagnosis
9	Aspvall	2020	32082991	Implementation of internet-delivered cognitive behaviour therapy for pediatric obsessive-compulsive disorder: Lessons from clinics in Sweden, United Kingdom and Australia	*Internet Interv*	D: Single-arm study N≥50, unadjusted
10	Aspvall	2021	2021-34763-236 (PsycINFO)	Novel treatment approaches for children and adolescents with obsessive-compulsive disorder	NA	D: Not a primary study
11	Ayres	2000	2000-95024-249 (PsycINFO)	Obsessive Compulsive Disorder in children and adolescents: A longitudinal study	NA	D: Not a peer-reviewed publication
12	Babiano-Espinosa	2022	35460057	eCBT Versus Standard Individual CBT for Paediatric Obsessive-Compulsive Disorder	*Child Psychiatry Hum Dev*	D: KQ2: not an RCT or adjusted NRCS

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
13	Bakhshaie	2020	32822898	Temporal precedence of the change in obsessive-compulsive symptoms and change in depressive symptoms during exposure and response prevention for pediatric obsessive-compulsive disorders	*Behav Res Ther*	D: Single-arm study of pooled treatments
14	Bastiani	1996	9162209	Comparison of obsessions and compulsions in patients with anorexia nervosa and obsessive compulsive disorder	*Biol Psychiatry*	P: Not a population <21 years with OCD
15	Baving	2000	10746297	[Obsessive-compulsive disorder, frontostriatal system and the effect of the serotonergic system]	*Z Kinder Jugendpsychiatr Psychother*	D: KQ2: not an RCT or adjusted NRCS
16	Beig	2017	27058836	[Effectiveness of cognitive-behavioral therapy in children and adolescents with obsessive-compulsive disorders treated in an outpatient clinic]	*Z Kinder Jugendpsychiatr Psychother*	D: Single-arm study N≥50, unadjusted
17	Benazon	2002	12038645	Cognitive behavior therapy in treatment-naive children and adolescents with obsessive-compulsive disorder: an open trial	*Behav Res Ther*	D: Single-arm study N≥50, unadjusted
18	Benazon	2003	14566164	Neurochemical analyses in pediatric obsessive-compulsive disorder in patients treated with cognitive-behavioral therapy	*J Am Acad Child Adolesc Psychiatry*	D: Single-arm study N≥50, unadjusted
19	Benito	2018	29939055	Measuring fear change within exposures: Functionally-defined habituation predicts outcome in three randomized controlled trials for pediatric OCD	*J Consult Clin Psychol*	D: Single-arm study N≥50, unadjusted

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
20	Benito	2020	33990231	Therapist Behavior During Exposure Tasks Predicts Habituation and Clinical Outcome in Three Randomized Controlled Trials for Pediatric OCD	*Behavior therapy*	D: Single-arm study N≥50, unadjusted
21	Bennett	2015	25843610	Evaluation of cognitive behaviour therapy for paediatric obsessive-compulsive disorder in the context of tic disorders	*J Behav Ther Exp Psychiatry*	D: Single-arm study N≥50, unadjusted
22	Berg	1986	1987-02850-001 (PsycINFO)	The Leyton Obsessional Inventory,ÄîChild Version	*Journal of the American Academy of Child Psychiatry*	O: No extractable or new outcomes of interest
23	Bernstein	2017	27830935	Use of Computer Vision Tools to Identify Behavioral Markers of Pediatric Obsessive-Compulsive Disorder: A Pilot Study	*J Child Adolesc Psychopharmacol*	I: Index test not used for diagnosis
24	Bettess	2023	35303769	Clinical characteristics of transformation obsessions in obsessive-compulsive disorder: A psychopathological study	*Aust N Z J Psychiatry*	P: Not a population <21 years with OCD
25	Björgvinsson	2008	18520782	Treatment outcome for adolescent obsessive-compulsive disorder in a specialized hospital setting	*J Psychiatr Pract*	D: Single-arm study N≥50, unadjusted
26	Bloch	2016	27027204	N-Acetylcysteine in the Treatment of Pediatric Tourette Syndrome: Randomized, Double-Blind, Placebo-Controlled Add-On Trial	*J Child Adolesc Psychopharmacol*	P: Not a population <21 years with OCD
27	Borda	2017	2017-34965-012 (PsycINFO)	Overvalued ideation in adolescents with obsessive-compulsive disorder	*Psychiatry Research*	D: Single-arm study N≥50, unadjusted
28	Bortoncello	2012	22306130	Psychometric properties of the Brazilian version of the Obsessive Beliefs Questionnaire (OBQ-44)	*J Anxiety Disord*	P: Not a population <21 years with OCD

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
29	Bose	2022	2022-17115-001 (PsycINFO)	Therapeutic alliance in psychosocial interventions for youth internalizing disorders: A systematic review and preliminary meta-analysis	*Clinical Psychology: Science and Practice*	P: Not a population <21 years with OCD
30	Brown	2017	28714753	Pediatric Acute-Onset Neuropsychiatric Syndrome Response to Oral Corticosteroid Bursts: An Observational Study of Patients in an Academic Community-Based PANS Clinic	*J Child Adolesc Psychopharmacol*	I: Not an intervention/index test of interest
31	Brown	2017	28696786	Effect of Early and Prophylactic Nonsteroidal Anti-Inflammatory Drugs on Flare Duration in Pediatric Acute-Onset Neuropsychiatric Syndrome: An Observational Study of Patients Followed by an Academic Community-Based Pediatric Acute-Onset Neuropsychiatric Syndrome Clinic	*J Child Adolesc Psychopharmacol*	P: Not a population <21 years with OCD
32	Canavera	2022	CN-02399450 (Cochrane)	A Five-Day Intensive Treatment for Pediatric Obsessive-Compulsive Disorder: a Multiple Baseline Design Pilot Study	*Evidence-based practice in child and adolescent mental health*	D: Single-arm study N≥50, unadjusted
33	Cervin	2019	30481695	Validation of an interview-only version of the Dimensional Yale-Brown Obsessive-Compulsive Scale (DY-BOCS) in treatment-seeking youth with obsessive-compulsive disorder	*Psychiatry Res*	O: No extractable or new outcomes of interest
34	Cervin	2021	33483124	Incompleteness and Disgust Predict Treatment Outcome in Pediatric Obsessive-Compulsive Disorder	*Behav Ther*	D: Single-arm study of pooled treatments

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
35	Cervin	2023	34978642	Symptom dimension breakpoints for the Obsessive-Compulsive Inventory-Child Version (OCI-CV)	*Child Psychiatry and Human Development*	I: Index test not used for diagnosis
36	Chai	2013	2014-08162-007 (PsycINFO)	Validity of the children's Yale-Brown obsessive compulsive scale in Singaporean children	*Advances in Mental Health*	O: No extractable or new outcomes of interest
37	Ching	2018	28681684	Association splitting of the sexual orientation-OCD-relevant semantic network	*Cogn Behav Ther*	P: Not a population <21 years with OCD
38	Chu	2015	25892174	Mediators of exposure therapy for youth obsessive-compulsive disorder: specificity and temporal sequence of client and treatment factors	*Behav Ther*	D: Single-arm study N≥50, unadjusted
39	Coles	2010	20577988	Development and initial validation of the obsessive belief questionnaire-child version (OBQ-CV)	*Depress Anxiety*	I: Index test not used for diagnosis
40	Cook	2001	11589530	Long-term sertraline treatment of children and adolescents with obsessive-compulsive disorder	*J Am Acad Child Adolesc Psychiatry*	O: No extractable or new outcomes of interest
41	De Caluwé	2014	2013-45490-001 (PsycINFO)	Development and validation of the Youth Obsessive,ÄìCompulsive Symptoms Scale (YOCSS)	*Child Psychiatry and Human Development*	P: Not a population <21 years with OCD
42	De Nadai	2015	26003507	Contemporary models of pediatric obsessive-compulsive disorder: An evaluation with a large clinical sample	*Psychiatry Res*	I: Index test not used for diagnosis

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
43	DeVeaugh-Geiss	1991	1993-97959-005 (PsycINFO)	Clomipramine hydrochloride (Anafranil) in the treatment of obsessive-compulsive disorder: Results from three multicentre trials	*Understanding obsessive-compulsive disorder (OCD).*	D: Not a peer-reviewed publication
44	Duholm	2022	36510026	Specific Contamination Symptoms are Associated with Experiencing a Limited Response of Cognitive-Behavioral Therapy in Pediatric Patients with OCD	*Child Psychiatry Hum Dev*	D: Single-arm study N≥50, unadjusted
45	Efe	2022	35905054	Impact of Attention-Deficit/Hyperactivity Disorder Comorbidity on Phenomenology and Treatment Outcomes of Pediatric Obsessive-Compulsive Disorder	*J Child Adolesc Psychopharmacol*	I: Not an intervention/index test of interest
46	Elsner	2022	35086513	Mechanisms of exposure and response prevention in obsessive-compulsive disorder: effects of habituation and expectancy violation on short-term outcome in cognitive behavioral therapy	*BMC Psychiatry*	P: Not a population <21 years with OCD
47	Farrell	2010	20181328	Cognitive-behavioral treatment of childhood obsessive-compulsive disorder in community-based clinical practice: clinical significance and benchmarking against efficacy	*Behav Res Ther*	D: Single-arm study N≥50, unadjusted
48	Farrell	2012	22633155	Comorbidity and treatment response in pediatric obsessive-compulsive disorder: a pilot study of group cognitive-behavioral treatment	*Psychiatry Res*	D: Single-arm study N≥50, unadjusted

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
49	Farrell	2016	27395805	Brief intensive CBT for pediatric OCD with E-therapy maintenance	*J Anxiety Disord*	D: Single-arm study N≥50, unadjusted
50	Farrell	2022	36591101	FAST CBT for pediatric OCD: A multiple-baseline controlled pilot trial of parent training in exposure and response prevention delivered via telehealth	*Front Psychol*	D: Single-arm study N≥50, unadjusted
51	Fernández de la Cruz	2015	2016-01377-007 (PsycINFO)	Phenomenology and treatment outcomes in children and adolescents from ethnic minorities with obsessive,Äìcompulsive disorder	*Journal of Obsessive-Compulsive and Related Disorders*	D: Single-arm study N≥50, unadjusted
52	Fernández de la Cruz		L601056186 (Embase)	Phenomenology and treatment outcomes in children and adolescents from ethnic minorities with obsessive-compulsive disorder	*Journal of Obsessive-Compulsive and Related Disorders*	D: Single-arm study N≥50, unadjusted
53	Fischer	1998	NA (From SRs)	Group behavioral therapy for adolescents with obsessive-compulsive disorder: Preliminary outcomes.	*Research on Social Work Practice*	D: Single-arm study N≥50, unadjusted
54	Flament	1985	3885292	A controlled trial of clomipramine in childhood obsessive compulsive disorder	*Psychopharmacol Bull*	O: No extractable or new outcomes of interest
55	Flament	1987	3548637	Biochemical changes during clomipramine treatment of childhood obsessive-compulsive disorder	*Arch Gen Psychiatry*	D: Single-arm study N≥50, unadjusted
56	Flessner	2010	19842168	The impact of neuropsychological functioning on treatment outcome in pediatric obsessive-compulsive disorder	*Depress Anxiety*	O: No extractable or new outcomes of interest

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
57	Flessner	2011	CN-00795157 (Cochrane)	Predictors of Parental Accommodation in Pediatric Obsessive-Compulsive Disorder: findings from the Pediatric Obsessive-Compulsive Disorder Treatment Study (POTS) Trial	*Journal of the American Academy of Child and Adolescent Psychiatry*	O: No extractable or new outcomes of interest
58	Foa	2010	20171333	Development and validation of a child version of the obsessive compulsive inventory	*Behav Ther*	I: Index test not used for diagnosis
59	Franklin	1998	9549962	Cognitive-behavioral treatment of pediatric obsessive-compulsive disorder: an open clinical trial	*J Am Acad Child Adolesc Psychiatry*	D: KQ2: not an RCT or adjusted NRCS
60	Franklin	2012	CN-01017907 (Cochrane)	Cognitive behavior therapy augmentation of pharmacotherapy in pediatric obsessive-compulsive disorder: the pediatric OCD treatment study II (POTS II) randomized controlled trial (JAMA - Journal of the American Medical Association (2011) 306, 11, (1224-1232))	*JAMA*	O: No extractable or new outcomes of interest
61	Franklin	2015	25771752	Cognitive-behavioral therapy for pediatric obsessive-compulsive disorder: Empirical review and clinical recommendations	*Psychiatry Res*	D: Not a primary study
62	Freeman	2011	21340599	The Children's Yale-Brown Obsessive Compulsive Scale: reliability and validity for use among 5 to 8 year olds with obsessive-compulsive disorder	*J Abnorm Child Psychol*	I: Index test not used for diagnosis
63	Gallant	2008	18329843	Convergent and discriminant validity of the Children's Yale-Brown Obsessive Compulsive Scale-Symptom Checklist	*J Anxiety Disord*	I: Index test not used for diagnosis

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
64	Geller	2004	15103533	Re-examining comorbidity of Obsessive Compulsive and Attention-Deficit Hyperactivity Disorder using an empirically derived taxonomy	*Eur Child Adolesc Psychiatry*	I: Index test not used for diagnosis
65	Geller	2019	30852257	Fear extinction learning as a predictor of response to cognitive behavioral therapy for pediatric obsessive compulsive disorder	*J Anxiety Disord*	D: Single-arm study of pooled treatments
66	Gittins Stone	2023	36749490	Examining the Effectiveness of an Intensive Telemental Health Treatment for Pediatric Anxiety and OCD During the COVID-19 Pandemic and Pediatric Mental Health Crisis.	*Child psychiatry and human development*	P: Not a population <21 years with OCD
67	Godoy	2011	21504689	[Factor structure and reliability of the Spanish adaptation of the Children's Yale-Brown Obsessive-Compulsive Scale--Self Report (CY-BOCS-SR)]	*Psicothema*	P: Not a population <21 years with OCD
68	Goodman	1997	9184625	Fluvoxamine in the treatment of obsessive-compulsive disorder and related conditions	*J Clin Psychiatry*	D: Not a primary study
69	Gordon	1992	1536276	Differential response of seven subjects with autistic disorder to clomipramine and desipramine	*Am J Psychiatry*	P: Not a population <21 years with OCD
70	Gorrell	2019	30734406	Rituals and preoccupations associated with bulimia nervosa in adolescents: Does motivation to change matter?	*Eur Eat Disord Rev*	P: Not a population <21 years with OCD

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
71	Gregory	2020	31864218	Cost-Effectiveness of Treatment Alternatives for Treatment-Refractory Pediatric Obsessive-Compulsive Disorder	*J Anxiety Disord*	O: No extractable or new outcomes of interest
72	Guggisberg	2005	2005-99016-280 (PsycINFO)	Methodological review and meta-analysis of treatments for child and adolescent obsessive-compulsive disorder	NA	D: Not a peer-reviewed publication
73	Guzick	2017	28966908	The link between ADHD-like inattention and obsessions and compulsions during treatment of youth with OCD	*J Obsessive Compuls Relat Disord*	D: Single-arm study N≥50, unadjusted
74	Guzick	2021	34134828	Irritability in Children and Adolescents With OCD	*Behav Ther*	D: Single-arm study of pooled treatments
75	Guzick	2023	36908861	Development and pilot testing of internet-delivered, family-based cognitive behavioral therapy for anxiety and obsessive-compulsive disorders in autistic youth	*J Obsessive Compuls Relat Disord*	P: Not a population <21 years with OCD
76	Haque		37489154	Early detection of paediatric and adolescent obsessive-compulsive, separation anxiety and attention deficit hyperactivity disorder using machine learning algorithms	*Health Inf Sci Syst 11(1):-*	I: Not an intervention/index test of interest
77	Harris	2010	2010-19252-014 (PsycINFO)	Disinhibition as a side effect of treatment with fluvoxamine in pediatric patients with obsessive-compulsive disorder	*Journal of Child and Adolescent Psychopharmacology*	D: Single-arm study N≥50, unadjusted
78	Henin	2017	CN-01439319 (Cochrane)	Long-term efficacy of cognitive-behavioral therapy for pediatric OCD with and without d-cycloserine augmentation	*Neuropsychopharmacology*	D: Not a peer-reviewed publication

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
79	Himle	2003	12621595	Group behavioral therapy for adolescents with tic-related and non-tic-related obsessive-compulsive disorder	*Depress Anxiety*	D: Single-arm study N≥50, unadjusted
80	Holmgren Melin	2015	CN-01070018 (Cochrane)	Treatment and 12-month outcome of children and adolescents with obsessive-compulsive disorder: a naturalistic study	*Journal of obsessive-compulsive and related disorders*	D: Single-arm study N≥50, unadjusted
81	Hudson	2015	NA (From SRs)	Comparing outcomes for children with diferent anxiety disorders following cognitive behavioural therapy.	*Behaviour Research and Therapy*	P: Not a population <21 years with OCD
82	Højgaard	2017	29096776	One-Year Outcome for Responders of Cognitive-Behavioral Therapy for Pediatric Obsessive-Compulsive Disorder	*J Am Acad Child Adolesc Psychiatry*	D: Single-arm study N≥50, unadjusted
83	Højgaard	2017	28032202	Pediatric obsessive,Äìcompulsive disorder with tic symptoms: Clinical presentation and treatment outcome	*European Child & Adolescent Psychiatry*	D: Single-arm study N≥50, unadjusted
84	Iniesta-Sepúlveda	2018	28389841	An Initial Case Series of Intensive Cognitive-Behavioral Therapy for Obsessive-Compulsive Disorder in Adolescents with Autism Spectrum Disorder	*Child Psychiatry Hum Dev*	D: Single-arm study N≥50, unadjusted
85	Ivarsson	2015	25591044	Sleep problems and cognitive behavior therapy in pediatric obsessive-compulsive disorder have bidirectional effects	*J Anxiety Disord*	D: Single-arm study N≥50, unadjusted
86	Ivarsson	2016	CN-01304673 (Cochrane)	The nordic long-term obsessivecompulsive disorder treatment study: effectiveness of a stepped-care treatment	*Journal of the American Academy of Child and Adolescent Psychiatry*	D: Not a peer-reviewed publication

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
87	Jacoby	2021	34428688	Longitudinal trajectory and predictors of change in family accommodation during exposure therapy for pediatric OCD	*J Anxiety Disord*	D: Single-arm study of pooled treatments
88	Jalenques	2018	29392455	The MOVES (Motor tic, Obsessions and compulsions, Vocal tic Evaluation Survey): cross-cultural evaluation of the French version and additional psychometric assessment	*J Neurol*	P: Not a population <21 years with OCD
89	Janzen	2001	2001-95020-060 (PsycINFO)	Assessment of obsessive-compulsive disorder in youth using parent and youth rating scales	NA	D: Not a peer-reviewed publication
90	Jaspers-Fayer	2017	28121463	Prevalence of Acute-Onset Subtypes in Pediatric Obsessive-Compulsive Disorder	*J Child Adolesc Psychopharmacol*	D: Single-arm study N≥50, unadjusted
91	Jassi	2020	32006302	The Work and Social Adjustment Scale, Youth and Parent Versions: Psychometric Evaluation of a Brief Measure of Functional Impairment in Young People	*Child Psychiatry Hum Dev*	I: Index test not used for diagnosis
92	Jensen	2020	2022-97309-001 (PsycINFO)	The Children's Yale-Brown Obsessive-Compulsive Scale's auxiliary items: Long-term outcome	*Journal of Obsessive-Compulsive and Related Disorders*	O: No extractable or new outcomes of interest
93	Jensen	2020	31736082	Distinct trajectories of long‚Äêterm symptom severity in pediatric obsessive‚Äìcompulsive disorder during and after stepped‚Äêcare treatment	*Journal of Child Psychology and Psychiatry*	D: Single-arm study of pooled treatments

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94	Jensen	2022	36265194	Long- term remission status in pediatric obsessive-compulsive disorder: Evaluating the predictive value of symptom severity after treatment	*Psychiatry Res*	O: No extractable or new outcomes of interest
95	Jensen	2022	33881628	Quality of life in pediatric patients with obsessive‚Äìcompulsive disorder during and 3¬†years after stepped-care treatment	*European Child & Adolescent Psychiatry*	D: Single-arm study of pooled treatments
96	Jones	2013	109867399 (CINAHL)	Psychometric properties of the obsessive compulsive inventory: child version in children and adolescents with obsessive-compulsive disorder	*Child Psychiatry & Human Development*	O: No extractable or new outcomes of interest
97	Joseph	2011	CN-01020479 (Cochrane)	A placebo-controlled trial of riluzole for treatment of childhood-onset obsessive compulsive disorder	*Neuropsychopharmacology*	D: Not a peer-reviewed publication
98	Kano	2013	24228477	[Treatment-refractory OCD from the viewpoint of obsessive-compulsive spectrum disorders: impact of comorbid child and adolescent psychiatric disorders]	*Seishin Shinkeigaku Zasshi*	D: Not a primary study
99	Kay	2016	27638964	Outcome of multidisciplinary, CBT-focused treatment for pediatric OCD	*Gen Hosp Psychiatry*	D: Single-arm study N≥50, unadjusted
100	Keeley	2011	2011-17425-001 (PsycINFO)	The therapeutic alliance in the cognitive behavioral treatment of pediatric obsessive‚Äìcompulsive disorder	*Journal of Anxiety Disorders*	D: Single-arm study N≥50, unadjusted

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
101	Khenavandi		38435766	Treatment and Family Involvement for Young Children with Obsessive-Compulsive Disorder: An Experimental Study	*Iran J Public Health 52(12):-*	D: KQ2: not an RCT or adjusted NRCS
102	Kim	2020	CN-02141314 (Cochrane)	Understanding Anxiety and Symptom Impact as Mediators Explaining Cognitive-Behavior Therapy and Pharmacotherapy Response in Childhood Obsessive-Compulsive Disorder	*Journal of psychopathology and behavioral assessment*	O: No extractable or new outcomes of interest
103	Kircanski	2011	21440853	Cognitive-behavioral therapy for obsessive-compulsive disorder in children and adolescents	*Child Adolesc Psychiatr Clin N Am*	D: Not a primary study
104	Kircanski	2014	23774008	Reduction of subjective distress in CBT for childhood OCD: nature of change, predictors, and relation to treatment outcome	*J Anxiety Disord*	O: No extractable or new outcomes of interest
105	Kircanski	2015	25052626	Exposure and response prevention process predicts treatment outcome in youth with OCD	*J Abnorm Child Psychol*	D: Single-arm study N≥50, unadjusted
106	Krebs	2013	22957831	Temper outbursts in paediatric obsessive,Äêcompulsive disorder and their association with depressed mood and treatment outcome	*Journal of Child Psychology and Psychiatry*	D: Single-arm study N≥50, unadjusted
107	Krebs	2015	25130442	How resistant is 'treatment-resistant' obsessive-compulsive disorder in youth?	*Br J Clin Psychol*	D: KQ2: not an RCT or adjusted NRCS
108	Krulewicz	2006	16601647	Analysis of electrocardiographic data following use of paroxetine in pediatric depression and obsessive-compulsive disorder	*J Am Acad Child Adolesc Psychiatry*	O: No extractable or new outcomes of interest

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109	Kurlan	1993	8477412	A pilot controlled study of fluoxetine for obsessive-compulsive symptoms in children with Tourette's syndrome	*Clin Neuropharmacol*	P: Not a population <21 years with OCD
110	Lavell	2016	27544784	Predictors of treatment response to group cognitive behavioural therapy for pediatric obsessive-compulsive disorder	*Psychiatry Research*	D: Single-arm study N≥50, unadjusted
111	Lee	2005	32806851	Broad Outcome Measures May Underestimate Effectiveness: An Instrument Comparison Study	*Child Adolesc Ment Health*	I: Index test not used for diagnosis
112	Lei	1986	3556093	[A cross-over treatment of obsessive-compulsive neurosis with imipramine and chlorimipramine]	*Zhonghua Shen Jing Jing Shen Ke Za Zhi*	P: Not a population <21 years with OCD
113	Lenhard	2014	24949622	Internet-delivered cognitive behavior therapy for adolescents with obsessive-compulsive disorder: an open trial	*PLoS One*	D: Single-arm study N≥50, unadjusted
114	Lenhard	2016	CN-01304706 (Cochrane)	Cost-effectiveness of internetdelivered cognitive-behavior therapy for obsessive-compulsive disorder: results from a randomized controlled trial	*Journal of the American Academy of Child and Adolescent Psychiatry*	D: Not a study design of interest
115	Lenhard	2017	28637745	Corrections: Cost-effectiveness of therapist-guided internet-delivered cognitive behaviour therapy for paediatric obsessive-compulsive disorder: results from a randomised controlled trial	*BMJ Open*	O: No extractable or new outcomes of interest

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116	Lenhard	2018	28752937	Prediction of outcome in internet-delivered cognitive behaviour therapy for paediatric obsessive-compulsive disorder: A machine learning approach	*Int J Methods Psychiatr Res*	O: No extractable or new outcomes of interest
117	Lenhard	2020	33043148	Long-term outcomes of therapist-guided Internet-delivered cognitive behavior therapy for pediatric obsessive-compulsive disorder	*NPJ Digit Med*	O: No extractable or new outcomes of interest
118	Lenhard	2022	2022-34077-293 (PsycINFO)	Internet-delivered cognitive behavior therapy for adolescents with obsessive-compulsive disorder	NA	D: Not a peer-reviewed publication
119	Leon	2018	29119300	Longitudinal outcomes of children with pediatric autoimmune neuropsychiatric disorder associated with streptococcal infections (PANDAS)	*Eur Child Adolesc Psychiatry*	P: Not a population <21 years with OCD
120	Leonard	1988	3290954	Treatment of childhood obsessive compulsive disorder with clomipramine and desmethylimipramine: a double-blind crossover comparison	*Psychopharmacol Bull*	D: KQ2: not an RCT or adjusted NRCS
121	Leonard	1993	8498877	A 2- to 7-year follow-up study of 54 obsessive-compulsive children and adolescents	*Arch Gen Psychiatry*	D: Single-arm study of pooled treatments
122	Leonard	1995	1996-23910-001 (PsycINFO)	Electrocardiographic changes during desipramine and clomipramine treatment in children and adolescents	*Journal of the American Academy of Child & Adolescent Psychiatry*	P: Not a population <21 years with OCD

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123	Leonard	2014	2014-33301-005 (PsycINFO)	The effect of depression symptom severity on OCD treatment outcome in an adolescent residential sample	*Journal of Obsessive-Compulsive and Related Disorders*	O: No extractable or new outcomes of interest
124	Leonard	2016	26308588	Residential treatment outcomes for adolescents with obsessive-compulsive disorder	*Psychother Res*	D: Single-arm study N≥50, unadjusted
125	Lewin	2012	22963592	Agreement between therapists, parents, patients, and independent evaluators on clinical improvement in pediatric obsessive-compulsive disorder	*J Consult Clin Psychol*	O: No extractable or new outcomes of interest
126	Liebowitz	1990	2309962	Fluoxetine for adolescents with obsessive-compulsive disorder	*Am J Psychiatry*	D: Not a primary study
127	Liu	2011	NA (From SRs)	Fluvoxamine combined with cognitive behavioral therapy in child and adolescent obsessive neurosis	*J Clin Psychosom Dis*	Unable to retrieve full text
128	Lopez	2012	2012-99020-383 (PsycINFO)	Effect of exposure-based parent-child interaction therapy on early childhood compulsive behaviors	NA	D: Not a primary study
129	López-Pina	2015	25010899	Reliability generalization study of the Yale-Brown Obsessive-Compulsive Scale for children and adolescents	*J Pers Assess*	I: Index test not used for diagnosis
130	Mancebo	2014	24952937	Long-term course of pediatric obsessive-compulsive disorder: 3 years of prospective follow-up	*Compr Psychiatry*	I: Not an intervention/index test of interest

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131	Martin	2005	16049647	Group cognitive-behavior therapy with family involvement for middle-school-age children with obsessive-compulsive disorder: a pilot study	*Child Psychiatry Hum Dev*	D: Single-arm study N≥50, unadjusted
132	Martin	2020	32008168	Co-occurring obsessive-compulsive disorder and autism spectrum disorder in young people: prevalence, clinical characteristics and outcomes	*Eur Child Adolesc Psychiatry*	D: Not a study design of interest
133	Masi	2007	17822342	Bipolar co-morbidity in pediatric obsessive-compulsive disorder: clinical and treatment implications	*J Child Adolesc Psychopharmacol*	D: Single-arm study of pooled treatments
134	Masi	2009	19320532	Pharmacotherapy in paediatric obsessive-compulsive disorder: a naturalistic, retrospective study	*CNS Drugs*	D: Single-arm study N≥50, unadjusted
135	Masi	2013	23664673	Antipsychotic augmentation of selective serotonin reuptake inhibitors in resistant tic-related obsessive-compulsive disorder in children and adolescents: a naturalistic comparative study	*J Psychiatr Res*	D: KQ2: not an RCT or adjusted NRCS
136	McBride	2020	32026260	The Impact of Comorbidity on Cognitive-Behavioral Therapy Response in Youth with Anxiety and Autism Spectrum Disorder	*Child Psychiatry Hum Dev*	P: Not a population <21 years with OCD
137	McGuire	2019	30824248	Defining Treatment Outcomes in Pediatric Obsessive-Compulsive Disorder Using a Self-Report Scale	*Behav Ther*	I: Index test not used for diagnosis
138	McGuire	2019	30644767	Symptom Dimension Response in Children and Adolescents with Obsessive-Compulsive Disorder	*J Clin Child Adolesc Psychol*	O: No extractable or new outcomes of interest

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139	McKay	2003	14692851	The Children's Yale-Brown Obsessive-Compulsive Scale: item structure in an outpatient setting	*Psychol Assess*	I: Index test not used for diagnosis
140	McKenzie	2020	2020-47546-001 (PsycINFO)	Variability in emotion regulation in paediatric obsessive-compulsive disorder: Associations with symptom presentation and response to treatment	*Journal of Obsessive-Compulsive and Related Disorders*	D: Single-arm study N≥50, unadjusted
141	McNamara	2014	103982872 (CINAHL)	Self-Regulation and Other Executive Functions Relationship to Pediatric OCD Severity and Treatment Outcome	*Journal of Psychopathology & Behavioral Assessment*	D: Not a primary study
142	Melin	2018	29502315	A solid majority remit following evidence-based OCD treatments: a 3-year naturalistic outcome study in pediatric OCD	*Eur Child Adolesc Psychiatry*	D: Single-arm study N≥50, unadjusted
143	Melin	2020	30768383	Treatment Gains Are Sustainable in Pediatric Obsessive-Compulsive Disorder: Three-Year Follow-Up From the NordLOTS	*J Am Acad Child Adolesc Psychiatry*	D: Single-arm study N≥50, unadjusted
144	Meyer	2014	23756717	Prospective relationship between obsessive-compulsive and depressive symptoms during multimodal treatment in pediatric obsessive-compulsive disorder	*Child Psychiatry Hum Dev*	D: Single-arm study of pooled treatments
145	Monzani	2015	25753746	Transformation obsessions in paediatric obsessive-compulsive disorder: Clinical characteristics and treatment response to cognitive behaviour therapy	*J Behav Ther Exp Psychiatry*	D: Single-arm study N≥50, unadjusted

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146	Moritz	1998	1998-95014-194 (PsycINFO)	Behavior therapy in game format for the treatment of childhood obsessive compulsive disorder	NA	D: Not a peer-reviewed publication
147	Murphy	2017	28358599	A Double-Blind Randomized Placebo-Controlled Pilot Study of Azithromycin in Youth with Acute-Onset Obsessive-Compulsive Disorder	*J Child Adolesc Psychopharmacol*	I: Not an intervention/index test of interest
148	Murray	2015	2015-19893-001 (PsycINFO)	Outcomes of cognitive behaviour therapy for obsessive,Äìcompulsive disorder in young people with and without autism spectrum disorders: A case controlled study	*Psychiatry Research*	D: Single-arm study N≥50, unadjusted
149	Muñoz-Solomando	2008	18520736	Cognitive behavioural therapy for children and adolescents	*Curr Opin Psychiatry*	D: Not a primary study
150	Nadeau	2015	25978743	A pilot trial of cognitive-behavioral therapy augmentation of antibiotic treatment in youth with pediatric acute-onset neuropsychiatric syndrome-related obsessive-compulsive disorder	*J Child Adolesc Psychopharmacol*	D: Single-arm study N≥50, unadjusted
151	Nadeau	2017	27215910	Further Psychometric Evaluation of the Child Disgust Scale	*Child Psychiatry Hum Dev*	I: Index test not used for diagnosis
152	Nakatani	2009	105418794 (CINAHL)	Outcomes of cognitive behaviour therapy for obsessive compulsive disorder in a clinical setting: a 10-year experience from a specialist OCD service for children and adolescents	*Child & Adolescent Mental Health*	D: Single-arm study N≥50, unadjusted

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153	Nevell	2021	2020-97492-083 (PsycINFO)	Outcomes and predictors of treatment in an intensive outpatient program for pediatric obsessive-compulsive disorder	NA	D: Not a peer-reviewed publication
154	Niemeyer	2022	36092975	Memantine as treatment for compulsivity in child and adolescent psychiatry: Descriptive findings from an incompleted randomized, double-blind, placebo-controlled trial	*Contemp Clin Trials Commun*	P: Not a population <21 years with OCD
155	Nissen	2017	28928194	Diagnostic validity of early-onset obsessive-compulsive disorder in the Danish Psychiatric Central Register: findings from a cohort sample	*BMJ Open*	I: Not an intervention/index test of interest
156	Nissen	2018	29993297	The importance of insight, avoidance behavior, not-just-right perception and personality traits in pediatric obsessive-compulsive disorder (OCD): a naturalistic clinical study	*Nord J Psychiatry*	O: No extractable or new outcomes of interest
157	Nogueira Arjona	2012	23079369	[Psychometric properties of the Spanish version of the Obsessive Belief Questionnaire-Children's Version in a non-clinical sample]	*Psicothema*	P: Not a population <21 years with OCD
158	Ogle	2021	2021-27921-238 (PsycINFO)	Executive function, self-efficacy, and school engagement among youth in clinical treatment for anxiety and obsessive-compulsive disorder	NA	D: Not a peer-reviewed publication
159	Olatunji	2013	22999486	Cognitive-behavioral therapy for obsessive-compulsive disorder: a meta-analysis of treatment outcome and moderators	*J Psychiatr Res*	D: Not a primary study

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160	Olatunji	2022	2022-25278-011 (PsycINFO)	Decoupling of obsessions and compulsions during cognitive behavioral therapy for youths with obsessive compulsive disorder	*Clinical Psychological Science*	D: Single-arm study of pooled treatments
161	Olino	2011	21456041	Evidence for successful implementation of exposure and response prevention in a naturalistic group format for pediatric OCD	*Depress Anxiety*	D: Single-arm study N≥50, unadjusted
162	Park	2014	24999301	Does d-Cycloserine Augmentation of CBT Improve Therapeutic Homework Compliance for Pediatric Obsessive-Compulsive Disorder?	*J Child Fam Stud*	O: No extractable or new outcomes of interest
163	Pedapati	2015	26228567	Neural correlates associated with symptom provocation in pediatric obsessive compulsive disorder after a single session of sham-controlled repetitive transcranial magnetic stimulation	*Psychiatry Res*	I: Not an intervention/index test of interest
164	Peris	2012	22309471	Family factors predict treatment outcome for pediatric obsessive-compulsive disorder	*J Consult Clin Psychol*	O: No extractable or new outcomes of interest
165	Perlmutter	1999	10513708	Therapeutic plasma exchange and intravenous immunoglobulin for obsessive-compulsive disorder and tic disorders in childhood	*Lancet*	I: Not an intervention/index test of interest
166	Petersen	2022	2022-18280-001 (PsycINFO)	Intensive outpatient acceptance and commitment therapy with exposure and response prevention for adolescents	*Journal of Contextual Behavioral Science*	D: Single-arm study N≥50, unadjusted

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167	Piacentini	2002	12194545	Open trial of cognitive behavior therapy for childhood obsessive-compulsive disorder	*J Anxiety Disord*	D: Single-arm study N≥50, unadjusted
168	Piacentini	2007	18088221	Functional impairment in childhood OCD: development and psychometrics properties of the Child Obsessive-Compulsive Impact Scale-Revised (COIS-R)	*J Clin Child Adolesc Psychol*	I: Index test not used for diagnosis
169	Piacentini	2016	CN-01304680 (Cochrane)	Neural correlates of cognitivebehavioral therapy-related changes in pediatric obsessive-compulsive disorder symptom dimensions	*Journal of the American Academy of Child and Adolescent Psychiatry*	D: Not a peer-reviewed publication
170	Pretzmann		37497354	Adverse events in cognitive behavioral therapy and relaxation training for children and adolescents with obsessive-compulsive disorder: A mixed methods study and analysis plan for the TECTO trial	*Contemp Clin Trials Commun 34():-*	O: No extractable or new outcomes of interest
171	Przeworski	2012	22090186	Maternal and child expressed emotion as predictors of treatment response in pediatric obsessive,Äìcompulsive disorder	*Child Psychiatry and Human Development*	C: Not a comparison of interest
172	Rapoport	1980	6996027	Clinical controlled trial of chlorimipramine in adolescents with obsessive-compulsive disorder	*Psychopharmacol Bull*	D: KQ2: not an RCT or adjusted NRCS
173	Rech	2020	35990243	Symptom Trajectories of Early Responders and Remitters among Youth with OCD	*J Obsessive Compuls Relat Disord*	D: Single-arm study of pooled treatments

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174	Reddihough	2019	31638682	Effect of Fluoxetine on Obsessive-Compulsive Behaviors in Children and Adolescents With Autism Spectrum Disorders: A Randomized Clinical Trial	*Jama*	P: Not a population <21 years with OCD
175	Reddy	2003	12752023	A follow-up study of juvenile obsessive-compulsive disorder from India	*Acta Psychiatr Scand*	D: Single-arm study of pooled treatments
176	Rees	2016	27381977	Online Obsessive-Compulsive Disorder Treatment: Preliminary Results of the 'OCD? Not Me!' Self-Guided Internet-Based Cognitive Behavioral Therapy Program for Young People	*JMIR Ment Health*	D: Single-arm study N≥50, unadjusted
177	Rodríguez-Jiménez	2016	2016-44724-002 (PsycINFO)	Metric invariance, reliability, and validity of the Child Version of the Obsessive Compulsive Inventory (OCI-CV) in community and clinical samples	*Journal of Obsessive-Compulsive and Related Disorders*	O: No extractable or new outcomes of interest
178	Rodríguez-Jiménez	2017	2015-29405-001 (PsycINFO)	Factor structure and measurement invariance of the Obsessive-Compulsive Inventory,ÄîChild Version (OCI-CV) in general population	*European Journal of Psychological Assessment*	P: Not a population <21 years with OCD
179	Rosa-Alcázar	2017	27792972	A preliminary study of cognitive-behavioral family-based treatment versus parent training for young children with obsessive-compulsive disorder	*J Affect Disord*	D: KQ2: not an RCT or adjusted NRCS
180	Rosa-Alcázar	2021	34867529	Predictors of Parental Accommodation and Response Treatment in Young Children With Obsessive-Compulsive Disorder	*Front Psychiatry*	D: Single-arm study N≥50, unadjusted

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181	Rozenman	2017	27225633	Distinguishing Fear Versus Distress Symptomatology in Pediatric OCD	*Child Psychiatry Hum Dev*	I: Not an intervention/index test of interest
182	Rozenman	2019	31075706	Improvement in anxiety and depression symptoms following cognitive behavior therapy for pediatric obsessive compulsive disorder	*Psychiatry Res*	D: Single-arm study N≥50, unadjusted
183	Rueda-Jaimes	2007	17306168	Validación del Inventario de Obsesiones de Leyton, versión corta, en niños y adolescentes de Bucaramanga (Colombia).	*Aten Primaria*	P: Not a population <21 years with OCD
184	Russman Block	2023	36475374	Resting-State Connectivity and Response to Psychotherapy Treatment in Adolescents and Adults With OCD: A Randomized Clinical Trial	*Am J Psychiatry*	C: Not a comparison of interest
185	Ruta	2010	19557496	Obsessive-compulsive traits in children and adolescents with Asperger syndrome	*Eur Child Adolesc Psychiatry*	I: Not an intervention/index test of interest
186	Sandoval-Lentisco	2023	35849418	Florida Obsessive-Compulsive Inventory¬†and Children's Florida Obsessive Compulsive Inventory: A reliability generalization meta-analysis	*J Clin Psychol*	I: Index test not used for diagnosis
187	Saxena	2002	11838621	Obsessive-compulsive hoarding: symptom severity and response to multimodal treatment	*J Clin Psychiatry*	P: Not a population <21 years with OCD
188	Scahill	1997	9183141	Children's Yale-Brown Obsessive Compulsive Scale: reliability and validity	*J Am Acad Child Adolesc Psychiatry*	I: Index test not used for diagnosis

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189	Scahill	2016	25882391	Sensitivity of the modified Children's Yale-Brown Obsessive Compulsive Scale to detect change: Results from two multi-site trials	*Autism*	P: Not a population <21 years with OCD
190	Schultz	2018	30383480	Psychometric validation of a Danish version of the Obsessive Beliefs Questionnaire - Child Version (OBQ-CV)	*Nord J Psychiatry*	I: Index test not used for diagnosis
191	Schwarzlose	2022	35238927	Picky Eating in Childhood: Associations With Obsessive-Compulsive Symptoms	*J Pediatr Psychol*	P: Not a population <21 years with OCD
192	Scully	2012	2012-99200-025 (PsycINFO)	Child and family predictors of treatment response in childhood obsessive compulsive disorder		D: Not a peer-reviewed publication
193	Selles	2020	2022-97307-001 (PsycINFO)	Family profiles in pediatric obsessive-compulsive disorder	*Journal of Obsessive-Compulsive and Related Disorders*	D: Single-arm study N≥50, unadjusted
194	Sen	2016	28269076	Classification of obsessive-compulsive disorder from resting-state fMRI	*Annu Int Conf IEEE Eng Med Biol Soc*	D: Not a study design of interest
195	Seol	2013	23482407	Korean self-report version of the yale-brown obsessive-compulsive scale: factor structure, reliability, and validity	*Psychiatry Investig*	P: Not a population <21 years with OCD
196	Sevilla-Cermeño	2019	2019-27571-020 (PsycINFO)	Insomnia in pediatric obsessive,Äìcompulsive disorder: Prevalence and association with multimodal treatment outcomes in a naturalistic clinical setting	*Sleep Medicine*	D: Single-arm study N≥50, unadjusted

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197	Shahni Fayz	2023	NA (ad hoc)	Effectiveness of mindfulness-based stress reduction program on emotion regulation and obsessive-compulsive symptoms of child	*Journal of Applied Family Therapy*	D: KQ2: not an RCT or adjusted NRCS
198	Shalev	2009	19542825	Long-term durability of cognitive behavioral therapy gains for pediatric obsessive-compulsive disorder	*J Am Acad Child Adolesc Psychiatry*	D: Single-arm study N≥50, unadjusted
199	Shavitt	2016	CN-01304664 (Cochrane)	Adaptive treatment strategies for children and adolescents with obsessive compulsive disorder	*Journal of the American Academy of Child and Adolescent Psychiatry*	D: Not a peer-reviewed publication
200	Simons	2006	16785776	Metacognitive therapy versus exposure and response prevention for pediatric obsessive-compulsive disorder. A case series with randomized allocation	*Psychother Psychosom*	O: No extractable or new outcomes of interest
201	Skarphedinsson	2015	CN-01471427 (Cochrane)	Continued cognitive-behavior therapy versus sertraline for children and adolescents with obsessive-compulsive disorder that were non-responders to cognitivebehavior therapy: treatment outcome and moderator analysis	*European child & adolescent psychiatry*	D: Not a peer-reviewed publication
202	Skarphedinsson	2015	26348088	Sertraline Treatment of Nonresponders to Extended Cognitive-Behavior Therapy in Pediatric Obsessive-Compulsive Disorder	*J Child Adolesc Psychopharmacol*	D: Single-arm study N≥50, unadjusted

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
203	Skarphedinsson	2016	CN-01304688 (Cochrane)	Long-term effectiveness of treatments for cognitive-behavioral therapy resistant youth with obsessive-compulsive disorder initially randomized to continued cognitive-behavioral therapy or sertraline	*Journal of the American Academy of Child and Adolescent Psychiatry*	D: Not a peer-reviewed publication
204	Skarphedinsson	2017	27209422	Defining cognitive,Äëbehavior therapy response and remission in pediatric OCD: A signal detection analysis of the Children,Äôs Yale,ÄëBrown Obsessive Compulsive Scale	*European Child & Adolescent Psychiatry*	D: Single-arm study N≥50, unadjusted
205	Skarphedinsson		37684419	Family Accommodation in Pediatric Obsessive-Compulsive Disorder: Investigating Prevalence and Clinical Correlates in the NordLOTS Study	*Child Psychiatry Hum Dev ():-*	O: No extractable or new outcomes of interest
206	Smárason	2022	35282768	Age differences in children with obsessive-compulsive disorder: symptoms, comorbidity, severity and impairment	*Nord J Psychiatry*	D: Not a peer-reviewed publication
207	Smárason	2023	37119789	Long-term functional impairment in pediatric OCD after and during treatment: An analysis of distinct trajectories	*Psychiatry Res*	D: Single-arm study of pooled treatments
208	Snider	2005	15820236	Antibiotic prophylaxis with azithromycin or penicillin for childhood-onset neuropsychiatric disorders	*Biol Psychiatry*	P: Not a population <21 years with OCD

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
209	Solmi	2020	32394557	Safety of 80 antidepressants, antipsychotics, anti-attention-deficit/hyperactivity medications and mood stabilizers in children and adolescents with psychiatric disorders: a large scale systematic meta-review of 78 adverse effects	*World Psychiatry*	P: Not a population <21 years with OCD
210	Sperling	2020	139885178 (CINAHL)	The impact of intensive treatment for pediatric anxiety and obsessive-compulsive disorder on daily functioning	*Clinical Child Psychology & Psychiatry*	P: Not a population <21 years with OCD
211	Sperling	2021	34165353	Associations between parental distress and pediatric anxiety and obsessive-compulsive disorder treatment outcomes	*Clin Child Psychol Psychiatry*	D: Single-arm study N≥50, unadjusted
212	Steinberger	2002	12121206	Classification of obsessive-compulsive disorder in childhood and adolescence	*Acta Psychiatr Scand*	O: No extractable or new outcomes of interest
213	Steinhausen	2009	18723315	Performance of the adolescent obsessive-compulsive scale in a community survey	*J Anxiety Disord*	P: Not a population <21 years with OCD
214	Stewart	2004	15180774	Long-term outcome of pediatric obsessive-compulsive disorder: a meta-analysis and qualitative review of the literature	*Acta Psychiatr Scand*	O: No extractable or new outcomes of interest
215	Storch	2004	15572188	Psychometric evaluation of the Children's Yale-Brown Obsessive-Compulsive Scale	*Psychiatry Res*	I: Index test not used for diagnosis

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
216	Storch	2007	17044015	Sequential cognitive-behavioral therapy for children with obsessive-compulsive disorder with an inadequate medication response: a case series of five patients	*Depress Anxiety*	I: Index test not used for diagnosis
217	Storch	2008	18356759	Impact of comorbidity on cognitive-behavioral therapy response in pediatric obsessive-compulsive disorder	*J Am Acad Child Adolesc Psychiatry*	D: Single-arm study N≥50, unadjusted
218	Storch	2008	2008-15242-004 (PsycINFO)	Somatic symptoms in children and adolescents with obsessive-compulsive disorder: Associations with clinical characteristics and cognitive-behavioral therapy response	*Behavioural and Cognitive Psychotherapy*	O: No extractable or new outcomes of interest
219	Storch	2008	105800628 (CINAHL)	Comorbidity of pediatric obsessive-compulsive disorder and anxiety disorders: impact on symptom severity and impairment	*Journal of Psychopathology & Behavioral Assessment*	D: Single-arm study N≥50, unadjusted
220	Storch	2009	2009-08447-010 (PsycINFO)	Children,Äôs Florida Obsessive Compulsive Inventory: Psychometric properties and feasibility of a self-report measure of obsessive,Äìcompulsive symptoms in youth	*Child Psychiatry and Human Development*	I: Index test not used for diagnosis
221	Storch	2010	20610140	Defining treatment response and remission in obsessive-compulsive disorder: a signal detection analysis of the Children's Yale-Brown Obsessive Compulsive Scale	*J Am Acad Child Adolesc Psychiatry*	I: Index test not used for diagnosis

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
222	Storch	2010	CN-01032125 (Cochrane)	D-cycloserine augmentation of cognitive-behavioral therapy in pediatric obsessive-compulsive disorder: a preliminary study	*Neuropsychopharmacology*	D: Not a peer-reviewed publication
223	Storch	2010	20390817	An open trial of intensive family based cognitive-behavioral therapy in youth with obsessive-compulsive disorder who are medication partial responders or nonresponders	*J Clin Child Adolesc Psychol*	D: Not a peer-reviewed publication
224	Storch	2011	20886284	Development and preliminary psychometric evaluation of the Children's Saving Inventory	*Child Psychiatry Hum Dev*	I: Index test not used for diagnosis
225	Storch	2016	CN-01304668 (Cochrane)	Augmentation of cognitivebehavioral therapy with d-cycloserine in pediatric obsessive-compulsive disorder: a randomized controlled trial	*Journal of the American Academy of Child and Adolescent Psychiatry*	D: Not a peer-reviewed publication
226	Storch	2018	28910139	Quality of Life in Children and Youth with Obsessive-Compulsive Disorder	*J Child Adolesc Psychopharmacol*	D: Single-arm study of pooled treatments
227	Storch	2019	30577944	Development and Psychometric Evaluation of the Children's Yale-Brown Obsessive-Compulsive Scale Second Edition	*J Am Acad Child Adolesc Psychiatry*	I: Index test not used for diagnosis
228	Storch	2019	30877851	Sudden gains in cognitive behavioral therapy among children and adolescents with obsessive compulsive disorder	*Journal of behavior therapy and experimental psychiatry*	D: Single-arm study N≥50, unadjusted
229	Storch		38154287	Randomized trial comparing standard versus light intensity parent training for anxious youth	*Behav Res Ther 173():-*	P: Not a population <21 years with OCD

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
230	Stárková	2002	2002-04255-003 (PsycINFO)	Fluvoxamin v pedopsychiatrick√© praxi (retrospektivn√≠ studie) = Fluvoxamine in child and adolescent psychiatry (retrospective study)	*Česká a Slovenská Psychiatrie*	P: Not a population <21 years with OCD
231	Sukhodolsky	2013	23602943	Exposure and response prevention with or without parent management training for children with obsessive-compulsive disorder complicated by disruptive behavior: a multiple-baseline across-responses design study	*J Anxiety Disord*	D: Single-arm study N≥50, unadjusted
232	Sullivan	2018	2018-13260-042 (PsycINFO)	A meta-analysis of the effectiveness and efficiency of d-cycloserine-augmented exposure therapy with treatment resistant pediatric OCD patients	NA	D: Not a peer-reviewed publication
233	Tan	2005	NA (From SRs)	A comparative study of clomipramine and paroxetine in the treatment of adolescents with obsessive-compulsive disorder	*Journal of Binzhou Medical College*	Unable to retrieve full text
234	Thamrin	2017	CN-01452332 (Cochrane)	Reducing different types of family accommodation for families of youth with obsessive-compulsive disorder: comparison of two family intervention approaches	*Journal of the American Academy of Child and Adolescent Psychiatry*	D: Not a peer-reviewed publication
235	Thienemann	2001	11699798	Manual-Driven group cognitive-behavioral therapy for adolescents with obsessive-compulsive disorder: a pilot study	*J Am Acad Child Adolesc Psychiatry*	D: Single-arm study N≥50, unadjusted

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
236	Thierfelder	2022	36085677	Multimodal Sensor-Based Identification of Stress and Compulsive Actions in Children with Obsessive-Compulsive Disorder for Telemedical Treatment	*Annu Int Conf IEEE Eng Med Biol Soc*	D: Single-arm study N≥50, unadjusted
237	Tini	2022	35248877	Therapeutic drug monitoring of sertraline in children and adolescents: A naturalistic study with insights into the clinical response and treatment of obsessive-compulsive disorder	*Compr Psychiatry*	D: Single-arm study N≥50, unadjusted
238	Tollefson	1994	7961535	Continuation treatment of OCD: double-blind and open-label experience with fluoxetine	*J Clin Psychiatry*	P: Not a population <21 years with OCD
239	Torp	2015	25463245	Effectiveness of cognitive behavior treatment for pediatric obsessive-compulsive disorder: acute outcomes from the Nordic Long-term OCD Treatment Study (NordLOTS)	*Behav Res Ther*	O: No extractable or new outcomes of interest
240	Torp	2017	2017-47863-013 (PsycINFO)	Early responders and remitters to exposure-based CBT for pediatric OCD	*Journal of Obsessive-Compulsive and Related Disorders*	D: Single-arm study N≥50, unadjusted
241	Turner	2009	19545482	A pilot study of telephone cognitive-behavioural therapy for obsessive-compulsive disorder in young people	*Behav Cogn Psychother*	D: Single-arm study N≥50, unadjusted
242	Uher	2008	18023139	Self-, parent-report and interview measures of obsessive-compulsive disorder in children and adolescents	*J Anxiety Disord*	I: Index test not used for diagnosis

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
243	Ulloa	2004	2004-18723-003 (PsycINFO)	Estudio de validez y confiabilidad de la versi√≥n en espa√±ol de la escala Yale-Brown del trastorno obsesivo-compulsivo para ni√±os y adolescentes = Validity and reliability of the Spanish version of Yale-Brown rating scale for children and adolescents	*Actas Espa√±olas de Psiquiatr√≠a*	I: Index test not used for diagnosis
244	Valderhaug	2007	16836977	An open clinical trial of cognitive-behaviour therapy in children and adolescents with obsessive-compulsive disorder administered in regular outpatient clinics	*Behav Res Ther*	D: Single-arm study N≥50, unadjusted
245	Vattimo	2016	CN-01304623 (Cochrane)	Predicting obsessive-compulsive disorder treatment response in pediatric patients using structural neuroimaging correlates: a comparison between simple linear regression and support vector regression	*Journal of the American Academy of Child and Adolescent Psychiatry*	D: Not a peer-reviewed publication
246	Vattimo	2017	CN-01439240 (Cochrane)	Treatment response prediction in pediatric patients with OCD using structural neuroimaging correlates: simple linear regression versus support vector regression	*Neuropsychopharmacology*	D: Not a peer-reviewed publication
247	Vattimo	2019	30972581	Caudate volume differences among treatment responders, non-responders and controls in children with obsessive-compulsive disorder	*European Child & Adolescent Psychiatry*	C: Not a comparison of interest

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
248	Vause	2017	CN-01714036 (Cochrane)	Preliminary Randomized Trial of Function-Based Cognitive-Behavioral Therapy to Treat Obsessive Compulsive Behavior in Children with Autism Spectrum Disorder	*Focus on autism and other developmental disabilities*	P: Not a population <21 years with OCD
249	Vause	2020	30293128	Functional Behavior-Based Cognitive-Behavioral Therapy for Obsessive Compulsive Behavior in Children with Autism Spectrum Disorder: A Randomized Controlled Trial	*J Autism Dev Disord*	P: Not a population <21 years with OCD
250	Vulink	2009	19497245	Quetiapine augments the effect of citalopram in non-refractory obsessive-compulsive disorder: a randomized, double-blind, placebo-controlled study of 76 patients	*J Clin Psychiatry*	P: Not a population <21 years with OCD
251	Wagner	2003	12880500	Remission status after long-term sertraline treatment of pediatric obsessive-compulsive disorder	*J Child Adolesc Psychopharmacol*	O: No extractable or new outcomes of interest
252	Walitza	2008	18200431	Children and adolescents with obsessive-compulsive disorder and comorbid attention-deficit/hyperactivity disorder: preliminary results of a prospective follow-up study	*J Neural Transm (Vienna)*	D: Single-arm study N≥50, unadjusted
253	Walkup	1999	CN-00319964 (Cochrane)	Fluvoxamine in childhood OCD: long-term treatment	*Journal of the european college of neuropsychopharmacology*	D: Not a peer-reviewed publication
254	Wei	2020	2020-48460-005 (PsycINFO)	Emotion regulation strategy use and symptom change during intensive treatment of transitional age youth patients with obsessive compulsive disorder	*Journal of Behavioral and Cognitive Therapy*	P: Not a population <21 years with OCD

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
255	Weir	2000	10920742	Treating obsessive-compulsive and tic disorders	*Cmaj*	P: Not a population <21 years with OCD
256	Wever	1997	9088493	Juvenile obsessive-compulsive disorder	*Aust N Z J Psychiatry*	D: Single-arm study N≥50, unadjusted
257	Whiteside	2010	20569789	An uncontrolled examination of a 5-day intensive treatment for pediatric OCD	*Behav Ther*	D: Single-arm study N≥50, unadjusted
258	Whiteside	2018	28918645	Increasing Availability of Exposure Therapy Through Intensive Group Treatment for Childhood Anxiety and OCD	*Behav Modif*	D: Single-arm study N≥50, unadjusted
259	Wilens	1999	10230189	Absence of cardiovascular adverse effects of sertraline in children and adolescents	*J Am Acad Child Adolesc Psychiatry*	O: No extractable or new outcomes of interest
260	Wolters	2011	21497051	Psychometric properties of a Dutch version of the Obsessive Beliefs Questionnaire--Child Version (OBQ-CV)	*J Anxiety Disord*	I: Index test not used for diagnosis
261	Wolters	2012	22197341	Psychometric properties of the Dutch version of the Meta-Cognitions Questionnaire-Adolescent Version (MCQ-A) in non-clinical adolescents and adolescents with obsessive-compulsive disorder	*J Anxiety Disord*	I: Index test not used for diagnosis
262	Wolters	2015	CN-01098688 (Cochrane)	Improving treatment: supplementing cognitive behavioral therapy with a cognitive bias modification training for children and adolescents with OCD	*European child & adolescent psychiatry*	D: Not a peer-reviewed publication

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
263	Wolters	2019	30032391	Mediating Mechanisms in Cognitive Behavioral Therapy for Childhood OCD: The Role of Dysfunctional Beliefs	*Child Psychiatry Hum Dev*	O: No extractable or new outcomes of interest
264	Wong	2020	32361667	Manipulating visual perspective for obsessional imagery and its impact on obsessive-compulsive symptoms in an analogue sample	*J Anxiety Disord*	P: Not a population <21 years with OCD
265	Wu	2009	19345557	Inferential confusion, obsessive beliefs, and obsessive-compulsive symptoms: a replication and extension	*J Anxiety Disord*	P: Not a population <21 years with OCD
266	Xia	2012	2012-02515-010 (PsycINFO)	Revision of the Children's Florida Obsessive Compulsive Inventory	*Chinese Mental Health Journal*	P: Not a population <21 years with OCD
267	Yamamuro	2016	27552672	A longitudinal event-related potential study of selective serotonin reuptake inhibitor therapy in treatment-na√Øve pediatric obsessive compulsive disorder patients	*Psychiatry Res*	D: Not a study design of interest
268	Yaryura-Tobias	2000	10870874	Parental obsessive,Äìcompulsive disorder as a prognostic factor in a year long fluvoxamine treatment in childhood and adolescent obsessive,Äìcompulsive disorder	*International Clinical Psychopharmacology*	D: Single-arm study N≥50, unadjusted
269	Yucelen	2006	16324902	Interrater reliability and clinical efficacy of Children's Yale-Brown Obsessive-Compulsive Scale in an outpatient setting	*Compr Psychiatry*	I: Index test not used for diagnosis

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
270	Zheng	2020	32364596	Association of Pediatric Acute-Onset Neuropsychiatric Syndrome With Microstructural Differences in Brain Regions Detected via Diffusion-Weighted Magnetic Resonance Imaging	*JAMA Netw Open*	D: Not a study design of interest
271	Ólafsdóttir	2023	35013848	Body Dysmorphic Symptoms in Youth with Obsessive-compulsive Disorder: Prevalence, Clinical Correlates, and Cognitive Behavioral Therapy Outcome	*Child Psychiatry Hum Dev*	D: Single-arm study N≥50, unadjusted
272	Şimşek	2022	35330724	Developing and Examining the Effectiveness of a Cognitive Behavioral Therapy-Based Psychoeducation Practice for Reducing Obsessive-Compulsive Symptoms in Adolescents: A Mixed-Methods Study With a Turkish Sample	*Front Psychol*	P: Not a population <21 years with OCD
273	.	2020	L2006956099 (Embase)	The effect of transdiagnostic emotion-focused treatment on obsessive-compulsive symptoms in children and adolescents	*Journal of Obsessive-Compulsive and Related Disorders*	P: Not a population <21 years with OCD
274	.	.	L2015668905 (Embase)	The Role of Intolerance of Uncertainty in Treatment for Pediatric Anxiety Disorders and Obsessive-Compulsive Disorder	*Evidence-Based Practice in Child and Adolescent Mental Health*	D: Single-arm study N≥50, unadjusted
275	.	.	NCT01302080 (CT.gov)	Sertraline Pediatric Registry for the Evaluation of Safety (SPRITES)	*CT.gov*	P: Not a population <21 years with OCD
276	.	.	NCT01281969 (CT.gov)	Intravenous Immunoglobulin for PANDAS	*CT.gov*	I: Not an intervention/index test of interest

No.	First Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
277	.	.	NCT01617083 (CT.gov)	Antibiotic Treatment Trial for the PANDAS/PANS Phenotype	*CT.gov*	I: Not an intervention/index test of interest
278	.	.	NCT02421315 (CT.gov)	Overlapping Neural Circuits in Pediatric OCD	*CT.gov*	I: Not an intervention/index test of interest
279	.	.	NCT01018056 (CT.gov)	Developing New Treatments for Tourette Syndrome: Therapeutic Trials With Modulators of Glutamatergic Neurotransmission	*CT.gov*	P: Not a population <21 years with OCD
280	.	.	NCT00592852 (CT.gov)	Fluoxetine for Obsessive-Compulsive Disorder in Children and Adolescents With Bipolar Disorder	*CT.gov*	D: Single-arm study N≥50, unadjusted
281	.	.	NCT01172873 (CT.gov)	D-Cycloserine Augmentation to CBT With Exposure and Response Prevention in Adults and Adolescents With OCD	*CT.gov*	D: Single-arm study N≥50, unadjusted
282	.	.	NCT02797808 (CT.gov)	Effects of Sertraline on Brain Connectivity in Adolescents With OCD	*CT.gov*	D: Single-arm study N≥50, unadjusted

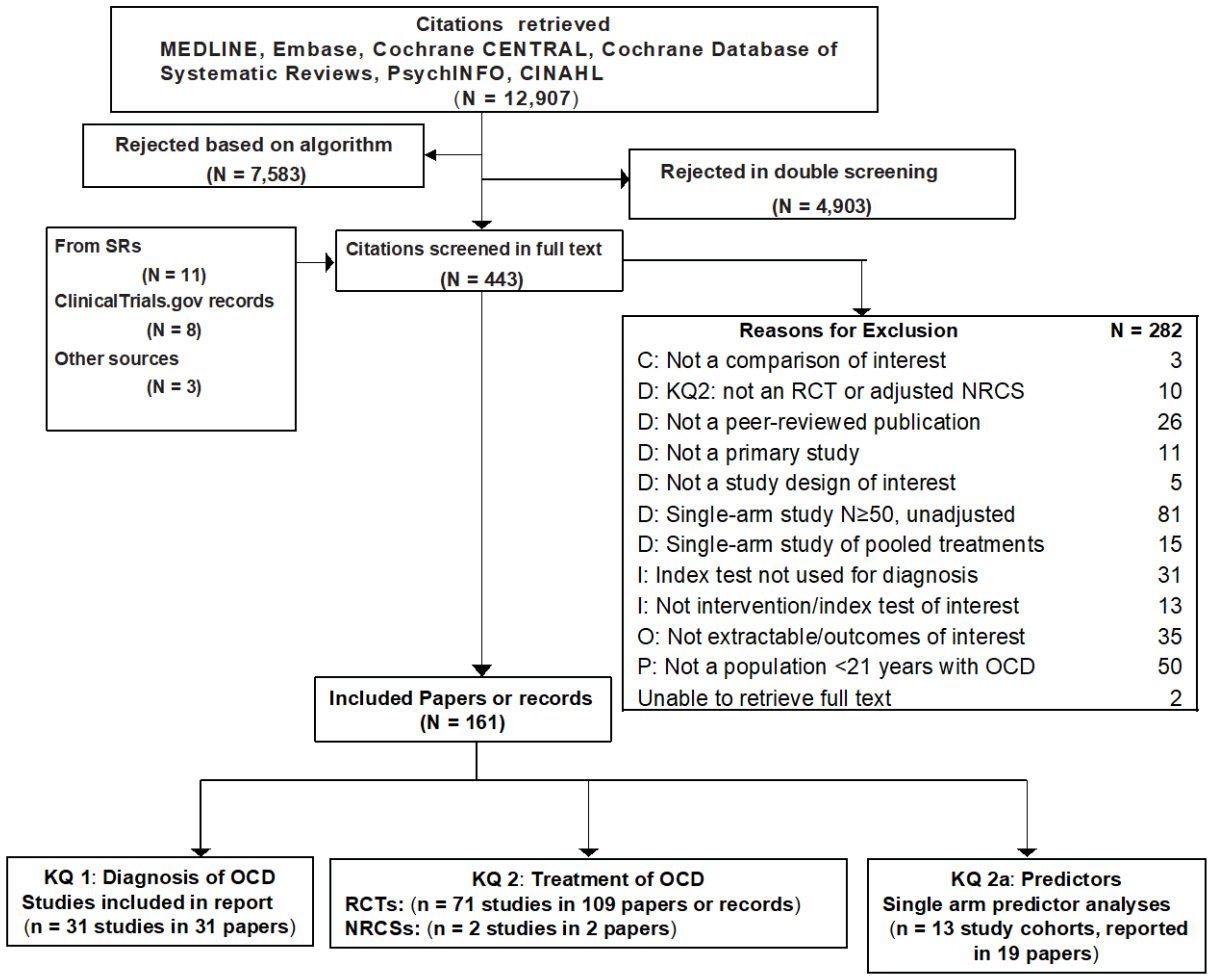
Abbreviations: ad hoc = not found in a search; Cochrane = Cochrane Register of Clinical Trials; CT.gov = clinicaltrials.gov; N = number of participants enrolled; NA = not applicable; No. = number; OCD = obsessive compulsive disorder; PICOD: = Population, Intervention or index test, comparator, outcome, design; PMID = PubMed identifier

Appendix C. Results: Design, Arm, and Sample Details

Results of Literature Searches

As illustrated by Figure C-1, our citation search retrieved a combined 12,907 citations. Of these, 421 were deemed potentially relevant and retrieved in full text. We identified and additional 22 papers and records from other sources. After full-text screening, our review includes 31 eligible studies for KQ1 (reported in 31 papers). For KQ 2, we included 71 RCTs reported in 109 papers or records and 2 NRCSs (in 2 papers). For KQ 2a, we included 19 papers that reported predictor analyses from 13 study cohorts.

Figure C-1. Flow diagram for studies



Abbreviations: CINAHL = Cumulative Index of the Nursing and Allied Health Literature, KQ = Key Question; N = number; NRCS = nonrandomized comparative study; OCD = obsessive compulsive disorder; P:I:C:O:D: = Population, Intervention or index test, comparator, outcome, design RCT = randomized controlled trial; SR = systematic review

Description of Included Studies

Overall Summary of Study and Patient Characteristics

Appendix Tables C-1.1 to C-2.3.2 summarize the design, arm, and patient characteristics in separate tables for each KQ.

Table C-1.1. Key Question 1: Baseline data for brief assessment tools, Part 1

Author, Year, PMID Country Years	OCD Group Source	Comparison Group Source	Diagnosis Criteria	Diagnosis: Specific Method/Evaluator
Abramovitch, 2022 35091252 US/Canada/Australia	Outpatient psychiatric clinic	Outpatient psychiatric clinic	DSM-IV	Structured Interview + Clinical Diagnosis MD/PhD
Abramovitch, 2022, 35697331 US/Canada/Australia	Outpatient psychiatric clinic	Outpatient psychiatric clinic	DSM-IV	Structured Interview + Clinical Diagnosis MD/PhD
Andersen, 2012, 23171745 Denmark 2000-2005	Child Psychiatric Outpatient Clinic	Child Psychiatric Outpatient Clinic	ICD-10/CBCL	Structured Interview Both
Bamber, 2002, 12364847 UK	Clinical services and depression research study	Secondary schools	DSM-IV (KSADS-PL)	Structured interview NR
Battle, 2013, 2013-15434-007 Spain	Clinical services receiving medical care in a child hospital	Primary health care child assistance units	DSM-IV-TR	NR
Hudziak, 2006, 16423147 US	Outpatient psychiatric clinic	Outpatient psychiatric clinic	DSM-III-R	Clinical Diagnosis MD/PhD
Ivarsson, 2008, 18280696 Sweden	Outpatient psychiatric clinic	Outpatient psychiatric clinic	DSM-IV	Structured Interview + Clinical Diagnosis MD/PhD
Lambe, 2021, 37431399 Canada	Outpatient psychiatric clinic	Tertiary care clinics	DSM-IV or DSM-V	Structured Interview + Clinical Diagnosis MD/PhD
Piqueras, 2015, 27703719 Spain	Outpatient psychiatric clinic	NR	NR	NR
Piqueras, 2017, 27283942 Spain	Child and adolescent psychiatry unit	Students in school	DSM-IV-TR (K-SADS-PL)	Structured Interview + Clinical Diagnosis MD/PhD
Rough, 2020, 32030629 US	Psychiatry clinic	NR	DSM-V, K-SADS-PL, SOCOBS, CY-BOCS	Structured Interview NR
Saad, 2017, 28151703 Brazil	Cohort Study for Psychiatric Disorders	Cohort Study for Psychiatric Disorders	DAWBA DSM-IV	Structured Interview + Clinical Diagnosis MD/PhD
Sattler, 2018, 2019-05127-008 US	Outpatient child and adolescent anxiety center at Mayo Clinic	Outpatient child and adolescent anxiety center at Mayo Clinic	DSM-IV TR	Structured Interview + Clinical Diagnosis MD/PhD
Shafran, 2003, 12550826 UK/Canada	Specialist OCD Clinic	Psychiatric clinics	DSM-IV	Structured Interview + Clinical Diagnosis MD/PhD
Skarphedinsson, 2021, 34293000 Sweden	Outpatient child and adolescent psychiatry (CAP) clinic	Outpatient child and adolescent psychiatry (CAP) clinic	DSM-IV	Structured Interview + Clinical Diagnosis MD/PhD
Stewart, 2005, 16379516 US	Clinical treatment program	NA	DSM-IV (K-SADS-E)	Structured Interview + Clinical Diagnosis MD/PhD

Author, Year, PMID Country Years	OCD Group Source	Comparison Group Source	Diagnosis Criteria	Diagnosis: Specific Method/Evaluator
Storch, 2006, 16046257 US 1998-2004	Outpatient psychiatric clinic	Patients undergoing psychodiagnostic testing	NR	Clinical Diagnosis MD/PhD
Storch, 2011, 21353458 US	Unclear	NA	DSM-IV-TR (ADIS-IV-P)	Structured Interview + Clinical Diagnosis MD/PhD
Uher, 2007, 17906247 UK	Clinic for Obsessive–Compulsive and Related Disorders	Clinic for Obsessive–Compulsive and Related Disorders	ICD-10	Structured Interview + Clinical Diagnosis MD/PhD
Whiteside, 2012, 22078243 US	Outpatient clinic for concerns regarding anxiety	Outpatient clinic for concerns regarding anxiety	DSM-IV	Structured Interview + Clinical Diagnosis Research Associate
Zemestani, 2021, 2021-61128-001 Iran	Psychiatric outpatient clinic	Schools	DSM-V (SCID-5-CV)	Structured Interview + Clinical Diagnosis MD/PhD
Zemestani, 2022, 33409771 Iran	psychiatric outpatient clinic	Elementary and high schools	DSM-5 (SCID-5-CV)	Structured interview MD/PhD

Abbreviations: ADIS-IV-P = ADIS-IV-P, based on the DSM-IV, parent report; CBCL = Child Behavior Checklist; CY-BOCS = Children's Yale-Brown Obsessive Compulsive Scale; DAWBA = Development and Well-Being Assessment; DSM = Diagnostic and Statistical Manual of Mental Disorders; ICD = International Classification of Diseases; K-SADS-E = Schedule for Affective Disorders and Schizophrenia for School-Age Children-Epidemiological samples; K-SADS-PL = Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version; MD = Doctor of medicine; NR = Not reported; OCD = Obsessive Compulsive Disorder; PhD = Doctor of philosophy; PMID = PubMed Identifier; SCID-5-CV = Structured Clinical Interview for DSM-5 Disorders—Clinician Version; SOCOBS = Schedule for Obsessive-Compulsive and Other Behavioral Syndromes; TR = Text revision; UK = United Kingdom; US = United States.

Table C-1.2. Key Question 1: Baseline data for brief assessment tools, Part 2

Author, Year, PMID Country Years	Age, Mean (SD) [Range] Male, N (%)	Race, N% Ethnicity, N%	Comorbidities; N%
Abramovitch, 2022 35091252 US/Canada/Australia	12.6 (2.9) Male, 380 (48.3)	White 666 (84.6) Black/African American 6 (0.8) Asian 16 (2) Hispanic 25 (3.2)	NR
Abramovitch, 2022, 35697331 US/Canada/Australia	12.6 (2.9) Male, 380 (48.3)	White 666 (84.6) Black/African American 6 (0.8) Asian 16 (2) Hispanic 25 (3.2)	NR
Andersen, 2012, 23171745 Denmark 2000-2005	11.7 (2.9) [4-17] Male, 78 (46.4)	NR	NR
Bamber, 2002, 12364847 UK	13.32 (0.95) Male, 4 (44)	NR	Depression 14 (60.9)

Author, Year, PMID Country Years	Age, Mean (SD) [Range] Male, N (%)	Race, N% Ethnicity, N%	Comorbidities; N%
Battle, 2013, 2013-15434-007 Spain	13.2 (2.6) [8-17] Male, 54 (69.23)	NR	NR
Hudziak, 2006, 16423147 US	NR	NR	Anxiety 31 (25); Depression 26 affective disorder 26% vs. 40% in clinical controls; Conduct disorder 32%; disruptive disorders 32% in clinical controls; ADHD 21% in OCD group vs. 47% in clinical controls;
Ivarsson, 2008, 18280696 Sweden	NR [4-17] Male, 190 (52.5)	NR	NR
Lambe, 2021, 37431399 Canada	11.71 (3.58) [6-21] Male, 32.4%	NR	NR
Piqueras, 2015, 27703719 Spain	14.62 (2.65) [9-19] Male, 46 (49)	NR	Anxiety 15 (16); Depression 2 (2.1); Tics/Tourette's 4 (4.3)
Piqueras, 2017, 27283942 Spain	14.62 (2.65) [8-19] Male, 46 (48.9)	NR	Anxiety 20 (21.3); Depression 7 (7.4); Bipolar spectrum disorders 2 (2.1); Tics/Tourette's 8 (8.5); ADHD 7 (7.4); ODD 3 (3.2)
Rough, 2020, 32030629 US	14.19 (3.30) [7-18] Male, 324 (71.4)	White 672 (89) Black/African American 1 (0.1) Asian 4 (0.8) American Indian 15 (3.4) Other 2 (0.4) Hispanic 35 (4.6)	Anxiety 164 (36.1); Depression 65 (14.3); Tics/Tourette's 34 (7.49); ADHD 115 (25.3)
Saad, 2017, 28151703 Brazil	8.86 (1.84) [6-12] Male, 1382 (55)	NR	Anxiety 74 (30.33); Depression 36 (14.75); Tics/Tourette's 8 (3.28); Conduct disorder 13 (5.33); ADHD 56 (22.95); ODD 27 (11.07)
Sattler, 2018, 2019-05127-008 US	12.2 (2.9) [5-18] Male, 501 (45.8)	White 951 (86.9)	NR
Shabani, 2019, 2019-80248-001 Iran	14.7 (1.8) [10-18] Male, 68 (53.1)	NR	NR
Shafran, 2003, 12550826 UK/Canada	11.9 (2.3) [7-17] Male, 38 (43)	NR	NR
Skarphedinsson, 2021, 34293000 Sweden 2010-2013	12.1 (3.2) [6.1-17.8] Male, 78 (56.2)	NR	Comorbidities: anxiety 50 (36), depression 41 (30), bipolar disorder 63 (45.5), conduct disorder 6 (4.5), ADHD 74 (53.2), Oppositional defiant disorder 32 (23.2)

Author, Year, PMID Country Years	Age, Mean (SD) [Range] Male, N (%)	Race, N% Ethnicity, N%	Comorbidities; N%
Stewart, 2005, 16379516 US	11.5 (3.1) Male, NR	NR	NR
Storch, 2006, 16046257 US 1998-2004	10.5 (3.3) [4-18] Male, 135 (71.0)	White 163 (86) Black/African American 15 (8.0) Other 8 (4) Hispanic 4 (2)	NR
Storch, 2011, 21353458 US	11.48 (2.76) [7-18] Male, 31 (62)	White 41 (82) Black 1 (2) Asian 2 (4) Other 4 (8) Hispanic 2 (4)	Comorbidities: Psychotic disorder, Bipolar disorder, ASD/PDD excluded
Uher, 2007, 17906247 UK	NR [11-15] NR	NR	NR
Whiteside, 2012, 22078243 US	12.81 (3.1) [7-18] Male, 83 (52)	White 154 (96.7)	NR
Zemestani, 2021, 2021-61128-001 Iran	15.82 (1.70) Male, 20 (32.3)	NR	Anxiety 30 (48.3); Depression 12 (19.4); ADHD 17 (27.6)
Zemestani, 2022, 33409771 Iran	15.82 (1.70) [7-17] Male, 20 (32.3)	NR	Anxiety 30 (48); Depression 30 (19.4); ADHD 17 (27.6)

Abbreviation: ADHD = Attention Deficit Hyperactivity Disorder; ASD = Autism Spectrum Disorder; NR = Not reported; OCD = Obsessive Compulsive Disorder; ODD = Oppositional Defiant Disorder; PDD = Pervasive Developmental Disorder; PMID = PubMed Identifier; PTSD = post-traumatic stress disorder; SD = Standard deviation; TS = Tourette Syndrome; UK = United Kingdom; US = United States, vs = versus.

Table C-2.1.1. Key Question 2: Design details, RCTs

Author, Year, PMID Study Name Country Years Registry Number	Industry Funding	Diagnostic Method, Evaluator CY-BOCS Cutoff	Excluded Comorbidities	Exclusion Criteria Regarding Previous Treatment	Previous Medication Status
Agrawal, 2024, India, CN-02530420	NR	DSM-5: K-SADS-PL CY-BOCS ≥14	All other psychiatric conditions excluded (except major depressive disorder)	NR	NR
Alaghband-Rad, 2009, 19190958 Iran 1999-2002	NR	DSM-IV: Clinical diagnosis MD/PhD	.	.	.

Author, Year, PMID Study Name Country Years Registry Number	Industry Funding	Diagnostic Method, Evaluator CY-BOCS Cutoff	Excluded Comorbidities	Exclusion Criteria Regarding Previous Treatment	Previous Medication Status
Asbahr, 2005, 16239861 Brazil 2000-2002	No	DSM-IV: Structured interview	ADHD; ASD/PDD; Tics/Tourette's; Psychotic disorders; Depressive disorders; Trauma/stressor related disorders; Bipolar spectrum disorders; BPD; any organic brain disorder.	Subjects with previous or current treatment were excluded.	.
Aspvall, 2021, 33974020 Sweden 2017-2020; NCT03263546	No	DSM-V: Clinical diagnosis MD/PhD ≥16	ASD/PDD; Psychotic disorders; Intellectual impairment Explicitly excluded	Course of CBT for OCD in the past 12 months or change in any psychotropic medication in the 6 weeks before the pretreatment assessment.	Dose optimized/stabilized
Barrett, 2003, 12647571 US <2003	NR	DSM-IV OCD: Structured interview MD/PhD	Tics/Tourette's; Psychotic disorders; other anxiety disorders, Depressive disorders Explicitly excluded	.	.
Barrett, 2004, 14691360 Australia	No	DSM-IV: Structured interview Research associate or similar	ADHD; ASD/PDD; Tics/Tourette's; Conduct Disorder; Psychotic disorders; other anxiety disorders; Depressive disorders; Intellectual impairment; ODD	Subjects receiving concurrent psychotherapy were excluded	Dose optimized/stabilized
Bolton, 2008, 17207457 UK 2008	No	DSM-IV: Clinical diagnosis		Concurrent medication treatment for OCD	.
Bolton, 2011, 21644984 UK 2011	No	DSM-IV	ASD/PDD; Psychotic disorders	.	Dose optimized/stabilized
Comer, 2017, 27869451 US 2012-2016	No	NR	PANS/PANDAS; ADHD; ASD/PDD; Tics/Tourette's; Conduct Disorder; Psychotic disorders; other anxiety disorders; Depressive disorders; Intellectual impairment; Trauma/stressor related disorders; ODD; Bipolar spectrum disorders	Child receiving medication or psychotherapy to manage emotional or behavioral problems	.

Author, Year, PMID Study Name Country Years Registry Number	Industry Funding	Diagnostic Method, Evaluator CY-BOCS Cutoff	Excluded Comorbidities	Exclusion Criteria Regarding Previous Treatment	Previous Medication Status
de Haan, 1998, 9785713 The Netherlands	NR	DSM-III-R: Clinical diagnosis + Structured interview MD/PhD	ASD/PDD; Tics/Tourette's; Psychotic disorders; Depressive disorders; Intellectual impairment	Treatment with behavior therapy or serotonergic antidepressants in the 6 months	.
DeVeaugh-Geiss, 1992, 1537780 US 1986-1988	Yes	DSM-III	ADHD; ASD/PDD; Tics/Tourette's; Psychotic disorders; Depressive disorders; Intellectual impairment; Bipolar spectrum disorders	Concomitant behavioral therapy.	.
Farrell, 2013, 23722990 Australia 2009-2010	No	≥19	.	.	.
Farrell, 2022, 35084071 Australia 2015-2019	No	ADIS-P CSR: Structured interview MD/PhD ≥16	ASD/PDD; Psychotic disorders; Bipolar spectrum disorders	Receiving concurrent psychological treatment.	Dose optimized/stabilized
Fatori, 2018, 30025255 Brazil 2018	No	DSM-IV MD/PhD ≥16	.	.	.
Flament, 1985, 3899048 US	NR	DSM-III: Clinical diagnosis MD/PhD	Tics/Tourette's; Psychotic disorders; Depressive disorders; Intellectual impairment	No response to previous therapy	.
Franklin, 2011, 21934055 POTS II United States 2004-2009 NCT00074815	No	NR: Clinical diagnosis MD/PhD ≥16	PANS/PANDAS; ADHD; ASD/PDD; Tics/Tourette's; Conduct Disorder; Psychotic disorders; other anxiety disorders; Depressive disorders; Intellectual impairment; Trauma/stressor related disorders; ODD; Bipolar spectrum disorders	Having failed an adequate CBT trial (>10 sessions)	Dose optimized/stabilized
Freeman, 2008, 18356758 US ~2008	No	DSM-IV MD/PhD ≥11	PANS/PANDAS; ADHD; ASD/PDD; Tics/Tourette's Conduct Disorder; other anxiety disorders; Depressive disorders; Intellectual impairment; Trauma/stressor related disorders; ODD; Bipolar spectrum disorders	No response to 10 sessions of E/RP; or 6 weeks of medication	Dose optimized/stabilized

Author, Year, PMID Study Name Country Years Registry Number	Industry Funding	Diagnostic Method, Evaluator CY-BOCS Cutoff	Excluded Comorbidities	Exclusion Criteria Regarding Previous Treatment	Previous Medication Status
Freeman, 2014, 24759852 POTS Jr US 2006-2011 NCT00533806	No	NR: Clinical diagnosis MD/PhD ≥16	PANS/PANDAS; ASD/PDD	.	.
Geller, 2001, 11437015 US 2001	Yes	DSM-IV: Clinical diagnosis ≥16	ADHD; Tics/Tourette's; Psychotic disorders; Depressive disorders; Bipolar spectrum disorders	Ongoing therapy for OCD or depression other than supportive psychotherapy.	.
Geller, 2003, 12880497 US 1997-1998	Yes	DSM-IV: Structured interview MD/PhD ≥16	ADHD; Psychotic disorders; Intellectual impairment	No medication ≤ 30 days; no previous psychological treatment	Dose optimized/stabilized
Geller, 2004, 15502598 US, Canada 2000-2001	Yes	DSM-IV: Structured interview MD/PhD ≥17	ASD/PDD; Tics/Tourette's; Psychotic disorders; Depressive disorders; Intellectual impairment; Bipolar spectrum disorders	Previous nonresponse to SSRIs; concurrent treatment.	.
Ghanizadeh, 2017, 28659986 Iran 2011-2012	No	DSM-IV-TR: Structured interview	ADHD; Psychotic disorders	.	.
Grant, 2014, 24356715 US 2011-2012 NCT00251303	No	DSM-IV: Structured interview MD/PhD ≥20	ASD/PDD; Psychotic disorders; other anxiety disorders	.	.
Guo, 2008; China 2001-2005	NR	CCMD-3 ≥16	Conduct Disorder	.	.
He, 2007; China; 2005-2006	NR	CCMD ≥16	Conduct Disorder	.	.
Himle, 2024; US 38103359	No	DSM-IV: KID-SCID ≥16	Bipolar disorder, psychosis, intellectual disability, hoarding disorder, substance dependence, suicidality, current or past major depressive disorder	Excluded if they had a previously failed course of ERP for OCD	Stable dose of SSRI or SNRI for at least 4 weeks. Not on antipsychotics, antidepressants, lithium or stimulants

Author, Year, PMID Study Name Country Years Registry Number	Industry Funding	Diagnostic Method, Evaluator CY-BOCS Cutoff	Excluded Comorbidities	Exclusion Criteria Regarding Previous Treatment	Previous Medication Status
Hollmann, 2022, 36329915 Germany 2019-2022 NCT05037344	No	DSM-V: Clinical diagnosis MD/PhD ≥16	Psychotic disorders; Intellectual impairment	.	.
Lenhard, 2017, 27993223 BiPOCD Sweden 2014-2015 NCT02191631	No	DSM-V: Clinical diagnosis + Structured interview MD/PhD ≥16	ASD/PDD; Psychotic disorders; Bipolar spectrum disorders	Completed CBT for OCD within the past 12 months, ongoing psychological treatment of OCD.	Dose optimized/stabilized
Leonard, 1989, 2686576, US	No	DSM 3: Structured interview + Clinical diagnosis MD/PhD	Tics/Tourette's; Psychotic disorders; Intellectual impairment	.	.
Lewin, 2014, 24657310 US 2011-2013 NCT01447966	No	DSM-IV: Clinical diagnosis MD/PhD ≥16	ADHD; ASD/PDD; Psychotic disorders; Intellectual impairment	Recent change in psychotropic medication, concurrent psychotherapy or behavioral intervention.	.
Li, 2020, 31800306 US 2012-2020 NCT01172275	Yes	Clinical diagnosis MD/PhD ≥16	Tics/Tourette's; Psychotic disorders; Intellectual impairment; Bipolar spectrum disorders	.	.
Liebowitz, 2002, 12447029 US 1991-1998	No	DSM-III-R or DSM-IV ≥16	Psychotic disorders	Previous fluoxetine treatment at 40 mg/day or more for at least 4 weeks	.
Liu, 2012 China 2010-2011	No	ICD-10 ≥16	Depressive disorders	.	.
Ma, 2014 China 2007-2013	NR	≥17	.	.	.
March, 1990, 19630661 US ~1990	Yes	DSM-III: Clinical diagnosis MD/PhD	ASD/PDD; Tics/Tourette's; Psychotic disorders; other anxiety disorders; Depressive disorders; Intellectual impairment; Trauma/stressor related disorders; Bipolar spectrum disorders	.	.

Author, Year, PMID Study Name Country Years Registry Number	Industry Funding	Diagnostic Method, Evaluator CY-BOCS Cutoff	Excluded Comorbidities	Exclusion Criteria Regarding Previous Treatment	Previous Medication Status
March, 1998, 9842950 US	Yes	DSM-III-R: Clinical diagnosis + Structured interview ≥16	ASD/PDD; Conduct Disorder; Intellectual impairment	Participated in a previous sertraline study or be treated with sertraline.	Dose optimized/stabilized
Mataix-Cols, 2014, 24262813 UK ISRCTN70977225	No	DSM-IV ≥17	ASD/PDD; Psychotic disorders; Bipolar spectrum disorders	.	Dose optimized/stabilized
Merlo, 2010, 19675960 US 2019	NR	NR: Structured interview ≥16	ASD/PDD; Psychotic disorders	.	.
Nai, 2009; China; 2005-2008	NR	CCMD-3 ≥16	Conduct Disorder	.	.
Nasiry, 2020 Cognitive Bias Modification of Interpretation (CBMI) Iran ~2020	No	DSM-V: Clinical diagnosis MD/PhD ≥15	ADHD; ASD/PDD; Tics/Tourette's; Conduct Disorder; Psychotic disorders; other anxiety disorders; Depressive disorders; Intellectual impairment; Trauma/stressor related disorders; ODD; Bipolar spectrum disorders	.	.
NCT01933919 Japan 2013-2015	NR	NR ≥16	ADHD; Tics/Tourette's; Psychotic disorders; Depressive disorders; Intellectual impairment; Bipolar spectrum disorders	Fluvoxamine ≤ 2 months	.
Neziroglu, 2000, 11191690 US 2000	No	DSM-IV MD/PhD	.	.	.
Noras, 2022, 35748547 Iran 2020-2021 IRCT20191127045521N1	No	DSM-V: Clinical diagnosis MD/PhD	Psychotic disorders	Exclude: Phenobarbital, Oxazepam, Sedative drug consumption	.

Author, Year, PMID Study Name Country Years Registry Number	Industry Funding	Diagnostic Method, Evaluator CY-BOCS Cutoff	Excluded Comorbidities	Exclusion Criteria Regarding Previous Treatment	Previous Medication Status
Peris, 2013, 22548378; US	No	DSM-IV-TR: Structured interview Research associate or similar ≥15	Conduct Disorder; Psychotic disorders	Failed CBT trials for anxiety or OCD within the last two years	Dose optimized/stabilized
Peris, 2017, 29173737 US 2008-20016 NCT01409642	No	DSM-IV ≥15	Psychotic disorders	Prior history of receiving CBT for OCD	Dose optimized/stabilized
Piacentini, 2011, 22024003 US 1998-2003 NCT 00000386	No	DSM-IV MD/PhD ≥16	ASD/PDD; Psychotic disorders; Bipolar spectrum disorders	Concurrent psychotropic medication for OCD at study entry	.
POTS Team, 2004, 15507582 POTS US 1997-2022	No	DSM-IV: Clinical diagnosis + Structured interview ≥17	Psychotic disorders; Depressive disorders; Intellectual impairment; Bipolar spectrum disorders	Concurrent psychotropic treatment; no response to 2 previous SRI trials or a CBT trial for OCD.	Dose optimized/stabilized
Rempel, 2023, 37048570 Germany 2019-2022 EK18012019	No	ICD-10: Clinical diagnosis MD/PhD ≥8	ASD/PDD; Psychotic disorders; Depressive disorders; Intellectual impairment	Treatment naïve	Dose optimized/stabilized
Reynolds, 2013, 24060194 UK 2013	No	DSM-IV	Psychotic disorders; Bipolar spectrum disorders	.	.
Rezvan, 2013, 23413047 Iran ~2013	No	DSM-IV: Clinical diagnosis + Structured interview MD/PhD	.	Previously treated with either pharmacotherapy or psychotherapy continuing medication during the study	.
Riddle, 1992, 1429406 US 1988-1990	No	DSM-III-R MD/PhD	Tics/Tourette's; Psychotic disorders; Depressive disorders; Intellectual impairment	Previous fluoxetine treatment	.

Author, Year, PMID Study Name Country Years Registry Number	Industry Funding	Diagnostic Method, Evaluator CY-BOCS Cutoff	Excluded Comorbidities	Exclusion Criteria Regarding Previous Treatment	Previous Medication Status
Riddle, 2001, 11211371; US 1991-1994	Yes	DSM-III-R ≥16	Tics/Tourette's; Psychotic disorders; Depressive disorders	Treatment with fluoxetine ≤ 30 days, a monoamine oxidase inhibitor ≤ 14 days, or tricyclic antidepressant or other psychotropic drug ≤ 7 days	Dose optimized/stabilized
Rosa-Alcázar, 2019, 31516500 Spain 2012-2018	No	DSM-IV-TR, DSM-V: Clinical diagnosis, MD/PhD, ≥16	ADHD; ASD/PDD; Psychotic disorders; Intellectual impairment	Medications not stable for > 8 weeks.	.
Salemink, 2015, 25724385 The Netherlands <2015	NR	DSM-IV ≥8	Psychotic disorders	.	.
Selles, 2021, 34079488 Canada 2018-2021 NCT03672565	No	NR: Clinical diagnosis MD/PhD ≥16	Explicitly included	Treatment naïve	.
Shabani, 2019 Iran IRCT20170326331 44N1	No	DSM-V: Clinical diagnosis MD/PhD ≥16	ADHD; ASD/PDD; Psychotic disorders; Depressive disorders; Intellectual impairment	Participants have not received a psychological intervention in the past year. SSRI (≥3 months)	Dose optimized/stabilized
Shen, 2020 China 2017-2018	NR	CCMD ≥16	.	.	.
Simons, 2006, 16785776 Germany 2006	NR	DSM-IV: Structured interview	ASD/PDD; Psychotic disorders; Intellectual impairment	Concomitant medications for OCD	.
Skarphedinsson, 2015, 25239489 NordLOTS Sweden, Denmark, Norway 2008-2012 ISRCTN66385119	No	DSM-IV ≥16	ASD/PDD; Psychotic disorders; Depressive disorders; Intellectual impairment	No response to CBT in step 1; no medications 6 months before step 1	.

Author, Year, PMID Study Name Country Years Registry Number	Industry Funding	Diagnostic Method, Evaluator CY-BOCS Cutoff	Excluded Comorbidities	Exclusion Criteria Regarding Previous Treatment	Previous Medication Status
Storch, 2007, 17420681 US	NR	DSM-IV-TR: Clinical diagnosis MD/PhD ≥16	Psychotic disorders; other anxiety disorders; Intellectual impairment; Bipolar spectrum disorders	.	Dose optimized/stabilized
Storch, 2010, 20817153 US 2007-2009 NCT00864123	No	DSM-IV: Clinical diagnosis MD/PhD ≥16	ASD/PDD; Psychotic disorders; Bipolar spectrum disorders	Received at least one DCS dose.	Dose optimized/stabilized
Storch, 2011, 21684018 US	No	DSM-IV-TR: Clinical diagnosis, MD/PhD ≥16	ASD/PDD; Conduct Disorder; Psychotic disorders; Bipolar spectrum disorders	Change in any psychotropic medications for at least 8 weeks	Dose optimized/stabilized
Storch, 2013, 24184429 US 2009-2011 NCT00382291	Yes	Current DSM-IV-TR: Clinical diagnosis ≥17	PANS/PANDAS; ASD/PDD; Psychotic disorders; Bipolar spectrum disorders	Concomitant psychotropic medications other than medication for ADHD or PRN sedative/hypnotics for insomnia. Prior adequate trial of (AACAP, 2012) or allergy to sertraline.	.
Storch, 2016, 27367832 US 2011-2015 NCT 00864123	No	DSM-IV-TR: Clinical diagnosis ≥16	ASD/PDD; Psychotic disorders; other anxiety disorders; Bipolar spectrum disorders	.	Dose optimized/stabilized
Tuerk, 2023 OC-Go US	NR	DSM-V: Structured interview	.	.	.
Turner, 2014, 25457928 UK 2008-2011 ISRCTN27070832	No	DSM-IV: Structured interview MD/PHD ≥16	ASD/PDD; Psychotic disorders; Intellectual impairment	Concurrent medication	Dose optimized/stabilized
Williams, 2010, 19921305 UK 2010	No	ADIS-C: Structured interview	ASD/PDD; Psychotic disorders	.	.

Author, Year, PMID Study Name Country Years Registry Number	Industry Funding	Diagnostic Method, Evaluator CY-BOCS Cutoff	Excluded Comorbidities	Exclusion Criteria Regarding Previous Treatment	Previous Medication Status
Wolters, 2016, The Netherlands 2007-2010 ISRCTN07851536	NR	DSM-IV: Structured interview ≥16	Psychotic disorders	Medication for OCD, CBT for OCD ≤ 6 months	.
Wolters, 2021, The Netherlands 2013-2016 NTR4275	No	DSM-IV ≥16	Psychotic disorders	No stable dosage of medication for at least 12 weeks (SSRI, TCA, or antipsychotic medication) or four weeks (methylphenidate, Risperidone), CBT ≤ 3 months	Dose optimized/stabilized
Xie, 2020, China 2016-2017	NR	CCMD-3 ≥16	.	.	.
Zhang, 2014, China 2008-2012	NR	ICD-10 ≥16	.	.	.
Zhu, 2008, China 2005-2007	NR	CCMD-3 ≥16	Conduct Disorder	.	.

Abbreviations: ADHD = Attention Deficit Hyperactivity Disorder; ADIS-C = Anxiety Disorders Interview Schedule-Child version for DSM-IV; ADISP = Anxiety Disorders Interview Schedule–Parent, based on the DSM-IV; ASD = Autism Spectrum Disorder; CBT= Cognitive Behavioral Therapy; BPD = Borderline Personality Disorder CCMD-3 = Chinese Classification and Diagnostic Criteria for Mental Disorder, 3rd edition, CY-BOCS = Children's Yale-Brown Obsessive Compulsive Scale; DCS = D-cycloserine; DSM = Diagnostic and Statistical Manual of Mental Disorders; ICD = International Classification of Diseases; KID-SCID = Structured Clinical Interview for DSM-IV Childhood Diagnoses; K-SADS-PL = Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version; MD = Doctor of medicine; NR = Not reported; OCD = Obsessive Compulsive Disorder; ODD = Oppositional Defiant Disorder; PANDAS = Pediatric Autoimmune Neuropsychiatric Disorders Associated with Strep Infection; PANS = Pediatric Acute-onset Neuropsychiatric Syndrome; PDD = Pervasive Developmental Disorder; PhD = Doctor of philosophy; PMID = PubMed Identifier; POTS = Pediatric OCD Treatment Study; PRN = As needed (from Latin phrase: pro re nata); RCTs = Randomized Controlled Trials; SNRI = serotonin norepinephrine reuptake inhibitor; SSRI = Selective Serotonin Reuptake Inhibitor; TR = Text revision UK = United Kingdom; US = United States.

Table C-2.1.2. Key Question 2: Design details, NRCSs

Author, Year, PMID Study Name Country Years Analysis Method	Industry Funding	Diagnostic Method, Evaluator CY-BOCS Cutoff	Excluded Comorbidities
Franklin, 2023 United States 2015-2022 propensity score analysis	No	DSM V: Clinical diagnosis MD/PhD ≥16	.
Schuberth, 2023; Canada 2011-2017 propensity score analysis	No	DSM-IV/5: Clinical diagnosis ≥16	Conduct Disorder; Depressive disorders

Abbreviations: CY-BOCS = Children's Yale-Brown Obsessive Compulsive Scale; DSM = Diagnostic and Statistical Manual of Mental Disorders; MD = Doctor of medicine; NRCS = Non Randomized Comparative Study; PhD = Doctor of philosophy; PMID= PubMed Identifier

Table C-2.1.3. Key Question 2: Design details of planned or ongoing trials registered in ClinicalTrials.gov

NCT Number	Study Title	Study URL	Study Acronym	Goal Enrollment	Start Date
NCT03595098	Treatment Effects of Family Based Cognitive Therapy in Children and Adolescents With Obsessive Compulsive Disorder	https://clinicaltrials.gov/study/NCT03595098	TECTO	128	8/28/2018
NCT03528109	Improving Access to Child Anxiety Treatment	https://clinicaltrials.gov/study/NCT03528109	IMPACT	379	7/1/2018
NCT04548609	Transcranial Direct Current Stimulation (tDCS) in Pediatric Obsessive Compulsive Disorder (OCD)	https://clinicaltrials.gov/study/NCT04548609		36	1/25/2021
NCT05104697	TMS for Improving Response Inhibition in Adolescents With OCD	https://clinicaltrials.gov/study/NCT05104697		25	4/1/2022
NCT05931913	TMS + Exposure Therapy for Pediatric OCD	https://clinicaltrials.gov/study/NCT05931913	NExT	60	10/1/2023
NCT04673578	Adjunctive Celecoxib in Childhood-onset OCD Study	https://clinicaltrials.gov/study/NCT04673578	ACE-OCD	80	6/1/2021
NCT04963257	Sertraline Combined With Fluvoxamine in the Treatment of Refractory Obsessive-compulsive Disorder	https://clinicaltrials.gov/study/NCT04963257		400	1/1/2020
NCT05609916	CBT Augmentation to Promote Medication Discontinuation in Pediatric OCD	https://clinicaltrials.gov/study/NCT05609916		200	11/30/2022

Table C-2.2. KQ 2: Arm details

Study Year PMID	Arm Name	Arms Description	Treatment Components	Sessions	Setting; Provider Type	Medication 1, Dose, Titration, Frequency, Duration	Medication 2, Dose, Titration, Frequency, Duration	Other Medications
Agrawal, 2024, India, CN-02530420	Neuromodulation	Transcranial direct current stimulation (tDCS)	2 mA for 20 minutes	10 sessions over 12 weeks	Tertiary care center, outpatients	Fluoxetine 20 mg daily, with dose increased to 40 mg/day after 1 week	.	.
Agrawal, 2024, India, CN-02530420	Sham treatment	Sham tDCS	Sham treatment (ramp-up and ramp-down periods of 20 seconds during each during the start and end of the session	10 sessions over 12 weeks		Fluoxetine 20 mg daily, with dose increased to 40 mg/day after 1 week	.	.
Alaghband-Rad 2009 19190958	Pharmacological intervention: Selective serotonin reuptake inhibitors (SSRI)	Fluoxetine	.	.	.	Fluoxetine, 20mg daily, 6 weeks	.	.
Alaghband-Rad 2009 19190958	Pharmacological intervention: Selective serotonin reuptake inhibitors (SSRI)	Citalopram	.	.	.	Citalopram, 20mg daily, 6 weeks	.	.
Asbahr 2005 16239861	Psychological/behavioral intervention	GCBT	Psychoeducation, Cognitive restructuring, ERP/Exposure, ACT/Acceptance and commitment	Twelve 90-minute sessions over 12 weeks	In person/clinic, MD/PhD Group family-focused	.	.	.
Asbahr 2005 16239861	Pharmacological intervention: Selective serotonin reuptake inhibitors (SSRI)	Sertraline	.	.	NR, MD Individual	Sertraline (SSRI), 25mg for the first week then gradually titrated (every 4 days) to a maximum daily dose of 200 mg, as much as could be tolerated, once/d, 12 weeks	.	.

Study Year PMID	Arm Name	Arms Description	Treatment Components	Sessions	Setting; Provider Type	Medication 1, Dose, Titration, Frequency, Duration	Medication 2, Dose, Titration, Frequency, Duration	Other Medications
Aspvall 2021 33974020	Psychological/behavioral intervention	iCBT implemented in a stepped-care model	Psychoeducation, ERP/Exposure	Fourteen sessions over 16 weeks	Virtual/home asynchronous, MD/PhD Individual family-focused	.	.	.
Aspvall 2021 33974020	Psychological/behavioral intervention	In-person CBT	Psychoeducation, ERP/Exposure	Fourteen 45–60-minute sessions over 16 weeks	In person/clinic, MD/PhD Individual	.	.	.
Barrett 2003 12647571	Psychological/behavioral intervention	CBT	General CBT/not specified	Fourteen 90-minute sessions over 14 weeks	Virtual/home synchronous, MD Individual family-focused	.	.	.
Barrett 2003 12647571	Placebo/no treatment	Waitlist	.	.	.	.	.	.
Barrett 2004 14691360	Psychological/behavioral intervention	CBFT (individual)	Psychoeducation, Cognitive restructuring, ERP/Exposure, manual: Freedom From Obsessions and Compulsions Using Cognitive-Behavioral Strategies (FOCUS)	Sixteen 90-minute sessions over 14 weeks	In person/clinic; NR Individual family-focused	.	.	.
Barrett 2004 14691360	Psychological/behavioral intervention	CBFT (group)	Psychoeducation, Cognitive restructuring, ERP/Exposure, manual: Freedom from Obsessions and Compulsions Using Cognitive-Behavioral Strategies (FOCUS)	Sixteen 90-minute sessions over 14 weeks	In person/clinic, NR Group family-focused	.	.	.
Barrett 2004 14691360	Placebo/no treatment	Waitlist	.	.	.	.	.	.

Study Year PMID	Arm Name	Arms Description	Treatment Components	Sessions	Setting; Provider Type	Medication 1, Dose, Titration, Frequency, Duration	Medication 2, Dose, Titration, Frequency, Duration	Other Medications
Bolton 2008 17207457	Psychological/behavioral intervention	E-RP	ERP/Exposure	NR	In person/clinic, MD/PhD Individual	.	.	.
Bolton 2008 17207457	Placebo/no treatment	.	.	.	.	.	.	.
Bolton 2011 21644984	Psychological/behavioral intervention	Full CBT	General CBT/not specified	Twelve sessions over 12 weeks	In person/clinic, NR Individual	.	.	.
Bolton 2011 21644984	Psychological/behavioral intervention	Brief CBT	General CBT/not specified	Five sessions over 12 weeks	NR, MD/PhD Individual	.	.	.
Bolton 2011 21644984	Placebo/no treatment	.	.	.	.	.	.	.
Comer 2017 27869451	Psychological/behavioral intervention	Computer-delivered family-based CBT	ERP/Exposure	Fourteen sessions over 14 weeks	Virtual/home synchronous, MD/PhD Individual family-focused	.	.	.
Comer 2017 27869451	Psychological/behavioral intervention	Clinic-based CBT	ERP/Exposure	Fourteen sessions over 14 weeks	In person/clinic, MD/PhD Individual family-focused	.	.	.
de Haan 1998 9785713	Psychological/behavioral intervention	ERP	Psychoeducation, ERP/Exposure	twelve sessions over 12 weeks	In person/clinic, MD/PhD Individual	.	.	.
de Haan 1998 9785713	Pharmacological intervention: Tricyclic antidepressants (TCA)	Clomipramine	.	.	.	Clomipramine, mean 2.5 (0.63) mg/kg/day (range = 1.4-3.3 mg/kg/day), 25-mg/day for the first week, titrated (every 4 days) to a maximum daily dosage of 3 mg/kg/day, with a maximum of 200 mg/day, daily, 12 weeks	.	.

Study Year PMID	Arm Name	Arms Description	Treatment Components	Sessions	Setting; Provider Type	Medication 1, Dose, Titration, Frequency, Duration	Medication 2, Dose, Titration, Frequency, Duration	Other Medications
DeVeaugh-Geiss 1992 1537780	Pharmacological intervention: Tricyclic antidepressants (TCA)	Clomipramine Hydrochloride	.	.	.	Clomipramine, 75-200mg, depending on BW, 25mg for the first 4 days, daily, 8 weeks	.	.
DeVeaugh-Geiss 1992 1537780	Placebo/no treatment	.	.	.	.	.	.	.
Farrell 2013 23722990	Psychological/behavioral intervention + Pharmacological intervention	D-cycloserine + ERP	.	Nine 90-minutes sessions 9 weeks.	In person Trained therapist Individual	D-cycloserine, 25-50mg, 1 hour before ERP sessions 5-9 (total 5 times/doses)	.	.
Farrell 2013 23722990	Psychological/behavioral	Placebo + ERP	.	Nine 90-minutes sessions, 9 weeks.	In person Trained therapist Individual	.	.	.
Farrell 2022 35084071	Psychological/behavioral intervention	Placebo augmentation of intensive exposure therapy (CBT)	ERP/Exposure	Four sessions over 4 weeks	Virtual/home synchronous In person/clinic; MD Individual	Antidepressant, NR	Antipsychotic, NR	.
Farrell 2022 35084071	Psychological/behavioral intervention + Pharmacological intervention	D-cycloserine + CBT	Psychoeducation, ERP/Exposure	Three 180-210minute weekly sessions, then 90-120 minutes final 1-month booster session	Virtual/home synchronous In person/clinic; MD Individual	Antidepressant, NR	Antipsychotic, NR	.
Fatori 2018 30025255	Psychological/behavioral intervention	CBT	General CBT/not specified	Fourteen 100-minute sessions over 14 weeks	In person/clinic; NR Group	.	.	.
Fatori 2018 30025255	Pharmacological intervention: Selective serotonin reuptake inhibitors (SSRI)	Fluoxetine	.	.	.	Fluoxetine, 10-60mg daily, 14 weeks	.	.

Study Year PMID	Arm Name	Arms Description	Treatment Components	Sessions	Setting; Provider Type	Medication 1, Dose, Titration, Frequency, Duration	Medication 2, Dose, Titration, Frequency, Duration	Other Medications
Flament 1985 3899048	Pharmacological intervention: Tricyclic antidepressants (TCA)	Clomipramine	.	.	.	Clomipramine, mean (SD): 141 (30) mg/day, range 100-200 mg., starting dose: 50 mg, increased daily by 50 mg, up to 3 mg/kg/day (maximum, 200 mg/day), as tolerated; at the end of the treatment phase, the dosage was tapered, daily, 5 weeks	.	.
Flament 1985 3899048	Placebo/no treatment	Placebo	.	.	.	.	.	.
Franklin 2011 21934055	Medication management (MM) + CBT	.	Psychoeducation, Cognitive restructuring, Coping/relaxation, ERP/Exposure, manual: OCD in Children and Adolescents: A Cognitive-Behavioral Treatment Manual	Fourteen 60-minute sessions over 12 weeks	In person/clinic; MD/PhD Individual	Sertraline 125 mg (mean recommended dose)	Fluoxetine 40 mg (mean recommended dose)	Fluvoxamine, Citalopram, Paroxetine Clomipramine Escitalopram Venalfaxine
Franklin 2011 21934055	Medication management (MM) + I-CBT	.	Psychoeducation, ERP/Exposure	Seven 45-minute sessions over 12 weeks	In person/clinic; MD/PhD Individual	Sertraline	Fluoxetine	Fluvoxamine, Citalopram, Paroxetine Clomipramine Escitalopram Venalfaxine

Study Year PMID	Arm Name	Arms Description	Treatment Components	Sessions	Setting; Provider Type	Medication 1, Dose, Titration, Frequency, Duration	Medication 2, Dose, Titration, Frequency, Duration	Other Medications
Franklin 2011 21934055	Medication management (MM)	.	.	Seven 35-minute sessions over 12 weeks	In person/clinic; MD Individual	Sertraline*, 109.1mg (9.2)	Fluoxetine*, 36.4mg (2.7)	Fluvoxamine*, 148.3mg (17.4); Citalopram*, 38.1mg (6.3); Paroxetine* 34.6mg (5.5); Clomipramine* 91.7mg (8.3); Escitalopram* 18.3mg (7.3); Venalfaxine* 100.0mg
Franklin 2023	Psychological/behavioral intervention	TH-CBT	ERP/Exposure	6hours/day 5days/week	Virtual/home synchronous; MD/PhD Group and Individual family-focused	.	.	.
Franklin 2023	Psychological/behavioral intervention	IP-CBT	ERP/Exposure	6hours/day 5days/week	In person/clinic; MD/PhD Group and Individual family-focused	.	.	.
Freeman 2008 18356758	Pharmacological intervention: supplement/complementary	Family-based relaxation treatment	Coping/relaxation	Twelve 90/60-minute sessions over 14 weeks	Virtual/home synchronous. MD Individual family-focused	.	.	.
Freeman 2008 18356758	Psychological/behavioral intervention	Family-based CBT	Psychoeducation, Cognitive restructuring, ERP/Exposure	Twelve 90/60-minute sessions over 14 weeks	Virtual/home synchronous. MD Individual family-focused	.	.	.
Freeman 2014 24759852	Complementary /Integrative therapies	FB-RT: Family-based Relaxation Treatment	Psychoeducation, Coping/relaxation	Twelve 60-minute sessions over 14 weeks	In person/clinic, PhD Individual family-focused	.	.	.

Study Year PMID	Arm Name	Arms Description	Treatment Components	Sessions	Setting; Provider Type	Medication 1, Dose, Titration, Frequency, Duration	Medication 2, Dose, Titration, Frequency, Duration	Other Medications
Freeman 2014 24759852	Psychological/behavioral intervention	EX/RP: exposure plus response prevention	Psychoeducation, Cognitive restructuring, Coping/relaxation, ERP/Exposure	Twelve 60-minute sessions over 14 weeks	In person/clinic, PhD Individual family-focused	.	.	.
Geller 2001 11437015	Pharmacological intervention: Selective serotonin reuptake inhibitors (SSRI)	Fluoxetine	.	.	.	Fluoxetine, 10mg and after 2 weeks 20mg daily, 13 weeks		.
Geller 2001 11437015	Placebo/no treatment	.	.	.	.	.	.	.
Geller 2003 12880497	Pharmacological intervention: Selective serotonin reuptake inhibitors (SSRI)	Paroxetine	.	.	.	Paroxetine, phase 1, 10-60 mg/day, started at 10mg/day; titrated up in 10mg increments ≤ once a week. dose ≤ 40 mg/day until after week 6, unless clinically indicated. The maximum daily dose allowed was 60mg/day., once daily, 16 weeks	Paroxetine, phase 2, final dose from Phase 1 once daily, subsequent 16 weeks	.

Study Year PMID	Arm Name	Arms Description	Treatment Components	Sessions	Setting; Provider Type	Medication 1, Dose, Titration, Frequency, Duration	Medication 2, Dose, Titration, Frequency, Duration	Other Medications
Geller 2003 12880497	Placebo/no treatment	.	.	.	.	Paroxetine, phase 1, 10-60mg/day, started at 10mg/day; titrated up in 10mg increments ≤ once a week. dose ≤ 40 mg/day until after week 6, unless clinically indicated. The maximum daily dose allowed was 60mg/day., once daily, 16 weeks	Placebo, phase 2 Dose tapering of patients randomized to placebo was achieved in a blind fashion such that decreases occurred in 10mg increments per week, beginning at the start of Phase II, once daily, subsequent 16 weeks	.
Geller 2004 15502598	Paroxetine	.	.	.	.	Paroxetine, 10-50mg/day (for the first week patient received 10 mg/day), upward in 10-mg/day increments, no more frequently than every 7 days, to a maximal dose of 50 mg/day., Once daily, 10weeks	.	.
Geller 2004 15502598	Placebo	.	.	.	.	.	.	.
Ghanizadeh 2017 28659986	Pharmacologic (citalopram + placebo)	.	.	.	.	Placebo	Citalopram, 20 to 40 mg daily, 10 weeks	.

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Ghanizadeh 2017 28659986	Pharmacologic (N-Acetylcystein) (NAC) + citalopram	.	.	.	.	N-Acetylcystein (NAC), 2400mg, during the first week 600 mg/day, increasing to 1200 mg/day in two divided doses in the second week. The patients were administered 1800 mg/day during weeks 4 and 5. The daily dose for NAC from week 6 to the end of this trial was 2400 mg/day, daily, 10 weeks	Citalopram, 20 to 40 mg daily, 10 weeks	.
Grant 2014 24356715	Pharmacological intervention: other	Riluzole	.	.	.	One capsule 10mg daily, then dose was increased daily by one capsule until maximum dose of 100mg/day (five 10-mg capsules twice daily), 12 weeks	.	Antipsychotic, NR Stimulant, NR Alpha agonist Anti-seizure
Grant 2014 24356715	Placebo/no treatment	.	.	.	.	.	.	.
Guo, 2008	Pharmacological intervention: Selective serotonin reuptake inhibitors (SSRI)	Sertraline	.	.	.	Sertraline, 50 mg/day, increased to 100-150 mg/day, once in the morning, 8 weeks	.	.
Guo, 2008	Pharmacological intervention: Tricyclic antidepressants (TCA)	Clomipramine	.	.	.	Clomipramine, 50 mg/day, increased to 150-250 mg/day, divided into 2 times, 8 weeks	.	.

Study Year PMID	Arm Name	Arms Description	Treatment Components	Sessions	Setting; Provider Type	Medication 1, Dose, Titration, Frequency, Duration	Medication 2, Dose, Titration, Frequency, Duration	Other Medications
He, 2007	Pharmacological intervention: Selective serotonin reuptake inhibitors (SSRI)	Fluvoxamine	.	.	.	Fluvoxamine, 25 mg/ day, increased to 100-200 mg/day, 8 weeks	.	.
He, 2007	Pharmacological intervention: Tricyclic antidepressants (TCA)	Clomipramine	.	.	.	Clomipramine, 25 mg/day, increased to 100-175 mg/day, 8 weeks	.	.
Himle, 2024 38103359	Exposure and response therapy (ERP)	ERP	Psychoeducation, ERP/Exposure	12 sessions weekly over 26 weeks	Individual, in-person/clinic MS level with PhD supervision			
Himle, 2024 38103359	Stress-management control therapy (SMT)		Psychoeducation, coping/relaxation therapy	12 sessions weekly over 26 weeks	Individual, in person/clinic MS level with PhD supervision			
Hollmann 2022 36329915	Psychological/behavioral intervention	CBT	Cognitive restructuring, ERP/Exposure	Fourteen 90-minute sessions over 14 weeks	Virtual/home synchronous, MD/PhD Individual family-focused	.	.	.
Hollmann 2022 36329915	Placebo/no treatment	Waitlist	.	.	.	.	.	.
Lenhard 2017 27993223	Psychological/behavioral intervention	Internet-based CBT	Psychoeducation, ERP/Exposure	Twelve sessions over 12 weeks	Virtual/home asynchronous, MD/PhD Individual family-focused	.	.	.
Lenhard 2017 27993223	Placebo/no treatment	Waitlist control	.	.	.	.	.	.

Study Year PMID	Arm Name	Arms Description	Treatment Components	Sessions	Setting; Provider Type	Medication 1, Dose, Titration, Frequency, Duration	Medication 2, Dose, Titration, Frequency, Duration	Other Medications
Leonard 1989 2686576	Pharmacological intervention: Tricyclic antidepressants (TCA)	Clomipramine	.	.	.	Clomipramine, targeting 3 mg/kg as tolerated, 25 mg (≤25 kg) or 50 mg (>25 kg) and increased by one capsule each week. The maximum dosage did not exceed 250 mg/d or 5 mg/kg, 5 weeks	.	.
Leonard 1989 2686576	Pharmacological intervention: Tricyclic antidepressants (TCA)	Desipramine	.	.	.	Desipramine, targeting 3 mg/kg as tolerated, 25 mg (≤25 kg) or 50 mg (>25 kg) and increased by one capsule each week. The maximum dosage did not exceed 250 mg/d or 5 mg/kg, 5 weeks	.	.
Leonard 1989 2686576	Pharmacological intervention: Tricyclic antidepressants (TCA)	Follow up study: clomipramine only	.	.	.	Clomipramine, daily dose did not exceed either 250 mg or 5 mg/kg., kept constant from part 1 8 months	.	.
Leonard 1989 2686576	Pharmacological intervention: Tricyclic antidepressants (TCA)	Follow up study: clomipramine then desipramine then clomipramine	.	.	.	Clomipramine, daily dose did not exceed either 250 mg or 5 mg/kg., kept constant from part 1 Months 1-3 and 6-8	Desipramine, daily dose did not exceed either 250 mg or 5 mg/kg., kept constant from part 1 Months 4-7	.
Lewin 2014 24657310	Placebo/no treatment	TAU	Unspecified TAU	NR	NR NR	.	.	.

Study Year PMID	Arm Name	Arms Description	Treatment Components	Sessions	Setting; Provider Type	Medication 1, Dose, Titration, Frequency, Duration	Medication 2, Dose, Titration, Frequency, Duration	Other Medications
Lewin 2014 24657310	Psychological/ behavioral intervention	E/RP	Psychoeducation, ERP/Exposure, manual: Freeman & Garcia, 2009	Twelve 60-minute sessions over 6 weeks	In person/clinic; MD Individual family-focused	.	.	.
Li 2020 31800306	Pharmacological intervention: supplement/complementary	N-acetylcysteine (NAC)	.	.	.	N-acetylcysteine (NAC), 2700mg, week1: 900mg/d, week2: 1800mg/d, week3-12: 2700mg/d, daily, 12 weeks	.	.
Li 2020 31800306	Placebo/no treatment	.	.	.	.	.	.	.
Liebowitz 2002 12447029	Pharmacological intervention: Selective serotonin reuptake inhibitors (SSRI)	Fluoxetine - first entrance	.	.	.	Fluoxetine, 20mg, week 1-2, daily, 2 weeks	Fluoxetine, 40 mg, 3-4, daily, 2 weeks	Fluoxetine, 60 mg, 5-6 daily, 2 weeks; Fluoxetine, 80mg, 7-8, daily, 2weeks
Liebowitz 2002 12447029	Pharmacological intervention: Selective serotonin reuptake inhibitors (SSRI)	Fluoxetine - Maintenance	.	.	.	Fluvoxamine	.	.
Liebowitz 2002 12447029	Placebo/no treatment	First entrance	.	.	.	.	.	.
Liebowitz 2002 12447029	Placebo/no treatment	Maintenance	.	.	.	.	.	.
Liu, 2012	Pharmacological intervention: combination of drugs	Fluvoxamine with risperidone	.	.	.	Fluvoxamine, 50mg/tablet, starting dose 25 mg/day, maximum dose 200mg/day	Risperidone, 1mg/tablet, starting dose 1mg/day, maximum dose 3mg/day	.

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Liu, 2012	Pharmacological intervention: Selective serotonin reuptake inhibitors (SSRI)	Fluvoxamine alone	.	.	.	Fluvoxamine	.	.
Ma, 2014	Psychological/behavioral intervention + Pharmacological intervention	.	ERP/Exposure	60–90-minute sessions 2/week	In person/clinic; NR Individual	.	.	.
Ma, 2014	Pharmacological intervention: Serotonin and norepinephrine reuptake inhibitors (SNRIs)	Sertraline	.	.	.	Sertraline, 12.5-200 mg/day, dose adjusted within 2 weeks, gradually increased, maximum 200 mg/day, daily, NR	.	.
March 1990 19630661	Pharmacological intervention: Selective serotonin reuptake inhibitors (SSRI)	Clomipramine	.	.	.	Clomipramine, 75-200mg, 3.5 mg/kg, daily, 8 weeks	.	.
March 1990 19630661	Placebo/no treatment	.	.	.	.	.	.	.
March 1998 9842950	Pharmacological intervention: Selective serotonin reuptake inhibitors (SSRI)	Sertraline	.	.	.	Sertraline, mean 167mg/day children/180mg/day adolescents, starting 25mg/day children and 50mg/day adolescents; titrated up 50mg/week over 4 weeks to a max of 200mg/day as tolerated, daily, 12 weeks	.	.
March 1998 9842950	Placebo/no treatment	Placebo	.	.	.	.	.	.

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Mataix-Cols 2014 24262813	Psychological/behavioral intervention + Pharmacological intervention	CBT + post-session DCS	Psychoeducation, ERP/Exposure	Fourteen sessions over 17 weeks	In person/clinic; NR Individual	D-cycloserine, 50 mg Immediately after each of the ten ERP sessions, 10 weeks	.	.
Mataix-Cols 2014 24262813	Psychological/behavioral intervention	CBT + Placebo	Psychoeducation, ERP/Exposure	Fourteen sessions over 17 weeks	NR Individual	Placebo, immediately after each of ten (CBT) sessions, ERP, 10weeks	.	.
Merlo 2010 19675960	Psychological/behavioral intervention	CBT + Motivational interviewing	General CBT/not specified	Three 20–30-minute sessions over 3 weeks	In person/clinic, MD/PhD NR	.	.	.
Merlo 2010 19675960	Psychological/behavioral intervention	CBT + psychoeducation	Psychoeducation, General CBT/not specified	Three 20–30-minute sessions over 3 weeks	NR, MD/PhD Family-focused	.	.	.
Nai 2009	Pharmacological intervention: Selective serotonin reuptake inhibitors (SSRI)	Sertraline	.	.	.	Sertraline, 50 mg/day, increased to 100-150 mg/day, once in the morning, 2 weeks	.	.
Nai 2009	Pharmacological intervention: Tricyclic antidepressants (TCA)	Clomipramine	.	.	.	Clomipramine, 50 mg/day within 2 weeks, 150~250mg/day divided into 2 times for 8 weeks	.	.
Nasiry 2020	Psychological/behavioral intervention	Cognitive Bias Modification of Interpretation (CBMI)	General CBT/not specified, manual: Cognitive Bias Modification of Interpretation (CBMI)	NR	Virtual/home synchronous, MD Individual	.	.	.
Nasiry 2020	Placebo/no treatment	.	.	.	.	.	.	.

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NCT01933919	Pharmacological intervention: Selective serotonin reuptake inhibitors (SSRI)	Fluvoxamine	.	.	.	Fluvoxamine, 25mg once a day, week 1 then increased 25 mg/day/week up to a max of 150 mg	.	.
NCT01933919	Placebo/no treatment	.	.	.	.	.	.	.
Neziroglu 2000 11191690	Psychological/behavioral intervention + Pharmacological intervention	Fluvoxamine + ERP	ERP/Exposure	Twenty 90-minute sessions weekly over 20 weeks	In person/clinic, MD/PhD Individual	Fluvoxamine, 50mg daily, 52 weeks	.	.
Neziroglu 2000 11191690	Pharmacological intervention: Selective serotonin reuptake inhibitors (SSRI)	Fluvoxamine	.	.	.	Fluvoxamine, 50mg daily, 52 weeks	.	.
Noras 2022 35748547	Pharmacological intervention: other	Fluvoxamine + placebo syrup	.	.	.	Fluvoxamine, NR	.	.
Noras 2022 35748547	Pharmacological intervention: Selective serotonin reuptake inhibitors (SSRI)	Fluvoxamine + herbal supplement (E. amoenum - M. officinalis)	.	.	.	Fluvoxamine, NR	.	.
Peris 2013 22548378	Psychological/behavioral intervention	Positive Family Interaction Therapy (PFIT)	Psychoeducation, Cognitive restructuring, ERP/Exposure, manual: Piacentini, Langley, & Roblek, 2007	Twelve 60-minute sessions over 14 weeks	In person/clinic; PhD Individual family-focused	.	.	.

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Peris 2013 22548378	Psychological/behavioral intervention	Standard Treatment	Psychoeducation, Cognitive restructuring, ERP/Exposure, manual: Piacentini, Langley, & Roblek, 2007	Twelve 60-minute sessions over 14 weeks	In person/clinic; PhD Individual family-focused	.	.	.
Peris 2017 29173737	Psychological/behavioral intervention	Positive Family Interaction Therapy PFIT	Psychoeducation	Twelve 60-minute sessions over 12 weeks and 60-minute of family therapy every other week.	In person/clinic; PhD Individual family-focused	.	.	.
Peris 2017 29173737	Psychological/behavioral intervention	ST	Psychoeducation, Cognitive restructuring, ERP/Exposure	Twelve 90-minute sessions over 12 weeks	In person/clinic; PhD Individual family-focused	.	.	.
Piacentini 2011 22024003	Psychological/behavioral intervention	FCBT (family CBT)	Psychoeducation, ERP/Exposure	Twelve 90-minute sessions over 14 weeks	In person/clinic; PhD Individual family-focused	.	.	.
Piacentini 2011 22024003	Psychological/behavioral intervention	Psychoeducation/Relaxation Training (PRT)	Psychoeducation, Coping/relaxation	Twelve 90-minute sessions over 14 weeks	In person/clinic; PhD Individual family-focused	.	.	.
POTS Team 2004 15507582	CBT	.	Psychoeducation, Cognitive restructuring, ERP/Exposure, manual: March 1998	Fourteen 60-minute sessions over 12 weeks	In person/clinic; NR Individual	.	.	.
POTS Team 2004 15507582	Pacebo	.	General CBT/not specified	Nine 30 minutes sessions over 12 weeks	In person/clinic; MD Individual	.	.	.

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POTS Team 2004 15507582	CBT+sertraline	.	Psychoeducation, Cognitive restructuring, ERP/Exposure, manual: March 1998	NR	In person/clinic; MD Individual	Sertraline, 20 mg/day to 200 mg/day, over 6 weeks, once a day	.	.
POTS Team 2004 15507582	Sertraline	.	General CBT/not specified	Nine 30 minutes sessions over 12 weeks	In person/clinic; MD Individual	Sertraline, 25 mg/day to 200 mg/day, over 6 weeks, once a day, 12 weeks	.	.
Rempel 2023 37048570	Psychological/behavioral intervention	App-based mindfulness meditation training	Psychoeducation, Cognitive restructuring, Coping/relaxation, manual: 7Mind	Sixteen 7–12 minutes sessions twice/week over 8 weeks	Virtual/home synchronous, MD Individual	.	.	.
Rempel 2023 37048570	Complementary /Integrative therapies	App-based audiobook	Coping/Relaxation	One hundred twelve sessions twice daily over 8 weeks	Virtual/home synchronous, MD Individual	.	.	.
Reynolds 2013 24060194	Psychological/behavioral intervention	Parent-enhanced CBT	General CBT/not specified	Fourteen sessions over 14 weeks	In person/clinic; MD/PhD Group	.	.	.
Reynolds 2013 24060194	Psychological/behavioral intervention	Individual CBT	General CBT/not specified	Fourteen sessions over 14 weeks	In person/clinic, MD/PhD Individual	.	.	.
Rezvan 2013 23413047	Psychological/behavioral intervention	Attachment-based therapy	Attachment-based therapy	Eight 60-minute sessions over 8 weeks	In person/clinic, MD Individual	.	.	.
Rezvan 2013 23413047	Placebo/no treatment	TAU	.	.	.	.	.	.
Riddle 1992 1429406	Pharmacological intervention: Selective serotonin reuptake inhibitors (SSRI)	Fluoxetine	.	.	.	Fluoxetine, 20mg Daily, 8 weeks	.	.
Riddle 1992 1429406	Placebo/no treatment	.	.	.	.	.	.	.

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Riddle 2001 11211371	Pharmacological intervention: Selective serotonin reuptake inhibitors (SSRI)	Fluvoxamine	.	.	.	Fluvoxamine, 25mg, 25mg at bedtime for 3 days, increased 25mg every 3-4 days until 200mg, 2 caps/day, weeks 4-10	.	.
Riddle 2001 11211371	Placebo/no treatment	.	.	.	.	.	.	.
Rosa-Alcázar 2017 27792972	Psychological/behavioral intervention	Cognitive-behavioral family-based treatment (CBFP)	Psychoeducation, Cognitive restructuring, Coping/relaxation, ERP/Exposure	Twelve 60-minute sessions over 12 weeks	In person/clinic, MD/PhD Individual family-focused	.	.	.
Rosa-Alcázar 2017 27792972	Psychological/behavioral intervention	Parent Training	Psychoeducation, ERP/Exposure	Twelve 60-minute sessions over 12 weeks	In person/clinic, MD/PhD Individual family-focused	.	.	.
Rosa-Alcázar 2019 31516500	Psychological/behavioral intervention	CBFT Parents and child	Psychoeducation, ERP/Exposure	Twelve 60-minute sessions over 12 weeks	In person/clinic, MD Individual family-focused	.	.	.
Rosa-Alcázar 2019 31516500	Psychological/behavioral intervention	CBFT Mother and child	Psychoeducation, ERP/Exposure	Twelve 60-minute sessions over 12 weeks	In person/clinic, MD Individual family-focused	.	.	.
Rosa-Alcázar 2019 31516500	Psychological/behavioral intervention	CBFT mother only	Psychoeducation, ERP/Exposure	Twelve 60-minute sessions over 12 weeks	In person/clinic, MD Individual	.	.	.
Salemink 2015 25724385	CBM-I	Cognitive Bias Modification training of Interpretations (CBM-I)	Psychoeducation	Eight 30-minute sessions over 11 days	Virtual/home synchronous, NR Individual	.	.	.
Salemink 2015 25724385	Placebo/no treatment	.	.	.	.	.	.	.

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Schuberth 2023	Psychological/behavioral intervention	CBT+ PMT (parent management training)	Psychoeducation, ERP/Exposure	Twelve 90-minute sessions over 12 weeks	In person/clinic; PhD Group family-focused	.	.	.
Schuberth 2023	Psychological/behavioral intervention	CBT	Psychoeducation	Twelve 90-minute sessions over 12 weeks	In person/clinic; PhD Group	.	.	.
Selles 2021 34079488	Psychological/behavioral intervention	Hospital-based CBT	Psychoeducation, Cognitive restructuring, ERP/Exposure	Seven 180-minute sessions biweekly over 12 weeks	In person/clinic; MD Individual	.	.	.
Selles 2021 34079488	Psychological/behavioral intervention	Home-based CBT	Psychoeducation, Coping/relaxation, ERP/Exposure	Seven 180-minute sessions biweekly over 12 weeks	Virtual/home synchronous, MD Individual	.	.	.
Shabani, 2019	Psychological/behavioral intervention + Pharmacological intervention	Acceptance and Commitment Therapy + SSRI	Psychoeducation, ACT/Acceptance and commitment, manual: Armstrong et al. (2013)	Ten 60-minute sessions over 10 weeks	In person/clinic, MD/PhD Group	Clomipramine, 25 mg, increasing every 3–4 days until maximum results were achieved with the fewest side effects	Fluoxetine 20 mg, increasing every 3–4 days until maximum results were achieved with the fewest side effects	Fluvoxamine 50 mg, increasing every 3–4 days until maximum results were achieved with the fewest side effects ; sertraline 50 mg, increasing every 3–4 days until maximum results were achieved with the fewest side effects

Study Year PMID	Arm Name	Arms Description	Treatment Components	Sessions	Setting; Provider Type	Medication 1, Dose, Titration, Frequency, Duration	Medication 2, Dose, Titration, Frequency, Duration	Other Medications
Shabani, 2019	Psychological/behavioral intervention + Pharmacological intervention	Cognitive Behavioral Therapy + SSRI	Psychoeducation, Cognitive restructuring, ERP/Exposure	Twelve 60-minute sessions over 12 weeks	In person/clinic, MD/PhD Group	Clomipramine 25 mg, increasing every 3–4 days until maximum results were achieved with the fewest side effects	Fluoxetine 20 mg, increasing every 3–4 days until maximum results were achieved with the fewest side effects	Fluvoxamine 50 mg, increasing every 3–4 days until maximum results were achieved with the fewest side effects; 50 mg, increasing every 3–4 days until maximum results were achieved with the fewest side effects
Shabani, 2019	Pharmacological intervention: Selective serotonin reuptake inhibitors (SSRI)	.	.	.	.	Clomipramine 25 mg, increasing every 3–4 days until maximum results were achieved with the fewest side effects	Fluoxetine 20 mg, increasing every 3–4 days until maximum results were achieved with the fewest side effects	Fluvoxamine 50 mg, increasing every 3–4 days until maximum results were achieved with the fewest side effects; sertraline 50 mg, increasing every 3–4 days until maximum results were achieved with the fewest side effects
Shen, 2020	Pharmacological intervention: Selective serotonin reuptake inhibitors (SSRI)	Escitalopram	.	.	.	Escitalopram, 10 mg per time, can increase up to 20 mg per time within 7~14 days, once a day, 6 weeks	.	.
Shen, 2020	Pharmacological intervention: Tricyclic antidepressants (TCA)	Clomipramine	.	.	.	Clomipramine, 25 mg per time, can increase up to 50 mg/day within 7~14 days, twice a day, 6 weeks	.	.

Study Year PMID	Arm Name	Arms Description	Treatment Components	Sessions	Setting; Provider Type	Medication 1, Dose, Titration, Frequency, Duration	Medication 2, Dose, Titration, Frequency, Duration	Other Medications
Simons 2006 16785776	Psychological/behavioral intervention	Metacognitive Therapy	Metacognitive Therapy	Twenty sessions over 20 weeks	In person/clinic, MD/PhD Individual	.	.	.
Simons 2006 16785776	Psychological/behavioral intervention	ERP	ERP/Exposure	Twenty sessions over 20 weeks	NR, MD/PhD Individual	.	.	.
Skarphedinsson 2015 25239489	Psychological/behavioral intervention	CBT	Psychoeducation, Cognitive restructuring, ERP/Exposure, manual: March and Mulle as well as an adapted version by Piacentini]	Ten 90-minute sessions over 16 weeks	In person/clinic, NR Individual family-focused	.	.	.
Skarphedinsson 2015 25239489	Pharmacological intervention: Selective serotonin reuptake inhibitors (SSRI)	Sertraline	ERP/Exposure	.	.	Sertraline, 100mg - 200 mg, A starting dose of 25 mg per day was titrated up to 100 mg per day by week 4; if response was considered inadequate, the dose was increased gradually up to a maximum of 200 mg per day by week 8, 6 sessions, 16 weeks	.	.
Storch 2007 17420681	Psychological/behavioral intervention	Intensive CBT	General CBT/not specified	Fourteen 90-minute sessions	In person/clinic; MD Individual family-focused	.	.	.
Storch 2007 17420681	Psychological/behavioral intervention	Weekly CBT	General CBT/not specified	Fourteen 90-minute sessions	NR, MD Individual family-focused	.	.	.

Study Year PMID	Arm Name	Arms Description	Treatment Components	Sessions	Setting; Provider Type	Medication 1, Dose, Titration, Frequency, Duration	Medication 2, Dose, Titration, Frequency, Duration	Other Medications
Storch 2010 20817153	Psychological/behavioral intervention + Pharmacological intervention	CBT+DCS	Psychoeducation, Cognitive restructuring, ERP/Exposure	Ten 60-minute sessions	In person/clinic, MD/PhD Individual	D-cycloserine, 0.7mg/kg. Children with weight 25–45kg took 25mg (0.56–1.0 mg/kg/day), between 46–90kg took 50mg (0.56–1.08mg/kg/day), NR, one hour before sessions 4–10, NR	.	.
Storch 2010 20817153	Psychological/behavioral intervention	CBT+ Placebo	Psychoeducation, Cognitive restructuring, ERP/Exposure	Ten 60-minute sessions	In person/clinic, MD/PhD Individual	Placebo, one hour before sessions 4–10	.	.
Storch 2011 21684018	Psychological/behavioral intervention	Web-camera CBT	Psychoeducation, Cognitive restructuring, ERP/Exposure	Fourteen 60–90-minute sessions over 12 weeks	Virtual/home synchronous, PhD Individual family-focused	.	.	.
Storch 2011 21684018	Placebo/no treatment	Waitlist	.	.	.	.	.	.
Storch 2013 24184429	Psychological/behavioral intervention + Pharmacological intervention	Regular Sertraline + CBT	Psychoeducation, Cognitive restructuring, ERP/Exposure, manual: the protocol used in POTS (POTS, 2004)	Fourteen 60-minute sessions over 14 weeks	In person/clinic; PhD Individual	Sertraline, 25 mg/d, from 25 mg/day to 200 mg/day over 9 weeks unless higher doses were not tolerated, after which the dosage was adjusted as a function of tolerability. Once daily dose, typically following breakfast, 18 weeks	.	.

Study Year PMID	Arm Name	Arms Description	Treatment Components	Sessions	Setting; Provider Type	Medication 1, Dose, Titration, Frequency, Duration	Medication 2, Dose, Titration, Frequency, Duration	Other Medications
Storch 2013 24184429	Psychological/behavioral intervention + Pharmacological intervention	Slow Sertraline + CBT	Psychoeducation, Cognitive restructuring, ERP/Exposure, manual: the protocol used in POTS (POTS, 2004)	Fourteen 60-minute sessions over 14 weeks	In person/clinic; PhD Individual	Sertraline, 25 mg/day, as previously unless unable to tolerate higher doses, children remained on 25mg/day for the first two weeks, 50mg/day from weeks 3-4, 75mg/day for weeks 5-6, 100mg/day for week 7, 150mg/day for week 8, and 200mg/day for week 9 until the end of the study, once daily dose, typically following breakfast, 18 weeks	.	.
Storch 2013 24184429	Placebo/no treatment	Placebo + CBT	Psychoeducation, Cognitive restructuring, ERP/Exposure, manual: the protocol used in POTS (POTS, 2004)	Fourteen 60-minute sessions over 14 weeks	In person/clinic; PhD Individual	Placebo, 25 mg/day, 18 weeks	.	.

Study Year PMID	Arm Name	Arms Description	Treatment Components	Sessions	Setting; Provider Type	Medication 1, Dose, Titration, Frequency, Duration	Medication 2, Dose, Titration, Frequency, Duration	Other Medications
Storch 2016 27367832	Psychological/behavioral intervention + Pharmacological intervention	D-Cycloserine Plus CBT	Psychoeducation, Cognitive restructuring, ERP/Exposure	Ten sessions weekly over 8 weeks	NR, PhD Individual family-focused	D-cycloserine, Children weighing 25 to 45 kg took 25 mg (approximately 0.56-1.0 mg/kg/d), and children weighing at least 46 kg took 50 mg provided in two 25-mg capsules (approximately 0.50-1.08 mg/kg/d) 1 hour before sessions 4 through 10	.	.
Storch 2016 27367832	Psychological/behavioral intervention	Placebo Plus CBT	Psychoeducation, Cognitive restructuring, ERP/Exposure	Approximately 10 sessions over 8 weeks	NR, PhD Individual family-focused	placebo	.	.
Tuerk, 2023	Psychological/behavioral intervention	CBT	General CBT/not specified	Twelve sessions over 12 weeks	In person/clinic, NR Individual	.	.	.
Tuerk, 2023	Psychological/behavioral intervention	ERP	ERP/Exposure	NR sessions over 12 weeks	Virtual/home asynchronous, NR Group	.	.	.
Turner 2014 25457928	Psychological/behavioral intervention	Telephone CBT	Psychoeducation, ERP/Exposure	Fourteen sessions over 17 weeks	Virtual/home synchronous, PhD Individual family-focused	.	.	.
Turner 2014 25457928	Psychological/behavioral intervention	CBT	Psychoeducation, ERP/Exposure	Fourteen sessions over 17 weeks	In person/clinic, PhD Individual family-focused	.	.	.
Williams 2010 19921305	Psychological/behavioral intervention	CBT	General CBT/not specified	Ten 60-minute sessions over 10 weeks	NR, MD/PhD NR	.	.	.
Williams 2010 19921305	Placebo/no treatment	.	.	.	.	.	.	.

Study Year PMID	Arm Name	Arms Description	Treatment Components	Sessions	Setting; Provider Type	Medication 1, Dose, Titration, Frequency, Duration	Medication 2, Dose, Titration, Frequency, Duration	Other Medications
Wolters 2016	Psychological/behavioral intervention	CBT	Psychoeducation, Cognitive restructuring, ERP/Exposure, manual: Dutch treatment manual 'Bedwing je dwang' ('Control your OCD'; De Haan & Wolters, 2009)	Sixteen 45–60-minute sessions over 16 weeks	In person/clinic, MD/PhD Individual family-focused	.	.	.
Wolters 2016	Placebo/no treatment	An eight-week waitlist followed by CBT	.	.	.	.	.	.
Wolters 2021	Psychological/behavioral intervention	CBM-I + CBT	Psychoeducation, Cognitive restructuring, ERP/Exposure, manual: 'Control your OCD' (De Haan & Wolters, 2009; Wolters, de Haan, Hogendoorn, Boer, & Prins, 2016	Twelve 60–75-minute sessions over 16 weeks	In person/clinic, MD/PhD Individual	.	.	.
Wolters 2021	Psychological/behavioral intervention	Waitlist + CBT	.	.	.	.	.	.
Xie, 2020	Pharmacological intervention: Selective serotonin reuptake inhibitors (SSRI)	Escitalopram	.	.	.	Escitalopram, <12 years: 5mg/day, >12 years, 10 mg/day once a day, 6 weeks	.	.

Study Year PMID	Arm Name	Arms Description	Treatment Components	Sessions	Setting; Provider Type	Medication 1, Dose, Titration, Frequency, Duration	Medication 2, Dose, Titration, Frequency, Duration	Other Medications
Xie, 2020	Pharmacological intervention: Tricyclic antidepressants (TCA)	Clomipramine	.	.	.	Clomipramine, <12 years: 12.5 mg, 2 times a day >12 years, 25 mg of 2 times a day, 6 weeks	.	.
Zhang, 2014	Psychological/behavioral intervention + Pharmacological intervention	CBT + Sertraline	Cognitive restructuring	Ten sessions biweekly over 12 weeks	In person/clinic, NR	Sertraline: average 138. 7 (56. 5) mg /day over 12 weeks	.	.
Zhang, 2014	Pharmacological intervention	Sertraline	.	.	.	Sertraline, initial dose 50 mg/day, increase up to 100 to 200 mg/day over 12 weeks over 12 weeks	.	.
Zhu, 2008	Pharmacological intervention: Selective serotonin reuptake inhibitors (SSRI)	Sertraline	.	.	.	Sertraline, 50 mg/ day, increased to 100-150 mg/day, once in the morning, 2 weeks	.	.
Zhu, 2008	Pharmacological intervention: Tricyclic antidepressants (TCA)	Clomipramine	.	.	.	Clomipramine, 50 mg/day within 2 weeks, 150~250mg/d divided into 2 times for 8 weeks	.	.

Abbreviations: App = Application; BW = Body weight; CBFT = Cognitive Behavioral Family-based Therapy; CBM-I = Cognitive Bias Modification training of Interpretation; CBT= Cognitive Behavioral Therapy; d = Day; DCS = D-cycloserine; E/RP, E-RP, ERP = Exposure and Response Prevention; GCBT = Group Cognitive Behavioral Therapy; iCBT, I-CBT = Internet-based Cognitive Behavioral Therapy; IP-CBT= In-person Cognitive Behavioral Therapy; max = Maximum; mA = milliampere; MD = Doctor of medicine; NR = Not reported; PhD = Doctor of philosophy; PMID = PubMed Identifier; POTS = Pediatric OCD Treatment Study; SMT = stress management control therapy; SSRI = Selective Serotonin Reuptake Inhibitor; ST = Standard Treatment; TAU = Treat as usual; tDCS = transcranial direct current stimulation; TH-CBT= Telehealth-based Cognitive Behavior Therapy. *Mean actual dose for all groups.

Table C-2.3.1. Key Question 2: Sample characteristics, Part 1

Study, Year, PMID	Age, Mean (SD) [Range]	Age at Symptom Onset, Mean (SD) [Range]	Male, N (%)	Race and Ethnicity, N (%)	Other Relevant SDH Factors, N (%)	Duration of OCD, Mean (SD) [Range]
Agrawal, 2024, India, CN-02530420	14.4 (2.5)	12.4 (2.8)	11 (61.1)	NR	Education (up to high school): 14 (77.7)	24.1 (24.5)
Alaghband-Rad, 2009, 19190958	.	.	17 (58.6)	.	.	.
Asbahr, 2005, 16239861	13.1 (2.54)	8.9 (2.92)	26 (65)	.	.	4.2 (2.44) years
Aspvall, 2021, 33974020	13.4 (2.6) [8-17]	9.3 (3.2) Onset OCD, (year) 11.75 (2.6)	29 (38.2)	.	Parent occupational status: Working 143 (94.1) Student 3 (2) On sick leave (3.9) Parent educational level: Primary school 2 (1.3) Secondary school 16 (10.5; College/university (<2y) 16 (10.5) College/university (>2y) 113 (74.3) Doctorate 5 (3.3)	.
Barrett, 2003, 12647571	11.21 [7-16]	.	14 (58.3)	.	.	.
Barrett, 2004, 14691360	11.9 (2.7)	.	38 (49.3)	.	.	.
Bolton, 2008, 17207457	13 [8-17]	.	14 (70)	.	.	22 months [8-60]
Bolton, 2011, 21644984	14.4 (2.1)	.	41 (42.7)	.	.	3.2 (2.7) years
Comer, 2017, 27869451	6.65 (1.3) [4-8]	.	13 (59.1)	White 20 (91.0) Biracial: 1 (4.5) Hispanic origin 1 (4.5)	.	>3months
de Haan, 1998, 9785713	13.7 (3.0) [9-19]	10.8 (3.2)	11 (50)	.	.	30.3 (30.7) months [7-144]
DeVeaugh-Geiss, 1992, 1537780	14.25	.	39 (65.0)	.	.	3.75 years
Farrell, 2013, 23722990	13.11 (3.33)	.	41	White 94% Asian 6%	.	.
Farrell, 2022, 35084071	11.95 (2.46) [7-17]	.	47	.	.	.

Study, Year, PMID	Age, Mean (SD) [Range]	Age at Symptom Onset, Mean (SD) [Range]	Male, N (%)	Race and Ethnicity, N (%)	Other Relevant SDH Factors, N (%)	Duration of OCD, Mean (SD) [Range]
Fatori, 2018, 30025255	11.8 (3.2)	6.4 (2.75)	40 (48.2)	White 76 (91.6) Black or African American 1 (1.2) Asian 1 (1.2) Mixed 5 (6.0)	.	.
Flament, 1985, 3899048	14.5 (2.3) [10-18]	10.2 (3.9) [8-16]	14 (73.7)	.	.	4 years [1-10]
Franklin, 2011, 21934055	13.60 (2.77) [7-17]	.	58 (46.8)	White 115 (92.7) Black or African American 3 (2.4) Asian 2 (1.6) Mixed: 1 (0.8) Not reported: 3 (2.4) Hispanic origin 2 (1.6)	.	.
Franklin, 2023	14.19 (2.31) [7-17]	.	500 (38.88)	White 961 (74.73) Black or African American 20 (1.56) Asian 40 (3.11) Alaska Native 8 (0.62) Native Hawaiian and Other Pacific Islander 3 (0.23) Multiracial 29 (2.26) Other 1 (0.08) Hispanic origin 72 (5.60)	.	.
Freeman, 2008, 18356758	7.11 (1.26) [4-8]	4.99 (1.27)	18 (43)	White 34 (80) Asian 1 (2) Alaska Native 1 (2) Multiracial: 1 (2) Unknown: 6 (12) Hispanic origin 1 (2)	Married and living together 35 (83.3)	>3 months
Freeman, 2014, 24759852	7.2 (1.12)	5.08 (1.7)	60 (47.2)	White 114 (89.76) Black or African American 2 (1.57) Asian 3 (2.36) Mixed: 4 (3.15) NR 4 (3.15) Hispanic origin 6 (4.7)	.	.
Geller, 2001, 11437015	11.4 (2.9)	.	49 (47.6)	White 85.6% Black or African American 1.9% Asian 0.96% Other 3.8% Hispanic origin 6.7%	.	.

Study, Year, PMID	Age, Mean (SD) [Range]	Age at Symptom Onset, Mean (SD) [Range]	Male, N (%)	Race and Ethnicity, N (%)	Other Relevant SDH Factors, N (%)	Duration of OCD, Mean (SD) [Range]
Geller, 2003, 12880497	11.7 (2.73) [6-18]	10 (3.15)	105 (54.4)	White 176 (91.2) Black or African American 3 (1.6) Asian 4 (2.1) Other 10 (5.2)	.	.
Geller, 2004, 15502598	11.3 (3.00) Children: 9.1 (1.49) Adolescents: 14.3 (1.62) [7-17]	7.5 (3.09)	117 (57.6)	White 179 (88.2) Black or African American 13 (6.4) Hispanic origin 11 (5.4)	.	4.2 (2.89) years
Ghanizadeh, 2017, 28659986	16.3 (3.2)	.	14 (48.3)	.	.	.
Grant, 2014, 24356715	14.5 (2.4) [7-17]	.	44 (73.3)	.	.	.
Guo, 2008,	15.1 (1.94) [12-18]	.	57.4%	Asian (100)	.	9.65 (7.92) months [1-36]
He, 2007,	13.9 (2.1) [8-16]	.	55	Asian (100)	.	10.7 (4.2) [6-22]
Himle, 2024 38103359	15.6 (1.62)		18 (31)	White 33 (57) Black 7 (12) Hispanic 4 (14)		NR
Hollmann, 2022, 36329915	13.2 (2.9) [7-18]	.	36 (60)	.	**Mother:** Undergraduate degree or higher, 35 (58.3) No academic degree, 22 (36.7) **Father:** Undergraduate degree or higher, 31 (51.7) No academic degree, 24 (40.0)	30.92 (30.8) months
Lenhard, 2017, 27993223	14.60 (1.71) [12-17]	10.55 (2.82)	21 (31)	.	Education: Primary 1%, High school 25%, College 4%, Vocational 4%, University 49%, Doctoral degree 1%, Other 13%	.
Leonard, 1989, 2686576	13.86 (2.87) [7-19]	10.23 (5.8) [5-16]	31 (63.3)	.	.	3.63 (2.74) years [1-10]

Study, Year, PMID	Age, Mean (SD) [Range]	Age at Symptom Onset, Mean (SD) [Range]	Male, N (%)	Race and Ethnicity, N (%)	Other Relevant SDH Factors, N (%)	Duration of OCD, Mean (SD) [Range]
Lewin, 2014, 24657310	5.8 (1.6) [3-8]	.	22 (71)	White 27 (87) Black or African American 1 (6) Asian 1 (6) Latinx 4 (13)	Married 81% Both parents (same) 77% Both parents (different residence) 6.5% Lives with single parent (mom) 13% Lives with mom/stepdad 3%	.
Li, 2020, 31800306	11.9 (3.0) [8-17]	.	3 (27)	White 11 (100)	.	.
Liebowitz, 2002, 12447029	12.7 (2.7)	.	18 (41.8)	White 35 (81.4) Black or African American 3 (7.0) Asian 1 (2.0) Alaska Native 1 (2.0) Other 1 (2.0) Hispanic origin 2 (5.0)	.	.
Liu, 2012	15.3 (5.4) [7-18]	.	51	Asian (100)	.	2.65 (1.16) [8 months - 5 years]
Ma, 2014	11.58 (0.05)	90% of population: 10 years, 10% of population: <7 years	.	.	.	5.8 (0.2) months [3-24]
March, 1990, 19630661	15.0 (2.2) [10-17]	.	11 (69)	.	.	41.2 (29.4) months
March, 1998, 9842950	12.6 (NR) [6-17]	.	71 (52)	White 116 (85) Black or African American 6 (4.4) Asian 1 (0.7) Other 8 (5.8) Hispanic origin 6 (4.4)	.	3.8 years
Mataix-Cols, 2014, 24262813	14.95 (2.1)	.	14 (51.9)	.	.	.
Merlo, 2010, 19675960	13.3 (3.0)	.	10 (62.5)	White 13 (81.3) Hispanic 2 (12.5) Mixed 1 (6.3)	.	.
Nai, 2009	15.1 (1.9) [12-18]	.	57.8%	Asian 100%	.	9.65 (7.92) months [1-36]

Study, Year, PMID	Age, Mean (SD) [Range]	Age at Symptom Onset, Mean (SD) [Range]	Male, N (%)	Race and Ethnicity, N (%)	Other Relevant SDH Factors, N (%)	Duration of OCD, Mean (SD) [Range]
Nasiry, 2020	9.46 (1.44) [7-12]	.	16 (45.7)	.	.	2.31 (1.49) years
NCT01933919	13.5 (2.74)	.	20 (54.1)	.	.	.
Neziroglu, 2000, 11191690	14.5 (2.4)	9.9 (11.7)	60%	.	.	.
Noras, 2022, 35748547	14.72 (1.43) [13-17]	.	21 (52)	.	Education: Father: HS: 16 (40) Bachelor's: 13 (37.5) Master's: 11 (27.5) Mother: HS: 22 (55) Bachelor's: 12 (30) Master's: 6 (15)	.
Peris, 2013, 22548378	12.35 (2.58)	.	11 (55)	White 12 (60) Black or African American 2 (10) Persian 3 (15) Hispanic origin Latino: 3 (15)	15 (75) came from homes with intact marriages	.
Peris, 2017, 29173737	13.12 (2.68)	.	57%	White 40 (65) Black or African American 2 (3) Asian 4 (7) Mixed racial/ethnic background 7% Iranian 5% Hispanic origin 8 (13)	.	.
Piacentini, 2011, 22024003	12.2 (2.5)	.	26 (36.6)	White 55 (77.5) Black or African American 2 (2.8) Asian 3 (4.2) Other 4 (5.6) Hispanic origin 7 (9.9)	Current Living Situation Both Biological Parents 73.2% Single Parent 18.3% Other 8.5%	.
POTS Team, 2004, 15507582	11.7 (2.7)		56 (50.0)	White 103 (92) Black or African American 4 (4) Asian 11 (1) Native Hawaiian and Other Pacific Islander 3 (3)	.	.
Rempel, 2023, 37048570	15.3 (2.1) [10-20]	.	25 (43.1)	.	.	.
Reynolds, 2013, 24060194	14.5 (1.5)	.	.	.	.	.
Rezvan, 2013, 23413047	[10-12]	10.3 years [7.5-12.5]	0 (0)	.	.	.

Study, Year, PMID	Age, Mean (SD) [Range]	Age at Symptom Onset, Mean (SD) [Range]	Male, N (%)	Race and Ethnicity, N (%)	Other Relevant SDH Factors, N (%)	Duration of OCD, Mean (SD) [Range]
Riddle, 1992, 1429406	11.8 (2.3)	.	6 (42.9)	.	.	.
Riddle, 2001, 11211371	12.9 (NR)	.	53.3%	White (95.8)	.	.
Rosa-Alcázar, 2019, 31516500	6.65 (0.74) [5.2-7.9]	.	33 (75)	White 44 (100)	.	0.65 (0.16) year
Salemink, 2015, 25724385	15.4 (2.3)	.	6 (37.5)	.	.	5.5 (3.6) years
Schuberth, 2023,	13.92 (2.57)	9.07 (3.01)	51 (43.6)	White 78 (66.7) Asian 13 (11.1) Mixed 10 (8.5) Hispanic origin 1 (0.9)	.	4.38 (2.74) years
Selles, 2021, 34079488	14.4 (2.7) [7-19]	10.0 (3.2)	14 (56)	White 15 (60) Asian 7 (28) Native Hawaiian and Other Pacific Islander 1 (4) Hispanic origin 2 (8)	Education: Father: ≤High school: 2 (8) college: 7 (28) Undergraduate: 10 (40) Advanced: 6 (24) Mother: ≤High school, 2 (8) college: 4 (16) Undergraduate: 11 (44) Advanced: 8 (32)	.
Shabani, 2019	14.96 (1.47)	12.42 (1.87)	38 (55.1)	.	.	.
Shen, 2020		.	75.7%	Asian 100%	.	.
Simons, 2006, 16785776	13.9 (3.1)	.	6 (60)	.	.	7.7 (11.2) months
Skarphedinsson, 2015, 25239489	14.0 (2.7)	.	24 (48)	At least one Scandinavian parent 49 (98)	Family status Biological parents living together 31 (62) divorced 19 (38) SES High 30 (62) Low 18 (37.5)	.
Storch, 2007, 17420681	13.3 (2.7)	.	18 (45)	White 37 (92.5) Native Hawaiian and Other Pacific Islander 3 (7.5)	Family income, mean $96,055 (49,855)	.

Study, Year, PMID	Age, Mean (SD) [Range]	Age at Symptom Onset, Mean (SD) [Range]	Male, N (%)	Race and Ethnicity, N (%)	Other Relevant SDH Factors, N (%)	Duration of OCD, Mean (SD) [Range]
Storch, 2010, 20817153	12.2 (2.8) [8–17]	.	19 (63)	Ethnicity Caucasia 29 (97)	.	.
Storch, 2011, 21684018	11.10 (2.59) [7-16]	.	19 (61.3)	White 23 (74) Black or African American 1 (3) Asian 2 (6.5) Other 4 (13) Hispanic origin 1 (3)	.	.
Storch, 2013, 24184429	11.9 (3.5)	.	61.2%	.	.	.
Storch, 2016, 27367832	12.8 (5.04)	.	66 (46.5)	White 126 (88.7) Black or African American 5 (3.5) Asian 3 (2.1) Alaska Native 0 (0.0) Native Hawaiian and Other Pacific Islander 0 (0.0) Unknown 8 (5.6), More than one race 0 (0.0) Hispanic origin 22 (15.5)	.	.
Tuerk, 2023	12.7 (2.1)	.	12 (43)	White 18 (64) Black or African American 0 (0) Asian 3 (11) Native Hawaiian and Other Pacific Islander 2 (7) Multiracial 2 (7) Hispanic/Latino origin 0 (0)	.	.
Turner, 2014, 25457928	14.35 (2.13)	11.0 (3.37)	39 (54.2)	.	.	.
Williams, 2010, 19921305	13 (NR)	.	13 (61.9)	.	.	.
Wolters, 2016,	12.5 (2.6)	.	16 (39.0)	.	.	.
Wolters, 2021,	13.6 (2.9)	.	40 (54)	.	.	.
Xie, 2020	15.0 (1.3) [2-18]	.	(59.3)	Asian 100%	.	13.5 (2.0) months [5-20]
Zhang, 2014	16. 01 (1. 85) [12-18]	.	(57. 5)	Asian 100%	.	.
Zhu, 2008	15.3 (1.9) [12-18]	.	0	Asian 100%	.	9.0 (7.7) months [1-35]

Abbreviations: HS = High school; N = Sample size; OCD = Obsessive Compulsive Disorder; PMID = PubMed Identifier; POTS = Pediatric OCD Treatment Study; SD = Standard deviation; SDH = Social Determinant History

Table C-2.3.2. Key Question 2: Sample characteristics, Part 2

Study, Year, PMID	CY-BOCS, Mean (SD)	CGI-S, Mean (SD)	Comorbidities; N%	Previous Treatment, N%
Agrawal, 2024, India, CN-02530420	22.8 (4.6)	.	Depression 1 (12.5)	.
Alaghband-Rad, 2009, 19190958	.	.	.	None of them had received previous treatment for OCD
Asbahr, 2005, 16239861	26.7 (5.8)	5.3 (0.8)	Anxiety 12 (30); Depression 7 (17.5); Bipolar spectrum disorders 1 (2.5); Tics/Tourette's 21 (52.5); ADHD 9 (22.5); ODD 6 (15)	.
Aspvall, 2021, 33974020	23 (3.7) Range: 16-33	.	Anxiety 7 (4.6); Depression 18 (11.8); Tics/Tourette's 14 (9.2); ADHD 10 (6.6);	CBT for OCD 15 (9.9), CBT for other 17 (11.2), Other 25 (16.4)
Barrett, 2003, 12647571	22.42	.		.
Barrett, 2004, 14691360	22.54 (5.31)	.	Anxiety 46 (59.7); Depression 6 (7.79)	.
Bolton, 2008, 17207457	.	.		.
Bolton, 2011, 21644984	22.7 (5.8)	.	Depression 8 (9.4); Tics/Tourette's 2 (2.1); ADHD 7 (8.3); ODD 12 (13.5)	.
Comer, 2017, 27869451	23.05 (3.7)	4.75 (0.8)	Anxiety 5 (22.7); 4 (18.2); 4 (18.2); Trauma /stressor related disorders 2 (9.1)	.
de Haan, 1998, 9785713	22.5 (6.6)	.	Anxiety 2 (9); Depression 1 (4.5); Tics/Tourette's1 (4.5)	Previous treatment (counseling) but no behavior therapy or drug therapy 8 (36.3)
DeVeaugh-Geiss, 1992, 1537780	.	.	.	.
Farrell, 2013, 23722990	.	.	Anxiety 8 (47.1); Depression 2 (11.7); ADHD 4 (23.5)	CBT 4 (24), CBT+SRI 13 (76)
Farrell, 2022, 35084071	27.3 (4.0)	.	.	.
Fatori, 2018, 30025255	.	.	Anxiety 65 (80.2); Depression 16 (19.8); Tics/Tourette's17 (21.)	Previous psychiatric treatment 27 (32.9), Previous psychotherapy 28 (34.1)
Flament, 1985, 3899048	.	.	.	Hospitalization: 8 (42.1); Psychotherapy: 13 (68.4); Behavioral therapy 5 (26.3); Medications 15 (78.9)
Franklin, 2011, 21934055 POTSII	26.29 (5.05)	4.93 (.90)	Anxiety/Mood 55 (44.4); Tics/Tourette's 19 (15.3); ADHD 27 (21.8); ODD: Externalizing 2 (1.6)	First SRI trial: 63/124 (50.8); One other past SRI trial: 36/124 (29); two past SRI trials: 11/124 (8.9); three past SRI trials: 8/124 (6.5); four past SRI trials: 3/124 (2.4); five past SRI trials: 2/124 (1.6) 61 (49.2)

Study, Year, PMID	CY-BOCS, Mean (SD)	CGI-S, Mean (SD)	Comorbidities; N%	Previous Treatment, N%
Franklin, 2023	24.04 (5.15)	.	Anxiety 735 (57.15); Depression 604 (46.97); Trauma /stressor related disorders 47 (3.65)	.
Freeman, 2008, 18356758	22.4 [11-32]	3.96 (0.95)	Anxiety 23 (54.8); Tics/Tourette's 4 (9.5); ADHD 8 (19)	Either medication and/or psychotherapy 7 (16)
Freeman, 2014, 24759852	25.55 (4.23)	4.69 (0.82)	Anxiety 59 (46.46); Depression 1 (0.79); Tics/Tourette's 29 (22.83)/14 (11.02); ADHD 18 (14.17); ODD 18 (14.17); ODD: Externalizing 31 (24.41)	.
Geller, 2001, 11437015	25.1 (5.0)	4.8 (2.4)	.	.
Geller, 2003, 12880497	9.75 (0.66)	.	Anxiety 44 (22.8); Depression 8 (4.1); Tics/Tourette's 22 (11.4); ADHD 26 (13.5); ODD 7 (3.6)	None 138 (71.5), psychotherapy 21 (10.9), pharmacotherapy 25 (13), psychotherapy + pharmacotherapy 9 (4.7)
Geller, 2004, 15502598	24.8 (5.01)	.	Anxiety 14 (6.9); ADHD 19 (9.4)	Psychotherapy 20 (9.8), Pharmacotherapy 25 (12.3), psychotherapy and pharmacotherapy 17 (8.4)
Ghanizadeh, 2017, 28659986	.	.	.	.
Grant, 2014, 24356715	28.2 (3.8)	.	Tics/Tourette's 28 (47); ASD/PDD 17 (28.3)	.
Guo, 2008	.	.	.	.
He, 2007	.	.	.	.
Himle, 2024 38103359	21.0 (6.83)	,	Anxiety 17 (57); Depression 3 (10), Tics 3 (10)	.
Hollmann, 2022, 36329915	24.6 (2.4)	5.0 (0.46)	Anxiety 12 (20); Depression 7 (11.7); Tics/Tourette's 6 (10); ASD/PDD 1 (1.67); ADHD 10 (16.7)	Any 31 (51.7)
Lenhard, 2017, 27993223	22.55 (4.10)	.	Anxiety 13% Panic anxiety disorder 7%; Social anxiety disorder 9%; Depression 7%; Tics/Tourette's 6%; Trauma /stressor related disorders 1%; ADHD 9%	CBT 1 (1.5), general counseling 25 (37.3)
Leonard, 1989, 2686576	.	.	.	Psychotherapy 37 (75.5), behavioral therapy 3 (6.1), antidepressants 19 (38.8), neuroleptic 8 (16.3), anxiolytic 4 (8.2), hospitalized 13 (26.5)
Lewin, 2014, 24657310	24.49 (5.74)	3.88 (0.77)	Anxiety 22 (71); ADHD 13 (42); ODD 11 (35)	.
Li, 2020, 31800306	.	.	Anxiety 1 (9); Depression 1 (9); Bipolar spectrum disorders 3 (2); Tics/Tourette's 3 (27)	.
Liebowitz, 2002, 12447029	.	.	Anxiety 19 (44.2); Depression 9 (20.9); ADHD 3 (0.07); ODD 4 (0.09)	.
Liu, 2012	.	.	.	.
Ma, 2014	.	.	.	.

Study, Year, PMID	CY-BOCS, Mean (SD)	CGI-S, Mean (SD)	Comorbidities; N%	Previous Treatment, N%
March, 1990, 19630661	.	.	.	.
March, 1998, 9842950	22.79 (NR)	4.7 (NR)	Anxiety 7 (3.7); Depression 4 (2.1); Tics/Tourette's 8 (4.3); ADHD 9 (4.8)	.
Mataix-Cols, 2014, 24262813	25.65 (3.6)	.	Anxiety 3 (11.1); Depression 1 (3.7); Tics/Tourette's 3 (11.1); ADHD 1 (3.7)	.
Merlo, 2010, 19675960	.	.	.	.
Nai, 2009	.	.	.	.
Nasiry, 2020	.	.	.	.
NCT01933919	26.2 (5.69)	.	.	.
Neziroglu, 2000, 11191690	25.4 (5.7)	5.3 (0.5)	.	.
Noras, 2022, 35748547	.	.	.	.
Peris, 2013, 22548378	25.45 (3.53)	5.45 (0.69)	.	.
Peris, 2017, 29173737	25.48 (3.51)	5.28 (0.80)	Anxiety 28 (45); Depression 9 (15); Tics/Tourette's 7 (12); ASD/PDD 3 (5); ADHD 14 (22); ODD/CD 6 (10)	At baseline, SSRIs 23%, stimulants 2%
Piacentini, 2011, 22024003	.	.	Anxiety 33 (46.5); Depression 3 (4.2); Tics/Tourette's 8 (11.3); ADHD 9 (13.9); ODD 3 (4.2)	Any Psychiatric 25.4%, SSRI/SRI 21.1%, Stimulant 7.0%, Other 3.7%
POTS Team, 2004, 15507582	24.6 (4.1)	4.8 (0.72)	Anxiety 70 (63); Tics/Tourette's 18 (16); ADHD 30 (27)	.
Rempel, 2023, 37048570	17.41 (0.88)	.	.	.
Reynolds, 2013, 24060194	.	.	Anxiety 33 (66%); Trauma /stressor related disorders 3 (6%)	.
Rezvan, 2013, 23413047	29.5 (3.0)	.	.	.
Riddle, 1992, 1429406	.	.	Anxiety 3 (21.0); Depression 2 (14.2); ADHD 1 (7.1)	.
Riddle, 2001, 11211371	.	.	.	Psychotherapy 40 (33.3), OCD medication 38 (31.7), Other medication 4 (3.3)
Rosa-Alcázar, 2019, 31516500	22.7 (3.95)	.	Anxiety 8 (18.2); Depression 2 (4.5); Trauma /stressor related disorders 16 (36.4)	.
Salemink, 2015, 25724385	22.4 (6.6)	.	.	.
Schuberth, 2023	.	.	Anxiety 25 (25.8); Depression 3 (3.1); Tics/Tourette's 18 (18.6); ASD/PDD 1 (1.0); ADHD 22 (22.7); ODD 4 (4.1)	Any OCD treatment 71 (78.9); CBT with ERP 17 (18.9); Medication(s) for OCD 58 (64.4)

Study, Year, PMID	CY-BOCS, Mean (SD)	CGI-S, Mean (SD)	Comorbidities; N%	Previous Treatment, N%
Selles, 2021, 34079488	.	.	Anxiety 10 (39); 1 (4); Depression 1 (4); Tics/Tourette's3 (12); ASD/PDD 1 (4); Trauma /stressor related disorders 1 (4); ADHD 5 (19); Social phobia 3 (12); Panic disorder 1 (4)	Prior psychosocial treatment for OCD 15 (60); SRIs 9 (36)
Shabani, 2019	24.33 (4.15)	.	.	.
Shen, 2020	.	.	.	.
Simons, 2006, 16785776	22.0 (7.9)	.	.	.
Skarphedinsson, 2015, 25239489	26.4 (5.6)	.	Anxiety 12 (24); Depression 3 (6); Tics/Tourette's 12 (24); ADHD 7 (14); ODD 1 (2)	.
Storch, 2007, 17420681	.	.	Anxiety 11 (27.5); Depression 7 (17.5); Tics/Tourette's 5 (12.5); ADHD 12 (30)	Medication alone 9 (22.5), Psychotherapy alone 2 (5.0), Medication and psychotherapy 18 (45.0)
Storch, 2010, 20817153	25.1 (4.1)	4.9 (0.8)	Anxiety 5 (16.7); Depression 3 (10); Tics/Tourette's 3 (10); ADHD 14 (46.7); ODD 4 (13.3)	SSRI 9 (30), Atomoxetine 2 (6.7), Alpha-2 adrenergic agonist 2 (6.7), TCA 1 (3.3), SNRI 1 (3.3), Stimulant 1 (3.3)
Storch, 2011, 21684018	23.3 (3.2)	3.24 (0.9)	.	Prior CBT 12 (38.7), supportive psychotherapy 7 (22.6)
Storch, 2013, 24184429	25.1 (4.7)	.	Tics/Tourette's 11 (23.4); Trauma /stressor related disorders: Internalizing 24 (51.1), Externalizing 10 (21.3)	.
Storch, 2016, 27367832	24.36 (5.41)	3.55 (3.3, 3.8)	Anxiety 41 (28.87); Depression 21 (14.79); ADHD 37 (26.1)	SSRI 42 (29.58), Atypical antipsychotic 3 (2.1), Stimulant 7 (4.9)
Tuerk	23.68 (4.61)	.	Tics/Tourette's 9 (32)	.
Turner, 2014, 25457928	24.88 (3.94)	.	Anxiety 39 (54.2); Depression 7 (9.7); Tics/Tourette's 6 (8.3); ADHD 1 (1.4); ODD 1 (1.4)	Previous CBT Treatment, 21 (29.17)
Williams, 2010, 19921305	.	.	Anxiety 8 (38.1); ADHD 2 (9.5)	.
Wolters, 2016	24.2 (3.8)	.	Anxiety 24 (58.5); Depression 8 (19.5); ADHD 6 (14.6)	.
Wolters, 2021	25.1 (5.6)	.	Anxiety 54 (73); Depression 53 (72); ADHD 14 (19)	.
Xie, 2020	.	.	.	.
Zhang, 2014	.	.	.	.
Zhu, 2008	.	.	.	.

Abbreviations: ADHD = Attention-deficit/Hyperactivity Disorder; ASD = Autism spectrum disorder; CBT= Cognitive behavioral Therapy; CD = Conduct Disorder; CGI-S = Clinical Global Impression-Severity; CY-BOCS = Children's Yale-Brown Obsessive Compulsive Scale; ERP = Exposure and Response Prevention; OCD = Obsessive Compulsive Disorder; ODD = Oppositional-defiant Disorder; PDD =Pervasive Developmental Disorder; PMID = PubMed Identifier; POTS = Pediatric OCD Treatment Study; SD = Standard deviation; SNRI = Serotonin Norepinephrine Reuptake Inhibitor; SRI = Serotonin Reuptake Inhibitor; SSRI = Selective Serotonin Reuptake Inhibitor; TCA = Tricyclic antidepressant.

Appendix D. Results: Risk of Bias and Assessment of Methodological Quality

Table D-1.1. KQ 1: Risk of bias for brief assessment tools

Study	Was a Consecutive or Random Sample of Patients Enrolled?	Was a Case-control Design Avoided?	Did the Study Avoid Inappropriate Exclusions?	Were the Index Test Results interpreted Without Knowledge of the Results of the Reference Standard?	If a Threshold Was Used, Was It Prespecified?	Is the Reference Standard Likely to Correctly Classify the Target Condition?	Were the Reference Standard Results interpreted Without Knowledge of the Results of the Index Test?	Did All Patients Receive a Reference Standard?	Did All Patients Receive the Same Reference Standard?	Were All Patients Included in the Analysis?	Overall Rating
Abramovitch, 2022, 35697331	Unclear	No	Yes	Unclear	No	Yes	Yes	Yes	Yes	Yes	Moderate
Abramovitch, 2022, 35091252	Unclear	No	Yes	Unclear	No	Yes	Yes	Yes	Yes	Yes	Moderate
Andersen, 2012, 23171745	Yes	No	Yes	Unclear	No	Unclear	Yes	Yes	Yes	Yes	Moderate
Bamber, 2002, 12364847	No	No	Unclear	Unclear	No	Unclear	Unclear	No	No	No	High
Battle, 2013,	Unclear	No	Unclear	Unclear	Unclear	Yes	Unclear	Yes	Yes	Yes	Moderate
Hudziak, 2006, 16423147	No	No	Yes	Unclear	No	Yes	Unclear	Yes	Yes	Yes	Moderate
Ivarsson, 2008, 18280696	Unclear	No	Yes	Unclear	No	Yes	Yes	Yes	No	Yes	High
Lambe, 2021, 37431399	No	No	Yes	Unclear	No	Yes	Yes	Yes	Yes	Yes	Moderate
Piqueras, 2017, 27283942	No	No	Unclear	Unclear	No	Yes	Yes	No	No	Yes	High
Piqueras, 2015, 27703719	No	No	Unclear	Unclear	No	Yes	Yes	Yes	No	Yes	High
Rough, 2020, 32030629	Yes	No	Yes	Unclear	No	Yes	Yes	Yes	No	Yes	High
Saad, 2017, 28151703	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Low

Study	Was a Consecutive or Random Sample of Patients Enrolled?	Was a Case-control Design Avoided?	Did the Study Avoid Inappropriate Exclusions?	Were the Index Test Results interpreted Without Knowledge of the Results of the Reference Standard?	If a Threshold Was Used, Was It Prespecified?	Is the Reference Standard Likely to Correctly Classify the Target Condition?	Were the Reference Standard Results interpreted Without Knowledge of the Results of the Index Test?	Did All Patients Receive a Reference Standard?	Did All Patients Receive the Same Reference Standard?	Were All Patients Included in the Analysis?	Overall Rating
Sattler, 2018, 2019-05127-008	No	No	Yes	Yes	No	Yes	Yes	Yes	No	Yes	High
Shafran, 2003, 12550826	No	No	Yes	Unclear	Unclear	Yes	Yes	Yes	No	Yes	High
Skarphedinsson, 2021, 34293000	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Moderate
Stewart, 2005, 16379516	No	No	Unclear	Yes	No	Yes	Yes	Yes	Yes	Yes	moderate
Storch, 2006, 16046257	No	No	Unclear	Yes	No	Yes	Yes	Yes	No	Yes	High
Storch, 2011, 21353458	No	No	Unclear	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Uher, 2007, 17906247	Yes	Yes	Unclear	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Low
Whiteside, 2012, 22078243	Unclear	No	Yes	Unclear	No	Yes	Yes	Yes	Yes	Yes	Moderate
Zemestani, 2022, 33409771	No	No	No	Yes	No	Unclear	Yes	No	No	Yes	High
Zemestani, 2021, 2021-61128-001	No	No	Unclear	No	No	Yes	Yes	No	No	Yes	High

Table D-2.1. KQ 2: ROB for RCTs

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessor	Incomplete outcome data	Selective Reporting	Intention-to-treat-analysis	Interventions adequately described	Cohorts similar	Clear reporting with no discrepancies	Overall rating
Agrawal, 2024, CN-02530420	Low	Low	Low	High	Low	Low	Low	Low	Low	Low	Low
Alaghband-Rad, 2009, 19190958	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear	Low	High	Low	Moderate
Asbahr, 2005, 16239861	Low	Unclear	High	Low	High	Low	High	Low	Low	Low	High
Aspvall, 2021, 33974020	Low	Unclear	High	Low	Low	Low	Low	Low	Low	Low	Low
Barrett, 2003, 12647571	Low	Low	Low	Low	Low	Low	Unclear	Low	Low	Low	Low
Barrett, 2004, 14691360	Low	Unclear	High	Low	High	Low	Low	Low	Unclear	Low	Moderate
Bolton, 2008, 17207457	Low	Low	High	Unclear	Low	Low	Low	Low	Low	Low	Moderate
Bolton, 2011, 21644984	Low	Unclear	High	Low	Low	Low	Low	Low	Low	Low	Low
Comer, 2017, 27869451	Low	Unclear	Low	Low	Low	Unclear	Low	Low	Low	Low	Low
de Haan, 1998, 9785713	Unclear	Unclear	High	High	Low	Low	Low	Low	Low	Low	High
DeVeaugh-Geiss, 1992, 1537780	Unclear	Unclear	Unclear	Unclear	Low	Low	Low	Low	Low	Low	Moderate
Farrell, 2013, 23722990	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
Farrell, 2022, 35084071	Low	Low	Low	Low	Low	Unclear	Low	Low	Low	Low	Low
Fatori, 2018, 30025255	Low	Low	High	Low	Low	Low	Low	Low	Low	Low	Low
Flament, 1985, 3899048	Unclear	Unclear	Low	Low	High	Low	Low	Low	Unclear	High	High
Franklin, 2011, 21934055	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessor	Incomplete outcome data	Selective Reporting	Intention-to-treat-analysis	Interventions adequately described	Cohorts similar	Clear reporting with no discrepancies	Overall rating
Freeman, 2008, 18356758	Unclear	Low	Low	Low	Unclear	Low	Low	Low	Low	Low	Low
Freeman, 2014, 24759852	Low	Low	Low	Low	Unclear	Low	Low	Low	Low	Low	Low
Geller, 2001, 11437015	Unclear	Unclear	Low	Low	Low	Low	Low	Low	Low	Low	Low
Geller, 2003, 12880497	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
Geller, 2004, 15502598	Low	Unclear	Low	Low	High	Low	Low	Low	Low	Low	Moderate
Ghanizadeh, 2017, 28659986	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
Grant, 2014, 24356715	Low	Low	Low	Low	High	Low	Low	Low	Low	Low	Moderate
Guo, 2008	Unclear	Unclear	Unclear	Unclear	Low	Low	Low	Low	Low	Low	Moderate
He, 2007	Unclear	Unclear	Unclear	Unclear	Low	Low	Low	Low	Low	Low	Moderate
Himle, 2024, 38103359	Low	Low	High	Low	Low	Low	Low	Low	Low	Low	Low
Hollmann, 2022, 36329915	Low	Low	Low	Unclear	Unclear	Low	Low	Low	Low	Low	Low
Lenhard, 2017, 27993223	Low	Low	High	Low	Low	Low	Low	Low	Low	Low	Low
Leonard, 1989, 2686576	Unclear	Unclear	Low	Low	Low	Low	Low	Low	Low	Unclear	Low
Lewin, 2014, 24657310	Low	Unclear	Low	Low	Unclear	Low	High	Low	Low	Low	Moderate
Li, 2020, 31800306	Low	Low	Low	Low	High	Low	Low	Low	Low	Low	Moderate
Liebowitz, 2002, 12447029	Unclear	Unclear	Unclear	Low	Low	Low	Low	Low	Low	Low	Low
Liu, 2012	Low	Unclear	Unclear	Unclear	Low	Low	Low	Low	Low	Unclear	Low
Ma, 2014	Unclear	Unclear	Unclear	Unclear	Low	Low	Low	Low	Low	High	High

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessor	Incomplete outcome data	Selective Reporting	Intention-to-treat-analysis	Interventions adequately described	Cohorts similar	Clear reporting with no discrepancies	Overall rating
March, 1990, 19630661	Low	Unclear	Low	Low	Low	Low	Low	Low	Low	Low	Low
March, 1998, 9842950	Low	Low	Low	Low	Low	Low	Low	Low	Low	Unclear	Low
Mataix-Cols, 2014, 24262813	Low	Unclear	Low	Low	Low	Low	Low	Low	Low	Low	Low
Merlo, 2010, 19675960	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear	Low	Unclear	Low	Moderate
Nai, 2009	Unclear	Unclear	Unclear	Unclear	Low	Low	Low	Low	Low	Low	Moderate
Nasiry, 2020,	Unclear	Unclear	Unclear	High	Low	Unclear	Unclear	Low	Low	Unclear	High
NCT01933919	Unclear	Unclear	Low	Unclear	Low	Low	Low	Low	Low	Low	Low
Neziroglu, 2000, 11191690	Unclear	Unclear	High	Unclear	Low	Low	Low	Low	Unclear	Low	Moderate
Noras, 2022, 35748547	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
Peris, 2013, 22548378	Low	Unclear	Unclear	Low	Low	Low	Unclear	Low	Low	Low	Low
Peris, 2017, 29173737	Low	Unclear	High	Low	Low	Low	Unclear	Low	Low	Low	Moderate
Piacentini, 2011, 22024003	Low	Unclear	Unclear	Low	Low	Low	Low	Low	Low	Low	Low
POTS Team, 2004, 15507582	Low	Low	Unclear	Low	Low	Low	Low	Low	Low	Low	Low
Rempel, 2023, 37048570	Low	Low	Unclear	Low	Low	Low	Low	Low	High	Low	Low
Reynolds, 2013, 24060194	Low	Low	High	Low	Low	Low	Low	Low	Low	Low	Low
Rezvan, 2013, 23413047	Low	Unclear	Low	Low	Unclear	Unclear	Unclear	Low	Unclear	High	Moderate
Riddle, 1992, 1429406	Unclear	Unclear	Low	Low	Low	Low	High	Low	Low	Low	Moderate
Riddle, 2001, 11211371	Unclear	Unclear	Low	Low	Low	Low	Low	Low	Low	Low	Moderate

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessor	Incomplete outcome data	Selective Reporting	Intention-to-treat-analysis	Interventions adequately described	Cohorts similar	Clear reporting with no discrepancies	Overall rating
Rosa-Alcázar, 2019, 31516500	Low	Low	Low	Low	Low	Unclear	Low	Low	Low	Low	Low
Salemink, 2015, 25724385	Unclear	Unclear	Low	Low	Low	Low	Low	Low	Low	Low	Low
Selles, 2021, 34079488	Low	Low	Low	Low	Unclear	Unclear	Low	Low	Low	Low	Low
Shabani, 2019,	Low	Low	High	Low	Low	Low	Low	Low	Low	Low	Moderate
Shen, 2020	Low	Unclear	Unclear	Unclear	Low	Low	Low	Low	Low	High	Moderate
Skarphedinsson, 2015, 25239489	Low	Unclear	High	High	High	Low	Low	Low	Low	Low	High
Storch, 2007, 17420681	Unclear	Unclear	High	Low	Low	Low	Low	Low	Low	Low	Low
Storch, 2010, 20817153	Low	Unclear	Low	Low	Low	Low	Low	Low	Low	Low	Low
Storch, 2011, 21684018	Low	Unclear	High	Low	High	Low	Low	Low	Low	Low	High
Storch, 2013, 24184429	Low	Unclear	Low	Low	Low	Low	Low	Low	Low	Low	Low
Storch, 2016, 27367832	Low	Unclear	Low	Low	Low	High	Low	Low	Low	Low	Low
Tuerk, 2023	Low	Low	High	Low	Low	Low	High	Low	Low	Low	Moderate
Turner, 2014, 25457928	Low	Low	High	Low	Low	Low	Low	Low	Low	Low	Low
Williams, 2010, 19921305	Low	Low	High	Low	Low	Low	Low	Low	Low	Low	Low
Wolters, 2016	Low	Unclear	High	Unclear	Low	Low	Low	Low	Low	Low	Moderate
Wolters, 2021	Low	Unclear	High	Low	Low	Low	Low	Low	Low	Low	Low
Xie, 2020	Unclear	Low	Unclear	Unclear	Low	Low	Low	Low	Low	High	High
Zhang, 2014	Unclear	Unclear	Unclear	Unclear	Low	Low	Low	Low	Low	Unclear	Moderate
Zhu, 2008	Unclear	Unclear	Unclear	Unclear	Low	Low	Low	Low	Low	Low	Moderate

Table D-2.2. KQ 2: ROB for NRCSs

Study	Blinding of participants and personnel	Blinding of outcome assessor	Incomplete outcome data	Selective Reporting	Intention-to-treat-analysis	Appropriate analysis method used to control for potential confounding domains?	Cohorts similar	Clear reporting with no discrepancies	Overall RoB
Franklin, 2023	High	High	Unclear	Low	High	Low: Propensity score (regression or matching)	High	Low	High
Schuberth, 2023	High	Unclear	Low	Low	High	Low RoB: Propensity score (regression or matching)	High	Low	High

Appendix E. Results: Evidence Tables

Key Question 1

For the full extractions and results for Key Question 1, please see Appendix G. Below are the summarized results for full diagnostic tools.

Semi-Structured Diagnostic Interviews, OCD-Specific: CY-BOCS

Three eligible studies evaluated the diagnostic accuracy of various CY-BOCS thresholds, compared to a reference standard that included specialist diagnostic interviews. The CY-BOCS includes 10 items, that evaluate the severity of obsessions and compulsions across 5 dimensions: frequency, interference, distress, resistance, and control in children and adolescents, aged 6 to 17 years.[5] The scale ranges from 0 to 40, with higher values representing more severe disease. Two studies were case-control designs with OCD prevalence of 79% in Novara 2020 and 55% in Shabni 2019,[6, 7] and the other study only included children with OCD.[8] RoB was high for two[7, 8] and moderate for the third.[6] Results for each study are shown in Table E-KQ1-1. Because only two studies provided both sensitivity and specificity data, the studies were not meta-analyzed. The studies were consistent in that a CY-BOCS score >16 has a sensitivity of at least 75%, with 100% specificity in one study; sensitivity was near 100% with a score >17 in one study, but with a lower specificity (79%). Shabani 2019, reported that, in a cohort of 128 children (70 with OCD; 58 with another anxiety disorder), the AUC for the CY-BOCS was high at 0.93 (95% CI 0.88 to 0.97).[7]

Table E-KQ1-1. Sensitivity and specificity for CY-BOCS

Study (N OCD/N Control) RoB	Cutoff	Sensitivity, % (95% CI)	Specificity, % (95% CI)
Novara 2020[6] (53/14) moderate	16	75 (62, 86)	100 (77, 100)
Shabani 2019[7] (58/70) high	17	99 (92, 100)	79 (67, 89)
Stewart 2005[8] (79/NA) high	16	76 (65, 85)	NA

Abbreviations: CI = confidence interval; OCD = obsessive compulsive disorder; RoB = overall risk of bias for study

The shading differentiates studies but does not provide any unique meaning.

Semi-Structured Diagnostic Interviews, Not OCD-Specific

We found 5 studies that addressed the diagnostic accuracy of non-OCD specific semi-structured diagnostic interviews[9-13] in 807 children. None of these tools is specific to OCD, and only one was evaluated by more than one study. Three low-risk-of-bias studies evaluated the Mini-International Neuropsychiatric Interview for Children and Adolescents (**MINI-KID**),[9, 11, 13] a structured clinical diagnostic interview for children 6 to 17 years old to identify DSM-IV and ICD-10 psychiatric and suicidality disorders, in populations where all children were at risk for OCD, and 6% to 7% were found to have OCD. The sensitivities of the MINI-KID for these populations ranged from 71% to 88% and the specificities ranged from 76% to 93% when compared to a full clinical diagnosis based on the Diagnostic and Statistical Manual of Mental Disorders (DSM).

The Development and Well-Being Assessment (**DABWA)** consists of a series of clinical interviews, which are designed to generate ICD-10 and DSM-IV or DSM-5 psychiatric diagnoses for subjects aged 2 to 65 years old. The performance of the DAWBA package was evaluated in a single low-risk-of bias study of 51 children (37 with OCD and 14 clinical controls). DABWA diagnosis, based on clinician rating or computer-generated diagnostic prediction, was compared to a consensus diagnosis.[12] Sensitivity was somewhat higher with the clinician than the computer rating (84%, 95% CI 69% to 94% compared to 74%, 95% CI 57% to 87%), but specificity was somewhat lower (54%, 95% CI 25% to 81% compared to 62%, 95% CI 32% to 86%). Compared to consensus, both the computer and clinicians tended or over-predict which children had comorbid disorders: 79% of OCD participants were identified as having one or more comorbid disorders in the computer-rated group, compared to 58% in the clinician-rated group and 50% in the consensus group.

The **DISC-2.1** is a structured diagnostic instrument to assess common psychiatric diagnoses in children 6 to 17 years old. The study that evaluated DISC-2.1 was at high RoB due to using a case-control design and different reference standards for cases and controls The combination of parent and child report had the best sensitivity (88%; 95% CI 64 to 99),[10] when compared to diagnoses based on parent or child report alone.

Key Question 2

Results tables for all studies included in KQ2 analyses are below. The full data are available in SRDR+.

Description of RCTs Evaluating Novel Interventions or Comparators

Behavioral Interventions—11 RCTs

One RCT[14] randomized 31 young children (ages 3 to 8 years) to ERP compared to treatment as usual (TAU). The TAU group received active behavioral and pharmacological interventions that were not well characterized.

Three RCTs evaluated variations in ERP delivery—intensity (daily sessions for 3 weeks vs. weekly sessions for 14 weeks),[15] location (home versus clinic)[16] and treatment provider (mother as treatment provider versus both parents and the child.[17]

Another 3 RCTs studies augmented ERP plus another behavioral intervention—one study evaluated the effect an additional motivational interview (MI) component to ERP[18], one study evaluated an app to create and push tailored assignments to patients on their mobile devices.[19] and one examined the effects of Cognitive Bias Modification of Interpretation (CMB-I) during the waiting period for ERP.[20]

Four studies evaluated other behavioral interventions—one study compared an attachment-based intervention with waitlist controls.[21], one compared CMB-I to ERP with or without pharmacotherapy[22], one compared CMB-I with behavioral control[23] and one study compared a mindfulness intervention with behavioral control.[24]

Pharmacological/Other Interventions—8 RCTs

Two trials, a randomized cross-over trial[25] that compared two TCAs (desipramine versus clomipramine) and an RCT[26] that compared two SSRIs (citalopram versus fluoxetine), compared medications belonging to the same drug class and therefore would be assigned to the same pharmacological treatment node in the network meta-analysis.

Two RCTs evaluated N-acetylcholine (NAC)— one compared NAC versus placebo[27] and another compared NAC plus SSRI versus placebo plus SSRI.[28]

A single RCT[29] evaluated treatment with an herbal syrup and fluvoxamine, compared to fluvoxamine and placebo syrup. One RCT evaluated the glutamate inhibitor riluzole compared to placebo.[30] Another RCT compared the atypical antipsychotic risperidone and SSRI with SSRI alone.[31] One study evaluated transcranial direct current stimulation (tDCS) plus fluoxetine versus fluoxetine alone.[32]

We also excluded novel treatment contrasts from 3 RCTs included in the NMA.

We excluded brief ERP versus waitlist and brief ERP versus ERP from a 3-arm RCT (retaining ERP versus waitlist).[33]

The POTS II study assigned participants to three arms: SSRI, medical management plus instruction in CBT (I-ERP+SSRI) and combined SSRI and ERP groups.[34] We excluded two treatment contrasts from the network —I-ERP+SSRI versus SSRI and I-ERP+SSRI versus ERP+SSRI—retaining SSRI+ERP vs. SSRI.

Another 3-arm study assigned participants to acceptance and commitment therapy (ACT) plus SSRI, ERP plus SSRI and SSRI alone. We excluded two treatment contrasts from the network—ACT+SSRI versus ERP+SSRI and ACT+SSRI versus SSRI—retaining the ERP+SSRI versus SSRI.[35]

Table E-KQ2-1. Randomized controlled trials evaluating novel interventions or comparators excluded from meta-analyses

Study	N	Comparison	Details	CY-BOCS NMD	Remission RR	CGI-S NMD	FAS NMD
Bolton, 2011	60	Brief ERP vs.Control (WL)	5 sessions of ERP s vs. 12 sessions over 12 weeks	**-8.1 (-12.1, -4.1)**	**6 (1.53, 23.53)**	NR	NR
Bolton, 2011	72	Brief ERP vs. ERP	5 sessions of ERP s vs. WL	3.8 (0.2, 7.4)	0.82 (0.54, 1.24)	NR	NR
Lewin, 2014	31	ERP vs. TAU	TAU not well characterized	**-11.7 (-16.2, -7.2)**	NR	**-1.42 (-2.10, -0.74)**	**-6.18 (-11.28, -1.08)**
Selles, 2021	26	Intensive ERP (home) vs. Intensive ERP (clinic)		-0.4 (-4.9, 4.1)	NR	NR	NR
Storch, 2007	40	Intensive ERP vs. ERP	Daily ERP for 3 weeks (14 session) vs. weekly ERP for 14 weeks	-3.8 (-8.2, 0.6)	0.94 (0.62, 1.42)	**-1.2 (-1.77, -0.63)**	**-8.7 (-14.61, -2.79)**
Merlo, 2010	16	MI+ERP vs. ERP	.	-6.6 (-15.4, 2.1)	NR	NR	NR
Nasiry, 2020	35	CMB-I vs. behavioral control	.	NR	NR	NR	NR
Salemink, 2015	16	CBM-I+ERP vs. ERP	.	-1.9 (-8.3, 4.5)	NR	NR	NR
Wolters, 2021	79	CMB-I+ERP vs. ERP	.	0.1 (-34.6, 34.8)	1.38 (0.88, 2.16)	NR	NR
Tuerk, 2023	28	App+ERP vs. ERP	.	-2.4 (-5.6, 0.8)	NR	NR	NR
Rezvan, 2013	24	ABI vs. WL	.	**-7.2 (-9.5, -5)**	NR	NR	NR
Rempel, 2023	76	Mindfulness vs. behavioral control	.	0.5 (-2.9, 3.8)	NR	NR	NR
Rosa-Alcázar, 2019	44	Parent training vs. ERP		1.2 (-1, 3.4)	NR	NR	1.5 (-1.23, 4.24)
Shabani, 2019	44	ACT+SSRI vs. ERP+SSRI	.	1.2 (-1.1, 3.5)	NR	NR	NR
Shabani, 2019	47	ACT+SSRI vs. SSRI	.	**-3.3 (-5.4, -1.2)**	NR	NR	NR
Franklin, 2011	82	iERP+SSRI vs. ERP+SSRI	.	-3.9 (-6.9. 0.9	NR	NR	NR
Franklin, 2011	84	iERP+SSRI vs. SSRI	.	**-6.5 (-9.4, -3.6)**	NR	NR	NR

Study	N	Comparison	Details	CY-BOCS NMD	Remission RR	CGI-S NMD	FAS NMD
Alaghband-Rad, 2009	29	citalopram vs. fluoxetine	both SSRIs	Mean CY-BOCS only	NR	NR	NR
Grant, 2014	60	riluzole vs. placebo	.	1.2 (-1.5, 3.8)	NR	0.05 (-0.35, 0.45)	NR
Leonard, 1989	48	desipramine vs. chlormipramine	both TCAs, CY-BOCS NR	NR	NR	NR	NR
Liu, 2012	96	AAP+SSRI vs. SSRI	.	**-2.6 (-4.5, -0.7)**	NR	NR	NR
Li, 2020	11	NAC vs. placebo	.	**-6 (-11.9, -0.1)**	NR	NR	NR
Ghanizadeh, 2017	29	NAC+SSRI vs. SSRI	.	**-6.9 (-13.3, -0.5)**	NR	NR	NR
Noras, 2022		herbal+SSRI vs. placebo+SSRI	No significant difference reported	NR	NR	NR	NR
Agrawal, 2024	18	tDCS+SSRI vs. sham+SSRI	.	-2.6 (-8.4, 3.3)	NR	NR	NR

Abbreviations: AAP = atypical antipsychotic mediation; ACT = acceptance and commitment therapy; CGI-S = Clinical Global Impression-Severity; CMB-I = cognitive bias modification of interpretation; CY-BOCS = Children's Yale-Brown Obsessive Compulsive Scale; ERP = Exposure and Response Prevention; iERP = instructions in ERP in the context of medication management; MI = motivational interviewing; NAC = N-acetyl cysteine; NR = not reported; OCD = Obsessive Compulsive Disorder; ODD = Oppositional-defiant Disorder; PDD =Pervasive Developmental Disorder; PMID = PubMed Identifier; POTS = Pediatric OCD Treatment Study; SD = Standard deviation; SNRI = Serotonin Norepinephrine Reuptake Inhibitor; SRI = Serotonin Reuptake Inhibitor; SSRI = Selective Serotonin Reuptake Inhibitor; TCA = Tricyclic antidepressant; WL = wait list.

Bold font has no independent meaning; it highlights statistical significance.

Children's Yale-Brown Obsessive Compulsive Scale Total (CY-BOCS)

Table E-KQ2-2. Randomized controlled trials—(C)Y-BOCS

Study, Year, PMID	Treatment Contrast	N	Treatment Duration (Wks)	CFB Treatment 1 (95% CI)	CFB Treatment 2 (95% CI)	NMD (95% CI)
Agrawal, 2024, CN-02530420 (Cochrane)	DCS+SSRI vs. shamDCS+SSRI	18	12	-7.4 (-9.5, -5.3)	-5.6 (-7.7, -3.5)	-2.6 (-8.4, 3.3)
Asbahr, 2005, 16239861	ERP vs. SSRI	40	12	-20.7 (-24.2, -17.2)	-20 (-23, -17.1)	-0.7 (-5.2, 3.9)
Aspvall, 2021, 33974020	Remote ERP vs. ERP	152	16	-10.3 (-11.5, -9.1)	-10.2 (-11.6, -8.8)	-0.1 (-1.9, 1.7)
Barrett, 2003, 12647571	ERP vs. WL	20	14	-15.7 (-19.9, -11.6)	1.2 (-2, 4.4)	**-17 (-22.2, -11.7)**
Barrett, 2004, 14691360	ERP vs. WL	75	14	-14 (-15.8, -12.3)	1.1 (-0.9, 3.1)	**-15.1 (-17.8, -12.5)**

Study, Year, PMID	Treatment Contrast	N	Treatment Duration (Wks)	CFB Treatment 1 (95% CI)	CFB Treatment 2 (95% CI)	NMD (95% CI)
Bolton, 2008, 17207457	ERP vs. WL	20	12	-10.6 (-13.2, -8)	-0.4 (-4.9, 4.1)	**-10.2 (-15.4, -5)**
Bolton, 2011, 21644984	briefERP vs. WL	60	12	-9 (-11.8, -6.2)	-0.9 (-3.8, 2)	**-8.1 (-12.1, -4.1)**
Bolton, 2011, 21644984	briefERP vs. ERP	72	12	-9 (-11.8, -6.2)	-12.8 (-15.1, -10.5)	3.8 (0.2, 7.4)
Bolton, 2011, 21644984	ERP vs. WL	60	12	-12.8 (-15.1, -10.5)	-0.9 (-3.8, 2)	**-11.9 (-15.6, -8.2)**
Comer, 2017, 27869451	Remote ERP vs. ERP	22	14	-8 (-11.7, -4.3)	-9 (-13, -5)	1 (-4.5, 6.5)
DeVeaugh-Geiss, 1992, 1537780	TCA vs. placebo	60	8	-10 (-12, -8)	-2.3 (-4.6, 0)	**-7.7 (-10.7, -4.7)**
Farrell, 2013, 23722990	DCS+ERP vs. ERP	17	9	-16.2 (-19.7, -12.7)	-15.1 (-19.9, -10.3)	-1.1 (-7.1, 4.9)
Farrell, 2022, 2022-28058-001 (PsycINFO)	DCS+ERP vs. ERP	100	12	-0.2 (-3, 2.6)	0.7 (-2.3, 3.7)	-0.9 (-4, 2.2)
Fatori, 2018, 30025255	ERP vs. SSRI	83	14	-11.7 (-14.2, -9.2)	-10.1 (-12.9, -7.3)	-1.6 (-5.3, 2.2)
Franklin, 2011, 21934055	ERP+SSRI vs. SSRI	82	12	-7.3 (-16.8, 2.1)	-4.7 (-13.6, 4.1)	-2.6 (-15.6, 10.3)
Freeman, 2008, 18356758	ERP vs. behavCntrl	42	14	-8.5 (-11.5, -5.5)	-4.6 (-7.5, -1.7)	-3.9 (-8, 0.2)
Freeman, 2014, 24759852	ERP vs. behavCntrl	127	14	-12.8 (-17.7, -8)	-6.3 (-11.2, -1.4)	-6.5 (-13.5, 0.4)
Geller, 2001, 11437015	SSRI vs. placebo	103	13	-9.5 (-11.6, -7.4)	-5.2 (-7.8, -2.6)	**-4.3 (-7.6, -1)**
Geller, 2004, 15502598	SSRI vs. placebo	203	10	-8.8 (-10.4, -7.2)	-5.3 (-6.8, -3.8)	**-3.4 (-5.6, -1.2)**
Ghanizadeh, 2017, 28659986	NAC+SSRI vs. SSRI	29	10	-9.7 (-13.1, -6.3)	-2.8 (-8.2, 2.6)	**-6.9 (-13.3, -0.5)**
Grant, 2014, 24356715	riluzole vs. placebo	60	12	-5.5 (-7.4, -3.5)	-6.7 (-8.5, -4.9)	1.2 (-1.5, 3.8)
Guo, 2008, Guo-2008_SR-35121274 (From SRs)	TCA vs. SSRI	54	8	-13.1 (-14.9, -11.3)	-12.6 (-14.9, -10.3)	-0.5 (-3.5, 2.5)
He, 2007, He-2007_SR-35121274 (From SRs)	TCA vs. SSRI	60	8	-11.8 (-13.2, -10.4)	-11.8 (-13.4, -10.2)	0 (-2.2, 2.2)
Himle, 0224, 38103359	ERP vs. behavCntrl	58	12			**-6.8 (-10.6, -2.9)**
Hollmann, 2022, 36329915	Remote ERP vs. WL	60	16	-13.5 (-16.4, -10.6)	-2.3 (-4, -0.7)	**-11.2 (-14.6, -7.8)**

Study, Year, PMID	Treatment Contrast	N	Treatment Duration (Wks)	CFB Treatment 1 (95% CI)	CFB Treatment 2 (95% CI)	NMD (95% CI)
Lenhard, 2017, 27993223	Remote ERP vs. WL	67	12	-6 (-7.9, -4.1)	-1.5 (-2.8, -0.1)	**-4.6 (-6.9, -2.2)**
Lewin, 2014, 24657310	ERP vs. TAU	31	6	-12.2 (-15.8, -8.6)	-0.5 (-3.2, 2.2)	**-11.7 (-16.2, -7.2)**
Li, 2020, 31800306	NAC vs. placebo	11	12	-7 (-11.5, -2.5)	-1 (-4.7, 2.7)	**-6 (-11.9, -0.1)**
Liebowitz, 2002, 12447029	SSRI vs. placebo	43	16	-9.7 (-13.5, -6)	-4.1 (-8, -0.3)	**-5.6 (-11, -0.2)**
Liu, 2012, Liu-2012_SR-37347947 (From SRs)	AAP+SSRI vs. SSRI	96	6	-12.1 (-13.5, -10.6)	-9.4 (-10.7, -8.1)	**-2.6 (-4.5, -0.7)**
Ma, 2014, Ma-2014_SR-35121274 (From SRs)	ERP+SSRI vs. SSRI	38	12	-7.5 (-9.6, -5.5)	-10.7 (-12.9, -8.4)	3.1 (0, 6.2)
March, 1990, 19630661	TCA vs. placebo	16	11	-5.2 (-10.4, 0)	-1.8 (-3.9, 0.3)	-3.4 (-9, 2.2)
March, 1998, 9842950	SSRI vs. placebo	187	12	-6.8 (-8.5, -5.1)	-3.4 (-5, -1.8)	**-3.4 (-5.7, -1.1)**
Mataix-Cols, 2014, 24262813	DCS+ERP vs. ERP	27	17	-15.9 (-19.4, -12.4)	-14.7 (-17.5, -11.9)	-1.2 (-5.7, 3.3)
Merlo, 2010, 19675960	MI+ERP vs. ERP	16	3	-21.6 (-26.6, -16.7)	-15 (-22.2, -7.8)	-6.6 (-15.4, 2.1)
Nai, 2009, Nai-2009_SR-35121274 (From SRs)	TCA vs. SSRI	64	8	-13.2 (-15.1, -11.3)	-12.8 (-14.9, -10.7)	-0.4 (-3.2, 2.4)
Neziroglu, 2000, 11191690	ERP+SSRI vs. SSRI	10	10	-10 (-14.5, -5.5)	-3.8 (-7.6, 0)	**-6.2 (-12.1, -0.3)**
POTS, 2004, 15507582	ERP vs. placebo	56	12	-12 (-15, -9)	-3.7 (-5.4, -2)	**-8.3 (-11.8, -4.8)**
POTS, 2004, 15507582	ERP vs. ERP+SSRI	56	12	-12 (-15, -9)	-12.6 (-15.4, -9.8)	0.6 (-3.5, 4.7)
POTS, 2004, 15507582	ERP vs. SSRI	56	12	-12 (-15, -9)	-7 (-9.9, -4.1)	**-5 (-9.2, -0.8)**
POTS, 2004, 15507582	SSRI vs. placebo	56	12	-7 (-9.9, -4.1)	-3.7 (-5.4, -2)	-3.3 (-6.7, 0.1)
POTS, 2004, 15507582	SSRI vs. ERP+SSRI	56	12	-7 (-9.9, -4.1)	-12.6 (-15.4, -9.8)	5.6 (1.6, 9.6)
POTS, 2004, 15507582	ERP+SSRI vs. placebo	56	12	-12.6 (-15.4, -9.8)	-3.7 (-5.4, -2)	**-8.9 (-12.2, -5.6)**
Peris, 2013, 22548378	FI+ERP vs. ERP	20	14	-14.5 (-18.5, -10.5)	-9.3 (-13.7, -4.9)	-5.2 (-11.2, 0.8)
Peris, 2017, CN-01446723 (Cochrane)	FI+ERP vs. ERP	62	12	-11.9 (-14.1, -9.8)	-8 (-10.3, -5.6)	**-4 (-7.1, -0.8)**

Study, Year, PMID	Treatment Contrast	N	Treatment Duration (Wks)	CFB Treatment 1 (95% CI)	CFB Treatment 2 (95% CI)	NMD (95% CI)
Piacentini, 2011, 22024003	ERP vs. Control	71	14	-11.4 (-20.2, -2.6)	-8.1 (-21.8, 5.6)	-3.3 (-19.6, 13)
Rempel, 2023, 37048570	Mindfullness vs. behavCntrl	58	8	4.3 (2.1, 6.6)	3.9 (2.1, 5.6)	0.5 (-2.9, 3.8)
Reynolds, 2013, 24060194	FI+ERP vs. ERP	50	14	-9.8 (-12.7, -6.8)	-10 (-12.9, -7.1)	0.2 (-3.9, 4.4)
Rezvan, 2013, 23413047	ABI vs. WL	24	12	-7.1 (-8.8, -5.4)	0.2 (-1.4, 1.7)	**-7.2 (-9.5, -5)**
Riddle, 1992, 1429406	SSRI vs. placebo	13	8	-10.7 (-15.1, -6.3)	-5.4 (-11.3, 0.5)	-5.3 (-12.3, 1.7)
Riddle, 2001, 11211371	SSRI vs. placebo	120	10	-6 (-7.9, -4.1)	-3.3 (-5.1, -1.5)	-2.7 (-5.4, 0)
Rosa-Alcázar, 2019, 31516500	ERP vs. parentTraining	44	12	-12.2 (-13.4, -11.1)	-11.1 (-12.9, -9.2)	-1.2 (-3.4, 1)
Shabani, 2019, CN-02003764 (Cochrane)	ACT+SSRI vs. ERP+SSRI	44	12	-7 (-8.7, -5.3)	-8.2 (-9.9, -6.6)	1.2 (-1.1, 3.5)
Shabani, 2019, CN-02003764 (Cochrane)	ACT+SSRI vs. SSRI	47	12	-7 (-8.7, -5.3)	-3.7 (-5, -2.4)	**-3.3 (-5.4, -1.2)**
Shabani, 2019, CN-02003764 (Cochrane)	ERP+SSRI vs. SSRI	47	12	-8.2 (-9.9, -6.6)	-3.7 (-5, -2.4)	**-4.5 (-6.6, -2.4)**
Shen, 2020, Shen-2020_SR-35121274 (From SRs)	TCA vs. SSRI	89	6	-8.7 (-12.6, -4.7)	-11.9 (-16.1, -7.7)	3.2 (-2.6, 9)
Storch, 2007, 17420681	intensiveERP vs. ERP	40	14	-16.4 (-19.2, -13.6)	-12.6 (-16, -9.2)	-3.8 (-8.2, 0.6)
Storch, 2010, 20817153	DCS+ERP vs. ERP	30	9	-17.3 (-20, -14.6)	-15 (-17.9, -12.1)	-2.3 (-6.3, 1.7)
Storch, 2011, 21684018	Remote ERP vs. Control	31	12	-14.2 (-18.8, -9.7)	-2.7 (-6.4, 0.9)	**-11.5 (-17.3, -5.7)**
Storch, 2013, 24184429	ERP+SSRI vs. ERP	47	19	-9.9 (-12.6, -7.2)	-9.5 (-12.3, -6.7)	-0.4 (-4.3, 3.5)
Storch, 2016, 27367832	DCS+ERP vs. ERP	142	9	-10.3 (-12.5, -8.2)	-9.4 (-11.5, -7.3)	-0.9 (-4, 2.1)
Tuerk, 2023, Tuerk-2023_adhoc (ad hoc)	App+ERP vs. ERP	28	6	-4 (-6.2, -1.8)	-1.6 (-3.8, 0.6)	-2.4 (-5.6, 0.8)
Turner, 2014, 25457928	Remote ERP vs. ERP	72	17	-12.7 (-15.1, -10.2)	-12.4 (-14.1, -10.6)	-0.3 (-3.2, 2.7)
Williams, 2010, 19921305	ERP vs. WL	21	12	-11 (-14.8, -7.2)	-1.4 (-5.3, 2.4)	**-9.6 (-14.9, -4.2)**
Wolters, 2016, CN-01166610 (Cochrane)	ERP vs. WL	41	8	-4.4 (-6.4, -2.4)	-0.3 (-2.6, 1.9)	**-4.1 (-7, -1.1)**

Study, Year, PMID	Treatment Contrast	N	Treatment Duration (Wks)	CFB Treatment 1 (95% CI)	CFB Treatment 2 (95% CI)	NMD (95% CI)
Wolters, 2021, CN-02248290 (Cochrane)	CMB-I+ERP vs. ERP	79		-14.3 (-39, 10.3)	-14.4 (-38.8, 9.9)	0.1 (-34.6, 34.8)
Xie, 2020, Xie-2020_SR-35121274 (From SRs)	TCA vs. SSRI	81	6	-9.2 (-18, -0.4)	-12.8 (-16.7, -8.9)	3.6 (-6.1, 13.2)
Zhang, 2014, Zhang-2014_SR-35121274 (From SRs)	ERP+SSRI vs. SSRI	40	12	-14.6 (-16.5, -12.7)	-10.3 (-12.4, -8.2)	**-4.3 (-7.1, -1.5)**
Zhu, 2008, Zhu-2008_SR-35121274 (From SRs)	TCA vs. SSRI	61	8	-13.1 (-15, -11.2)	-12.5 (-14.5, -10.5)	-0.6 (-3.3, 2.1)
de Haan, 1998, 9785713	ERP vs. TCA	22	12	-12.4 (-16.9, -7.9)	-6.2 (-12.6, 0.2)	-6.2 (-14, 1.6)
NCT01933919, 2017, NCT01933919 (from SRs)	SSRI vs. placbo	37	10	-10.5 (-12.9, -8.1)	-6.6 (-10.1, -3.1)	-3.9 (-8.1, 0.3)

Abbreviations: AAP = atypical antipsychotic mediation; ACT = acceptance and commitment therapy; behavCntrl = behavioral control; CMB-I = cognitive bias modification of interpretation; CY-BOCS = Children's Yale-Brown Obsessive Compulsive Scale; ERP = Exposure and Response Prevention; iERP = instructions in ERP in the context of medication management; MI = motivational interviewing; NAC = N-acetyl cysteine; OCD = Obsessive Compulsive Disorder; ODD = Oppositional-defiant Disorder; PDD =Pervasive Developmental Disorder; placebo = pill placebo; PMID = PubMed Identifier; POTS = Pediatric OCD Treatment Study; SD = Standard deviation; SNRI = Serotonin Norepinephrine Reuptake Inhibitor; SRI = Serotonin Reuptake Inhibitor; SSRI = Selective Serotonin Reuptake Inhibitor; TAU = treatment as usual; TCA = Tricyclic antidepressant; WL = wait list.

Bold font has no independent meaning; it highlights statistical significance.

Remission

Table E-KQ2-3. Randomized controlled trials—remission

Study, Year, PMID	Treatment Contrast	Total N	Treatment Duration (Wks)	n/N Treatment 1	n/N Treatment 2	RR (95% CI)
Asbahr, 2005, 16239861	ERP vs. SSRI	33	12	7/16	13/17	0.57 (0.31, 1.06)
Barrett, 2003, 12647571	ERP vs. WL	24	14	11/12	0/12	**23 (1.51, 349.42)**
Bolton, 2011, 21644984	briefERP vs. WL	60	12	18/36	2/24	**6 (1.53, 23.53**)

Study, Year, PMID	Treatment Contrast	Total N	Treatment Duration (Wks)	n/N Treatment 1	n/N Treatment 2	RR (95% CI)
Bolton, 2011, 21644984	briefERP vs. WL	72	12	18/36	22/36	0.82 (0.54, 1.24)
Bolton, 2011, 21644984	ERP vs. WL	60	12	22/36	2/24	**7.33 (1.9, 28.35)**
Comer, 2017, 27869451	remoteERP vs. ERP	22	14	7/11	7/11	1 (0.53, 1.88)
Farrell, 2022, 35084071	DCS+ERP vs. ERP	100	12	18/49	18/51	1.04 (0.62, 1.76)
He, 2007, He-2007_SR-35121274 (From SRs)	TCA vs. SSRI	60	8	26/30	27/30	0.96 (0.8, 1.16)
Himle, 2024, 38103359	ERP vs. behavCntrl	58	12	10/30	3/28	3.11 (0.95, 10.15)
Hollmann, 2022, 36329915	remoteERP vs. WL	47	16	18/28	12/19	1.02 (0.66, 1.58)
Lenhard, 2017, 27993223	remoteERP vs. WL	67	12	5/33	0/34	11.33 (0.65, 196.98)
Peris, 2017, CN-01446723 (Cochrane)	FI+ERP vs. ERP	61	12	18/31	8/30	**2.18 (1.12, 4.23)**
Piacentini, 2011, 22024003	ERP vs. behavCntrl	57	14	17/40	3/17	2.41 (0.81, 7.15)
POTS Team, 2004, 15507582	ERP vs. placebo	56	12	15/28	1/28	**15 (2.12, 105.99)**
POTS Team, 2004, 15507582	ERP vs. ERP+SSRI	56	12	15/28	6/28	**2.5 (1.14, 5.5)**
POTS Team, 2004, 15507582	ERP vs. SSRI	56	12	15/28	11/28	1.36 (0.77, 2.42)

Study, Year, PMID	Treatment Contrast	Total N	Treatment Duration (Wks)	n/N Treatment 1	n/N Treatment 2	RR (95% CI)
POTS Team, 2004, 15507582	SSRI vs. Control	56	12	11/28	1/28	**11 (1.52, 79.59)**
POTS Team, 2004, 15507582	SSRI vs. ERP+SSRI	56	12	11/28	6/28	**1.83 (0.79, 4.27)**
POTS Team, 2004, 15507582	ERP+SSRI vs. placebo	56	12	6/28	1/28	**6 (0.77, 46.66)**
Shen, 2020, Shen-2020_SR-35121274 (From SRs)	TCA vs. SSRI	89	6	15/44	19/45	0.81 (0.47, 1.38)
Skarphedinsson, 2015, 25239489	SSRI vs. ERP	50	17	6/22	9/28	0.85 (0.36, 2.02)
Storch, 2011, 21684018	remoteERP vs. WL	31	12	9/16	2/15	**4.22 (1.08, 16.45)**
Storch, 2016, 27367832	DCS+ERP vs. ERP	142	9	35/70	33/72	1.09 (0.77, 1.54)
Turner, 2014, 25457928	remoteERP vs. ERP	66	17	19/33	20/33	0.95 (0.64, 1.42)
Wolters, 2021, CN-01166610 (Cochrane)	CMB-I+ERP vs. ERP	63	8	20/31	15/32	1.38 (0.88, 2.16)

Abbreviations: AAP = atypical antipsychotic mediation; ACT = acceptance and commitment therapy; CGI-S = Clinical Global Impression-Severity; CMB-I = cognitive bias modification of interpretation; CY-BOCS = Children's Yale-Brown Obsessive Compulsive Scale; ERP = Exposure and Response Prevention; iERP = instructions in ERP in the context of medication management; MI = motivational interviewing; NAC = N-acetyl cysteine; OCD = Obsessive Compulsive Disorder; ODD = Oppositional-defiant Disorder; PDD =Pervasive Developmental Disorder; PMID = PubMed Identifier; POTS = Pediatric OCD Treatment Study; remoteERP = remote ERP; SD = Standard deviation; SNRI = Serotonin Norepinephrine Reuptake Inhibitor; SRI = Serotonin Reuptake Inhibitor; SSRI = Selective Serotonin Reuptake Inhibitor; TCA = Tricyclic antidepressant; WL = wait list.

Bold font has no independent meaning; it highlights statistical significance.

CGI-S (Clinical Global Impression–Severity)

Behavioral Interventions

Eight studies assessed the comparative effect of CBT (ERP) delivered alone, and one as a combination with pharmacological agent.

Behavioral Intervention Versus No Active Treatment

Four studies assessed OCD severity on CGI-S in participants receiving different types of CBT (ERP) versus Control (noActive Treatment)

ERP Versus Control

Two studies compared family-based ERP to Control (no active treatment).[14, 36] The OCD severity on CGI-S significantly decreased in family ERP group compared to Control.

Table E-KQ2-4. OCD severity on CGI-S: ERP versus control

Study, Year, PMID, Study Name	Arm	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)[a]	NMD (95% CI)
Freeman, 2014, 24759852 RCT POTS Jr	ERP	PE/CoRe/CR/ ERP	CGI-S	62: 4.71 (0.89)	59: -2.1 (1.17)	**-1.07 (-1.48, -0.66)**
	Control	BehavCntrl	.	64: 4.67 (0.76)	64: -1.03 (1.17)	.
Lewin, 2014, 24657310 RCT	ERP	ERP	CGI-S	17: 3.82 (0.81)	17: -1.35 (1.19)	**-1.42 (-2.1, -0.74)**
	Control	None	.	14: 3.93 (0.73)	14: 0.07 (0.71)	.

Abbreviations: BehavCntrl = Behavioral Control, CGI-S = Clinical Global Impression-Severity; CI = confidence interval; CoRe = coping and relaxation; CR = cognitive restructuring; ERP = exposure and Response Therapy; meanCFB = Mean change form baseline, N= sample size; NMD = net mean difference; PE = psychoeducation; PMID = PubMed ID; RCT = Randomized clinical trial; SD = standard deviation.

Bold font has no independent meaning; it highlights statistical significance.

[a]Calculated by research team.

Remote ERP Versus Control

Two studies assigned participants to either remote ERP: Therapist-guided, internet-delivered ERP and internet-delivered family ERP[37, 38] or waitlist. The OCD severity on CGI-S significantly decreased in remote CBT compared to waitlist.

Table E-KQ2-5. OCD severity on CGI-S: Remote ERP versus control

Study, Year, PMID, Study Name	Arm	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)[a]	NMD (95% CI)
Hollmann, 2022, 36329915 RCT	Remote ERP	CR/ERP	CGI-S	30: 4.93 (0.52)	30: -2.58 (1.38)	**-2.1 (-2.65, -1.55)**
	Waitlist	None	.	30: 5.07 (0.37)	30: -0.48 (0.70)	.
Storch, 2011, 21684018 RCT	Remote ERP	PR/CR/ERP	CGI-S	16: 3.75 (0.93)	16: -2.19 (1.52)	**-1.93 (-2.87, -0.99)**
	Waitlist	None	.	15: 2.73 (0.84)	15: -0.26 (1.14)	.

Abbreviations: CGI-S = Clinical Global Impression-Severity; CI = confidence interval; CR = cognitive restructuring; ERP = exposure and Response Therapy; meanCFB = Mean change form baseline, N= sample size; NMD = net mean difference; PE = psychoeducation; PMID = PubMed ID; RCT = Randomized clinical trial; Remote ERP = internet-delivered ERP, SD = standard deviation.

Bold font has no independent meaning; it highlights statistical significance.

[a]Calculated by research team.

Behavioral Intervention Versus Behavioral Intervention

Three studies each compared different types of CBT (ERP).

Remote ERP Versus ERP

Two RCTs assigned participants to either internet-delivered ERP or traditional ERP.[39, 40] The two RCTs found no evidence of significant difference between internet-delivered ERP and in-person ERP.

Table E-KQ2-6. OCD severity on CGI-S: Remote ERP versus ERP

Study, Year, PMID, Design	Arm	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)[a]	NMD[a] (95% CI)
Aspvall, 2021, 33974020 RCT	Remote ERP	PE/ERP	CGI-S	74: 4.36 (0.67)	74: -1.45 (1.0)	0.02 (-0.30, 0.34)
	ERP	PE/ERP	.	78: 4.26 (0.67)	78: -1.47 (1.04)	.
Comer, 2017 278694 RCT	Remote ERP	ERP	CGI-S	11: 4.9 (0.7)	11: -1.7 (1.3)	-0.4 (-1.52, 0.72)
	ERP	ERP	.	11: 4.6 (0.9)	11: -1.3 (1.39)	.

Abbreviations: CGI-S = Clinical Global Impression-Severity; CI = confidence interval; ERP = exposure and Response Therapy; meanCFB = Mean change form baseline, N= sample size; NMD = net mean difference; PE = psychoeducation; PMID = PubMed ID; RCT = Randomized clinical trial; Remote ERP = internet-delivered ERP; SD = standard deviation.

[a]Calculated by research team.

Intensive ERP Versus ERP

Only one study compared daily (intensive) ERP to weekly ERP.[15] The OCD severity on CGI-S significantly decreased in daily ERP compared to weekly ERP.

Table E-KQ2-7. OCD severity on CGI-S: Intensive ERP versus ERP

Study, Year, PMID, Design	Arm	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)[a]	NMD[a] (95% CI)
Storch, 2007, 17420681 RCT	Intensive ERP (daily)	Not specified	CGI-S	20: 4.2 (0.8)	20: -2.8 (0.85)	**-1.2 (-1.77, -0.63)**
	ERP (weekly)	Not specified	.	20: 3.5 (0.8)	20: -1.6 (0.98)	.

Abbreviations: CGI-S = Clinical Global Impression-Severity; CI = confidence interval; ERP = exposure and Response Therapy; meanCFB = Mean change form baseline, N= sample size; NMD = net mean difference; PE = psychoeducation; PMID = PubMed ID; RCT = Randomized clinical trial; SD = standard deviation

Bold font has no independent meaning; it highlights statistical significance.

[a]Calculated by research team.

Behavioral Intervention Versus Pharmacological Intervention

ERP Versus SSRI

Only one study for this outcome,[41], assigned participants to either group ERP or SSRI. Participants in group ERP had a greater reduction in OCD severity reported on CGI-S than sertraline.

Table E-KQ2-8. OCD severity on CGI-S: ERP versus SSRI

Study, Year, PMID, Study Design	Arm Name	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)[a]	NMD (95% CI)
Asbahr, 2005, 16239861 RCT	EPR	PE/ERP	CGI-S	20: 5.35 (0.88)	20: -2.85 (NR)	-0.85[b]
.	SSRI	Sertraline	.	19: 5.30 (0.73)	19: -2 (NR)	.

Abbreviations: CGI-S = Clinical Global Impression-Severity; CI = confidence interval; ERP = exposure and Response Therapy; meanCFB = Mean change form baseline, N= sample size; NMD = net mean difference; PE = psychoeducation; PMID = PubMed ID; RCT = Randomized clinical trial; SD = standard deviation; SSRI = Selective Serotonin Reuptake Inhibitor.

[a]Calculated by research team.

[b]95% CI could not be calculated due to missing data.

Combination of Behavioral Treatment

Behavioral Plus Pharmacological Intervention Versus Pharmacological Intervention

ERP Plus SSRI Versus SSRI

Only one study[42] for this outcome assigned participants to either ERP plus fluvoxamine or fluvoxamine alone. OCD severity reported on CGI-S significantly decreased in ERP plus fluvoxamine compared to fluvoxamine alone.

Table E-KQ2-9. OCD severity on CGI-S: ERP plus SSRI versus SSRI

Study, Year, PMID, Study Design	Arm Name	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)[a]	NMD (95% CI)
Neziroglu, 2000, 11191690 RCT	ERP + SSRI	Fluvoxamine + ERP	CGI-S	5: 5.6 (0.55)	5: -1.2 (0.52)	**-0.1 (-1.63, -0.37)**
	SSRI	Fluvoxamine	.	5: 5 (0)	5: -0.2 (0.49)	.

Abbreviations: CGI-S = Clinical Global Impression-Severity; CI = confidence interval; ERP = exposure and Response Therapy; meanCFB = Mean change form baseline, N= sample size; NMD = net mean difference; PE = psychoeducation; PMID = PubMed ID; RCT = Randomized clinical trial; SD = standard deviation; SSRI = Selective Serotonin Reuptake Inhibitor.

Bold font has no independent meaning; it highlights statistical significance.

[a]Calculated by research team.

Pharmacological Interventions

Pharmacological Intervention Versus No Active Treatment

Five studies assessed OCD severity in participants randomized to pharmacological intervention alone versus Control (placebo).

SSRI Versus Control

Three RCTs,[43-45] and one RCT crossover[46] compared SSRI to placebo.[46] reported OCD severity on subscale of CGI-S (CGI-OCD). The net improvement in OCD severity reported on CGI-S/CGI-OCD varied across studies, with two studies[43, 46] reporting a significant net improvement favoring SSRI.

Table E-KQ2-10. OCD severity on CGI-S: SSRI versus control

Study, Year, PMID, Study Design	Arm Name	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)[a]	NMD (95% CI)
Geller, 2001, 11437015	SSRI	Fluoxetine	CGI-S	71: 4.6 (0.7)	71: -1.3 (1.3)	**-0.7 (-1.16, -0.24)**

Study, Year, PMID, Study Design	Arm Name	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)[a]	NMD (95% CI)
RCT	Placebo	None	.	32: 4.8 (0.8)	32: -0.6 (1.0)	.
Liebowitz, 2002, 12447029 RCT	SSRI	Fluoxetine	CGI-S	21: 4.38 (0.67)	21: -1.09 (1.2)	-0.43 (-1.15, 0.29)
	Placebo	None	.	22: 4.57 (0.87)	22: -0.66 (1.21)	.
March, 1998, 9842950 RCT	SSRI	Sertraline	CGI-S	92: NR	92: -1.0 (1.34)	-0.3 (-0.67, 0.07)
	Placebo	None	.	95: NR	95: -0.7 (1.27)	.
Riddle, 1992, 1429406 RCT (cross-over)	SSRI	Fluoxetine	CGI-OCD	7: 4.6 (0.8)	7: -1.5 (0.75)	**-1 (-1.79, -0.21)**
	Placebo	None	.	6: 4.3 (0.5)	6: -0.5 (0.7)	.

Abbreviations: CGI-S = Clinical Global Impression-Severity; CI = confidence interval; meanCFB = Mean change form baseline, N= sample size; NMD = net mean difference; NR = Not reported; PMID = PubMed ID; RCT = Randomized clinical trial; SD = standard deviation; SSRI = Selective Serotonin Reuptake Inhibitor.

Bold font has no independent meaning; it highlights statistical significance.

[a]Calculated by research team.

Riluzole Versus. Control

Only one study for this outcome assessed the comparative effect of riluzole.[30] There was no significant net difference in CGI-S score between riluzole and placebo.

Table E-KQ2-11. OCD severity on CGI-S: Riluzole versus control

Study, Year, PMID, Study Design	Arm Name	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)[a]	NMD (95% CI)
Grant, 2014, 24356715 RCT	Riluzole	Riluzole	CGI-S	30: 5.59 (0.63)[b]	30: -0.55[c] (0.81)	0.05[d] (-0.35, 0.45)
	Placebo	Placebo	.	30: 5.63 (0.67)[b]	30: -0.6[c] (0.77)	.

Abbreviations: CGI-S = Clinical Global Impression-Severity; CI = confidence interval; meanCFB = Mean change form baseline, N= sample size; NMD = net mean difference; PMID = PubMed ID; RCT = Randomized clinical trial; SD = standard deviation.

[a]Calculated by research team.

[b]Estimated marginal mean.

[c]Difference in estimated marginal means.

[d]Net estimated marginal mean difference.

Combination of Pharmacological Treatment

Pharmacological Plus Behavioral Intervention Versus Behavioral Intervention

Four studies compared a combination of pharmacological agent plus behavioral intervention to behavioral intervention.

DCS Plus ERP Versus Placebo Plus ERP

Three RCTs measured CGI-S in participants received either a combination of D-cycloserine (DSC) plus ERP or placebo plus ERP.[47-49] The three RCTs did not find significant net difference in CGI-S between DSC plus ERP and placebo plus ERP.

Table E-KQ2-12. OCD severity on CGI-S: DCS plus ERP versus placebo plus ERP

Study, Year, PMID, Study Design	Arm Name	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)[a]	NMD (95% CI)
Farrell, 2013, 23722990 RCT	DCS+ERP	DCS + ERP	CGI-S	9: 5.67 (0.7)	9: -2.67 (1.43)	0.08 (-1.14, 1.30)
	ERP	Placebo + ERP	.	8: 5.38 (0.7)	8: -2.75 (1.13)	.
Storch, 2010, 20817153 RCT	DCS+ERP	DCS + PE/CR/ERP	CGI-S	15: 4.6 (0.83)	15: -2.6 (0.93)	-0.5 (-1.20, 0.21)
	ERP	Placebo + PE/CR/ERP	.	15: 5.1 (0.74)	15: -2.1 (1.04)	.
Storch, 2016, 27367832 RCT	DCS+ERP	DCS + PE/CR/EPR	CGI-S	70: 3.67 (1.13)	70: -1.39 (1.33)	-0.19 (-0.63, 0.25)
	ERP	Placebo + PE/CR/ERP	.	72: 3.43 (1.13)	72: -1.2 (1.32)	.

Abbreviations: CGI-S = Clinical Global Impression-Severity; CI = confidence interval; CR = Cognitive restructuring; DSC = D-cycloserine; ERP = exposure and Response Therapy; meanCFB = Mean change form baseline, N= sample size; NMD = net mean difference; PE = psychoeducation; PMID = PubMed ID; RCT = Randomized clinical trial; SD = standard deviation.

SSRI Plus ERP Versus Placebo Plus ERP

One three arm study[50] randomized participants to regular or slow sertraline or placebo. All participants received ERP. The change in OCD severity reported on CGI-S did not significantly differ in participants assigned to regular or slow sertraline plus ERP compared to placebo plus ERP.

Table E-KQ2-13. OCD severity on CGI-S: SSRI plus ERP versus placebo plus ERP

Study, Year, PMID, Study Design	Arm Name	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)[a]	NMD (95% CI)
Storch, 2013, 24184429	SSRI + ERP	Regular sertraline + PE/ CR/ERP	CGI-S	14: 4.36 (0.49)	14: -1 (1.17)	0.26 (-0.47, 0.99)

Study, Year, PMID, Study Design	Arm Name	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)[a]	NMD (95% CI)
RCT	ERP	Placebo + PE/ CR/ERP	.	16: 4.63 (0.72)	16: -1.26 (0.82)	.
Storch, 2013, 24184429 RCT	SSRI + ERP	Slow sertraline + PE/ CR/ERP	CGI-S	17: 4.82 (0.64)	17: -1.17 (0.97)	0.09 (-0.52, 0.70)
	ERP	Placebo + PE/ CR/ERP	.	16: 4.63 (0.72)	16: -1.26 (0.82)	.

Abbreviations: CGI-S = Clinical Global Impression-Severity; CI = confidence interval; CR = Cognitive restructuring; DSC = D-cycloserine; ERP = exposure and Response Therapy; meanCFB = Mean change form baseline, N= sample size; NMD = net mean difference; PE = psychoeducation; PMID = PubMed ID; RCT = Randomized clinical trial; SD = standard deviation; SSRI = Selective Serotonin Reuptake Inhibitors.

[a]Calculated by research team

Functional Impairment

Twelve studies, all RCTs[15, 16, 33, 36-38, 44, 49-53] enrolling a total of 844 participants assessed function impairment using the Child Obsessive–Compulsive Impact Scale (COIS) at baseline and at the end of intervention. COIS is a 56-item, parent- or child-report measuring the degree to which the child experiences OCD-related impairment across several domains of functioning: school, social, and home/family activities.[38] The COIS-R (the revised version) is a 33-item, using a 0 (not at all) to 3 (very much) Likert-scale.[53]

Eight studies assessed the comparative effect of CBT (basically ERP) alone or as a combination, and four studies assessed a medication as a primary intervention or as combination. Studies which delivered ERP alone differed in setting (remote versus in-person, home versus hospital), and intensity (daily versus weekly). Seven studies compared ERP alone with no active treatment (Control) or another form of ERP[15, 16, 33, 36-38, 53]; and one study compared ERP as a combination with family intervention to ERP alone.[52] Only one study compared pharmacological agent alone (SSRI) with placebo.[44] Three studies compared a combination of pharmacological agents (e.g., DSC, SSRI) plus ERP to placebo plus ERP.[49-51]

Three studies were rated as moderate risk of bias overall,[33, 49, 52] primarily for lack of blinding or incomplete outcome data. Two studies were rated as high risk of bias overall,[15, 38] for the combination of lack of blinding and incomplete outcome data. Seven studies were rated as low risk of bias overall[16, 36, 37, 44, 50, 51, 53]

COIS (Child Obsessive–Compulsive Impact Scale)

Behavioral Interventions

Seven studies assessed the comparative effect of CBT (ERP) delivered alone, and one as a combination with family intervention.

Behavioral Intervention Versus No Active Treatment

ERP Versus Control

Three RCTs assessed functional impairment in participants randomized to either ERP or no active treatment (Control).[33, 36, 53] The three RCTs were different in regard to the setting (e.g., full ERP versus brief), or component of the ERP delivered (e.g., family-based ERP). One study was three-arm RCT assigned participants to full or brief ERP versus waitlist.[33] There was significant net improvement in functioning reported on COIS-C (COIS-child rated) in ERP compared to waitlist. Similar significant net improvement in COIS-P (COIS-parent rated) was reported in ERP compared to waitlist[33, 36, 53] showed no significant net difference in functioning on COIS-RP between ERP and waitlist.

Table E-KQ2-14. Functional impairment on COIS: ERP versus control

Study, Year, PMID, Study Name	Arm	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)[a]	NMD (95% CI)[a]
Bolton, 2011, 21644984 RCT	ERP	General ERP/NS	COIS-C	36: 21.7 (12.7)	36: -15.1 (11.19)	**-17.1 (-23.04, -11.16)**
	Control	None	.	24: 22.4 (11.4)	24: 2 (11.71)	.
Bolton, 2011, 21644984 RCT	Brief ERP	Brief ERP/NS	COIS-C	36: 21.6 (13.8)	36: -15.3 (11.95)	**-17.3 (-23.4, -11.20)**
	Control	None	.	24: 22.4 (11.4)	24: 2 (11.71)	.
Bolton, 2011, 21644984 RCT	ERP	General CBT/NS	COIS-M	36: 23.2 (12.2)	36: -15.2 (10.77)	**-16 (-22.42, -9.58)**
	Control	None	.	24: 27.6 (9.8)	24: 0.8 (13.42)	.
Bolton, 2011, 21644984 RCT	Brief ERP	Brief ERP/NS	COIS-M	36: 19.5 (14.2)	36: -7.7 (13.28)	**-8.5 (-15.40, -1.60)**
	Control	None	.	24: 27.6 (9.8)	24: 0.8 (13.42)	.
Freeman, 2014, 24759852 RCT POTS Jr	ERP	Family-PE/CoRe/CR/ ERP	COIS-R	63: 23.97 (16.43)	63: -12.29 (14.64)	**-5.35 (-10.05, -0.65)**
	Control	behavCntrl	.	64: 23.46 (12.68)	64: -6.94 (12.27)	.
Piacentini, 2011, 22024003 RCT	ERP	PE/ERP	COIS-RC	48: 15.4 (10.6)	39: -9.8 (8.71)	**-9.2 (-15.81, -2.59)**
	Control	behavCntrl	.	22: 14.9 (13.64)	16: -0.6 (12.29)	.
Piacentini, 2011, 22024003 RCT	ERP	PE/ERP	COIS-RP	47: 22.4 (11.89)	39: -11.8 (10.99)	-1.6 (-9.03, 5.83)
	Control	behavCntrl	.	22: 21.4 (18.19)	17: -10.2 (13.85)	.

Abbreviations: behavCntrl = Behavioral control; CI = confidence interval; COIS-C = The Child Obsessive–Compulsive Impact Scale-child rated, COIS-M = The Child Obsessive–Compulsive Impact Scale-mother rated, COIS-P= The Child Obsessive–Compulsive Impact Scale-parent rated, COIS-R = The Children's OCD Impact Scale-Revised; COIS-RC = Child Obsessive Compulsive Impact Scale-Revised Child-Report; COIS-RP = Child Obsessive Compulsive Impact Scale-Revised Parent-Report; CoRe = Coping and relaxation; CR = Cognitive restructuring; ERP = exposure and Response Therapy; meanCFB = Mean change from baseline; N = Sample size; NMD =Net mean difference; Control = No active treatment; PE= Psychoeducation; PMID= PubMed ID; SD= Standard deviation; **Bold** = statistically significant

Bold font has no independent meaning; it highlights statistical significance.

[a]Calculated by research team.

Remote ERP Versus Control

Two studies compared the effect of remote ERP: Therapist-guided, internet-delivered ERP[37] and internet-delivered family ERP[38] to no active treatment (Control); Functional impairment on COIS-C (COIS-child rated) significantly decreased in internet-delivered ERP compared to Control.[37, 38] Functional impairment on COIS-P (COIS-parent rated) varied across these two studies, with significant net improvement favoring internet-delivered ERP.[38]

Table E-KQ2-15. Functional impairment on COIS: Remote ERP versus control

Study, Year, PMID, Study Name	Arm	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)[a]	NMD[a] (95% CI)
Hollmann, 2022, 36329915 RCT	remoteCBT	CR + ERP	COIS-C	30: 19.7 (17.04)	30: -11.69 (14.84)	-6.42 (-12.85, 0.006)[a]
	Control	None	.	30: 17.44 (10.86)	30: -5.27 (10.11)	.
Hollmann, 2022, 36329915 RCT	remoteCBT	CR + ERP	COIS-P	30: 25.87 (18.1)	30: -13.77 (16.18)	-6.94 (-14.22, 0.34)
	Control	None	.	30: 22.75 (12.14)	30: -6.83 (12.33)	.
Storch, 2011, 21684018 RCT	remoteCBT	PE/CR/ERP	COIS-C	16: 38.77 (24.09)	16: -22.71 (22.0)	**-30.76 (-44.27, -17.25)**
	Control	None	.	15: 15.40 (9.59)	15: 8.05 (16.08)	.
Storch, 2011, 21684018 RCT	remoteCBT	PE/CR/ERP	COIS-P	16: 42.81 (23.43)	16: -26 (24.0)	**-24.61 (-39.45, -9.77)**
	Control	None	.	15: 28.59 (13.34)	15: -1.39 (17.87)	.

Abbreviations: CI = confidence interval; COIS-C = The Child Obsessive–Compulsive Impact Scale-child rated; COIS-P= The Child Obsessive–Compulsive Impact Scale-parent rated; CR = Cognitive restructuring; ERP = Exposure and Response Therapy; meanCFB = Mean change from baseline; N = Sample size; NMD = Net mean difference; Control = No active treatment; PE= Psychoeducation; PMID= PubMed ID; Remote ERP = Remote ERP (internet-delivered ERP); SD= Standard deviation.

Bold font has no independent meaning; it highlights statistical significance.

[a]Calculated by research team.

Behavioral Intervention Versus Behavioral Intervention

Intensive ERP Versus ERP

Two RCTs each compared different types of ERP.[15, 16] Selles 2021 assigned participants to either home-intensive or hospital-intensive ERP. Storch 2007 assigned participants to daily or weekly ERP. The two RCTs found no evidence of difference in functioning between the comparative ERP groups.

Table E-KQ2-16. Functional impairment on COIS: Intensive ERP versus ERP

Study, Year, PMID, Study Name	Arm	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)[a]	NMD (95% CI)[a]
Selles, 2021, 34079488 RCT	Home-intensive ERP	PE/CoRe/ERP	COIS-C	12: NR	12: -6.1 (12.9)	-4.8 (-14.64, 5.04)
	IntensiveERP	hospital clinic PE/CoRe/ERP	.	14: NR	14: -1.3 (12.6)	.
Selles, 2021, 34079488 RCT	Home-intensive ERP	PE/CoRe/ERP	COIS-P	12: NR	12: -13.7 (12.11)	-9 (-18.79, 0.79)
	IntensiveERP	hospital clinic PE/CoRe/ERP	.	14: NR	14: -4.7 (13.36)	.
Storch, 2007, 17420681 RCT	IntensiveERP (daily)	Not specified	COIS-P	20: 44.2 (25.9)	20: -26 (22.46)	-12.8 (-28.99, 3.39)
	ERP	Not specified	.	20: 39.1 (29.8)	20: -13.2 (29.31)	.

Abbreviations: CI = confidence interval; COIS-C = The Child Obsessive–Compulsive Impact Scale-child rated; COIS-P= The Child Obsessive–Compulsive Impact Scale-parent rated; CoRe = coping and relaxation; ERP = Exposure and Response Therapy; intensiveERP = Intensive ERP; meanCFB = Mean change from baseline; N = Sample size; NMD =Net mean difference; PE = Psychoeducation; PMID= PubMed ID; SD= Standard deviation.

[a]Calculated by research team.

Combination With Behavioral Intervention

One study for this outcome assessed the comparative effect of a combination of behavioral intervention with other behavioral intervention.

PFIT Plus ERP Versus ERP

Only one RCT assessed functioning in participants assigned to either a combination ERP plus PFIT (Positive Family Interaction Therapy) or ERP.[52] The study found a significant net difference in functioning between PFIT plus ERP and ERP alone.

Table E-KQ2-17. Functional impairment on COIS: PFIT plus ERP versus ERP

Study, Year, PMID, Study Name	Arm	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)[a]	NMD[a] (95% CI)
Peris, 2017, 29173737 RCT	PFIT + ERP	ERP	COIS-RP	32: 26.91 (14.76)	32: -12.97 (13.39)	**-12.67 (-19.93, -5.41)**
	ERP	ERP	.	30: 26.52 (12.90)	30: -0.3 (15.59)	.

Abbreviations: CI = confidence interval; COIS-RP= Child Obsessive-Compulsive Disorder (OCD) Impairment Scale Parent-Report Revised; ERP = Exposure and Response Therapy; meanCFB = Mean change from baseline; N = Sample size; NMD =Net mean difference; PFIT = Positive Family Interaction Therapy; PMID= PubMed ID; SD= Standard deviation.

Bold font has no independent meaning; it highlights statistical significance.

[a]Calculated by research team.

Pharmacological Interventions

One study assessed the comparative effect of CBT (ERP) delivered alone, and three studies as a combination with behavioral intervention.

Pharmacological Intervention Versus No Active Treatment

SSRI Versus Control

Only one study assessed functioning in participants randomized to SSRI or no active treatment (placebo).[44] The study showed a significant net improvement in functioning on COIS-P in SSRI (fluoxetine) compared to placebo.

Table E-KQ2-18. Functional impairment on COIS: SSRI versus control

Study, Year, PMID, Study Name	Arm	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)[a]	NMD[a] (95% CI)
Liebowitz, 2002, 12447029 RCT	SSRI	Fluoxetine	COIS-P	21: 62.61 (33.71)	21: -36.08 (29.91)	**-22.36 (-42.97, -1.75)**
	Control	None	.	22: 58.29 (39.32)	22: -13.72 (38.69)	.

Abbreviations: CI = confidence interval; COIS-P= The Child Obsessive–Compulsive Impact Scale-parent rated; meanCFB = Mean change from baseline; N = Sample size; NMD =Net mean difference; Control = No active treatment (Placebo); PMID= PubMed ID; SD= Standard deviation; SSRI = Selective Serotonin Reuptake Inhibitor.

Bold font has no independent meaning; it highlights statistical significance.

[a]Calculated by research team.

Combination With Pharmacological Intervention

Pharmacological Plus Behavioral Intervention Versus Behavioral Intervention

Three RCTs compared a combination of pharmacological agent plus behavioral intervention to behavioral intervention.

DCS Plus ERP Versus Placebo Plus ERP

Two RCTs assessed functioning in participants assigned to either a combination of DSC (D-cycloserine) plus ERP or placebo plus ERP.[49, 51] One study reported non-significant net increase in functional impairment rated by parents in DSC plus ERP compared to placebo plus ERP.[51] The other study found non-significant net improvement in functioning rated by parents in DCS plus ERP group compared to placebo group.[49]

Table E-KQ2-19. Functional impairment on COIS: DCS plus ERP versus placebo plus ERP

Study, Year, PMID, Study Name	Arm	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)[a]	NMD[a] (95% CI)
Farrell, 2022, 35084071 RCT	DCS + ERP	DCS + ERP	COIS-P	49: 39.2 (26.5)	49: -20 (24.42)	4.6 (-5.49, 14.69)
	ERP	ERP	.	51: 49.3 (29.3)	51: -24.6 (27)	.
Storch, 2016, 27367832 RCT	DCS + ERP	DCS + PE/CR/EPR	COIS-P	70: 16.28 (13.77)	70: -6.34 (13.93)	-0.6 (-5.2, 4.0)
	ERP	PE/CR.ERP	.	72: 14.88 (13.83)	72: -5.74 (14)	.

Abbreviations: CI = confidence interval; COIS-P= The Child Obsessive–Compulsive Impact Scale-parent rated; CR = cognitive restructuring; DCS = D-cycloserine; ERP = Exposure and Response Therapy; meanCFB = Mean change from baseline; N = Sample size; NMD =Net mean difference; PE = Psychoeducation; PMID= PubMed ID; SD= Standard deviation.

[a]Calculated by research team.

SSRI Plus ERP Versus Placebo Plus ERP

One three arm study,[50] assigned participants to regular or slow sertraline or placebo. All participants received ERP. Results showed no significant net difference in functioning between regular or slow SSRI (sertraline) and placebo.

Table E-KQ2-20. Functional impairment on COIS: SSRI plus ERP versus placebo plus ERP

Study, Year, PMID, Study Name	Arm	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)	NMD[a] (95% CI)
Storch, 2013, 24184429 RCT	SSRI + ERP	Regular sertraline + PE/ CR/ERP	COIS-C	14: 14.31 (11.62)	14: -8.14 (10.43)	-1.47 (-9.38, 6.44)
	ERP	PE/ CR/ERP	.	16: 16.27 (13.03)	16: -6.67 (11.66)	.

Study, Year, PMID, Study Name	Arm	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)	NMD[a] (95% CI)
Storch, 2013, 24184429 RCT	SSRI + ERP	Slow sertraline + PE/ CR/ERP	COIS-C	17: 17.2 (12.97)	17: -8.73 (13.56)	-2.06 (-10.67, 6.55)
	ERP	PE/ CR/ERP	.	16: 16.27 (13.03)	16: -6.67 (11.66)	.
Storch, 2013, 24184429 RCT	SSRI + ERP	Regular sertraline + PE/ CR/ERP	COIS-P	14: 19.92 (13.27)	14: -2.65 (14.69)	2.08 (-8.47, 12.63)
	ERP	PE/ CR/ERP	.	16: 17.4 (15.17)	16: -4.73 (14.72)	.
Storch, 2013, 24184429 RCT	SSRI + ERP	Slow sertraline + PE/ CR/ERP	COIS-P	17: 24.6 (18.86)	17: -9.96 (17.37)	-5.23 (-16.19, 5.73)
	ERP	PE/ CR/ERP	.	16: 17.4 (15.17)	16: -4.73 (14.72)	.

Abbreviations: CI = confidence interval; COIS-C = The Child Obsessive–Compulsive Impact Scale-child rated; COIS-P= The Child Obsessive–Compulsive Impact Scale-parent rated; CR = cognitive restructuring; ERP = Exposure and Response Therapy; meanCFB = Mean change from baseline; N = Sample size; NMD =Net mean difference; PE = Psychoeducation; PMID= PubMed ID; SD= Standard deviation; SSRI = Selective Serotonin Reuptake Inhibitor.

Family Accommodation

Family accommodation is a change in the family's behavior with the goal of reducing distress in children with OCD, but "high degrees of family accommodation are associated with greater symptom severity and with poorer response to treatment."[54] Among 13 studies, 11 RCTs[14-17, 38-40, 52, 53, 55-57] and two NRCSs[58, 59] that enrolled a total of 702 participants assessed family accommodation using the Family Accommodation Scale (FAS). FAS (The Family Accommodation Scale) (FAS; Calvocoressi et al., 1995) is a 13-item parent-rated Questionnaire. It is scored on a 5-point Likert-type scale that assesses the degree to which family members have accommodated the child's OCD symptoms during the previous month (9 items) and the level of distress/impairment that the family members and patient experience as a result of the family accommodating or not accommodating the child (4 items).[15] For FAS the low score the better.

All studies assessed the comparative effect of CBT. No study assessed a medication as a primary intervention or as a combination with CBT. CBT in the 13 studies was delivered alone or in combination with another intervention (e.g., family therapy). Studies that delivered CBT alone differed in setting, specific components (e.g., psychoeducation, cognitive restructuring, exposure and response therapy), and intensity. Seven studies compared CBT with another form of CBT,[15-17, 39, 40, 53, 59] three studies compared a combination of CBT plus a family intervention with CBT alone,[52, 57, 58] and three studies compared CBT to a nonactive treatment (TAU or waitlist).[14, 38, 56]

Five RCTs were rated as moderate risk of bias overall,[14, 39, 52, 56] primarily for lack of blinding or incomplete outcome data. One NRCS was rated as moderate risk of bias.[59]Three studies were rated as high risk of bias overall,[15, 38, 58] for the combination of lack of blinding and incomplete outcome data, and in the case of one NRCS for possible confounding based on baseline differences between arms.[58] Five studies were rated as low risk of bias overall.[16, 17, 40, 53, 57]

Family Accommodation Scale (FAS)

Seven studies assessed FAS in participants receiving a specific type of CBT or general CBT.[16, 17, 38-40, 53, 59] The FAS was assessed before and after treatment.

The seven studies each compared different CBT types or approaches [I'm going by the table that differentiates stepped from internet CBT, but I don't know the studies or the interventions.] Three RCTs found statistically significant (or near-significant) net improvements in FAS for CBT (including Psychoeducation and ERP/Exposure) versus Psychoeducation plus Relaxation Training (PRT) (Piacentini 2011[53]), CBT with the child together with either their mother or both parents versus CBT with the mother alone (Rosa-Alcázar 2019[17]), and daily (intensive) CBT versus weekly CBT (Storch 2007[15]).

Two RCTs and the two NRCSs found no evidence of differences between internet-delivered and in-person CBT (Aspvall 2021[39] and Comer 2017[40]), [Whatever Rosa-Alcázar 2017 is comparing] (Rosa-Alcázar 2017[59]), and home-based versus hospital clinic based CBT (Selles 2021[16]).

Table E-KQ2-21. Family accommodation on FAS: CBT versus CBT

Study, Year, PMID, Design	Arm	CBT Components	Scale	Baseline N: Mean (SD)	N: MD (SD)[a]	NMD[a] (95% CI)
Aspvall, 2021, 33974020 RCT	Internet CBT	PE + ERP	FAS-self rated	74: 19.5 (14.4)	74: -12.5 (12.61)	0 (-4.29, 4.29)
	CBT	PE + ERP	.	78: 21.4 (16)	78: -12.5 (14.37)	.
Comer, 2017 278694 RCT	Internet CBT	ERP	FAS	11: 21.1 (6.7)	11: -10 (8.9)	-3.7 (-10.32, 2.92)
	CBT	ERP	.	11: 15.79 (11.25)	11: -6.3 (6.8)	.
Piacentini, 2011, 22024003 RCT	CBT with ERP	PE + ERP	FAS-Parent	48: 17.5 (10.6)	39: -8.2 (9.4)[a]	**-5.4 (-10.79, -0.007)**
	CBT	PE + CoRe	FAS- Parent	22: 18 (10.29)	17: -2.8 (9.5)[a]	.
Rosa-Alcázar, 2019, 31516500 RCT	CBT (parents + child)	PE + ERP	FAS-Mother	14: 22.36 (2.13)	14: -10.43 (1.88)	**-5.16 (-6.92, -3.41)[a]**
	CBT (mother + child)	PE + ERP	FAS-Mother	15: 23.33 (3.02)	15: -9.26 (2.81)	**-3.99 (-6.02, -1.96)[b]**
	CBT (mother only)	PE + ERP	FAS-Mother	15: 23.00 (2.70)	15: -5.27 (2.86)	.
Rosa-Alcázar, 2019, 31516500 RCT	CBT (parents + child)	PE + ERP	FAS-Father	14: 18 (2.26)	14: -8.64 (2.12)	**-6.11 (-8.08, -4.13)[a]**
	CBT (mother + child)	PE + ERP	FAS-Father	15: 19.4 (2.03)	15: -4.8 (2.41)	**-2.27 (-4.30, -0.23)[b]**
	CBT (mother only)	PE + ERP	FAS-Father	15: 19.53 (3.23)	15: -2.53 (3.22)	.

Study, Year, PMID, Design	Arm	CBT Components	Scale	Baseline N: Mean (SD)	N: MD (SD)[a]	NMD[a] (95% CI)
Selles, 2021, 34079488 RCT	Home- based CBT	PE + CoRe + ERP	FAS- self rated	12: NR	12: -9.5 (13.17)	4.7 (-5.87, 15.27)
	Intensive CBT at hospital clinic	PE + CoRe + ERP	FAS- self rated	14: NR	14: -14.2 (14.32)	.
Storch, 2007, 17420681 RCT	Intensive CBT (daily)	Not specified	FAS	20: 24.2 (10.0)	20: -13.5 (9.58)	**-8.7 (-14.61, -2.79)**
	CBT (weekly)	Not specified	FAS	20: 16.3 (10.4)	20: -4.8 (9.49)	.

Statistically significant net mean differences are in bold font.
Abbreviations: CBT = Cognitive behavior therapy; CBFT = Cognitive-Behavioral Family-Based Treatment; CI = confidence interval; CoRe = coping and relaxation; CR = cognitive restructuring; ERP = exposure and response therapy; FAS-P = Family Accommodation Scale-parent version; MD = mean difference; N= sample size; NMD = net mean difference; NR = not reported; NRCS = nonrandomized comparative study, NS = not significant; PE = psychoeducation; PMID = PubMed ID; RCT = randomized controlled trial.

Bold font has no independent meaning; it highlights statistical significance.

[a] This is three arm study. The calculated comparisons are versus CBT mother only (the control group).

[b]Time point of assessment one month after end of treatment.

Three studies, all RCTs, assessed family accommodation in participants randomized to CBT or waitlist/TAU.[14, 38, 56] The three RCTs were different in regard to the setting or component of the CBT delivered. Two studies assigned participants to virtual CBT: Therapist-guided, internet-delivered CBT and internet-delivered family CBT,[38, 56] or waitlist. One RCT assigned participants to ERP versus TAU (Lewin, 2014). The three RCTs found statistically significant net improvements in FAS in participants assigned to CBT compared to TAU or waitlist. Results provided evidence that family accommodation reported on FAS significantly improved in CBT groups, regardless of CBT setting or component, compared to those who were in control group (summary NMD –6.18, 95% CI –9.44 to -2.91).

Table E-KQ2-22. Family accommodation on FAS: CBT versus treatment as usual/waitlist

Study, Year, PMID, Study Name	Arm	CBT components	Scale/ Subscale	Baseline N: Mean (SD)	N: MD (SD)	NMD (95% CI)
Lenhard, 2017, 27993223 RCT	Internet CBT	PE/ERP	FAS-PR	33: 15.79 (11.25)	33: -4.56 (10.38)	**-5.51 (-10.79, -0.23)** P=0.003
	Waitlist	None	FAS-PR	34: 16.18 (10.93)	34: 0.95 (11.66)	.
Lewin, 2014, 24657310 RCT	Family CBT	ERP	FA[a]	17: 19.71 (6.76)	17: -8.47 (7.11)	**-6.18 (-11.28, -1.08)**

Study, Year, PMID, Study Name	Arm	CBT components	Scale/ Subscale	Baseline N: Mean (SD)	N: MD (SD)	NMD (95% CI)
	TAU	None	FA	14: 25.93 (6.86)	14: -2.29 (7.28)	.
Storch, 2011, 21684018 RCT	Internet CBT	PR/CR/ERP	FAS[a,b]	16: 25.67 (8.62)	16: -9.61 (12.17)	**-7.4 (-14.57, -0.23)**
	Waitlist	None	FAS	15: 16.21 (6.93)	15: -2.21 (7.87)	.

Abbreviations: CBT = Cognitive behavior therapy; CI = confidence interval; CoRe = coping and relaxation; CR = cognitive restructuring; ERP = exposure and Response Therapy; FAS-P = Family Accommodation Scale-parent version; MD = mean difference; N= sample size; NMD = net mean difference; NR = not reported; NS = not specified; PE = psychoeducation; PMID = PubMed ID.

Bold font has no independent meaning; it highlights statistical significance.

[a]FA, measure of family accommodation adapted from Calvocoressi et al., 1999.

[b]Administrated by clinician.

Three studies, two RCTs[52, 57] and one NRCS[58] assessed family accommodation in participants assigned to either CBT plus a family intervention or CBT only. In general, the results were variable, with only one study reporting a significant net mean difference favoring CBT combined with parent training.

Table E-KQ2-23. FAS: Combined CBT plus family intervention versus CBT only

Study, Year, PMID, Study Design	Arm Name	Arm Description	Scale	Baseline N: Mean (SD)	N: MD (SD)	NMD (95% CI)
Peris, 2013, 22548378 RCT	FI + CBT	PE/CR/ERP	FAS	10: 25.9 (10.97)	10: -18 (9.51)	-6 (-13.86, 1.86)
	CBT	PE/CR/ERP	FAS	10: 26.5 (8.25)	10: -12 (8.4)	.
Peris, 2017, 29173737 RCT	FI + CBT	ERP	FAS	32: 27.94 (11.02)	32: -17.13 (10.44)	**-9.89 (-15.10, -4.67)**
	CBT	ERP	FAS	30: 25.44 (8.95)	30n up.: -7.24 (10.51)	.
Schuberth, 2023, NR, NRCS	PMT + CBT	PE/ERP	FAS	37: NR	37: -7.73 (9.37)	MD: -1.23 (-4.24, 1.78)[a]
	CBT	PE/ERP	FAS	80: NR	80: NR	.

Abbreviations: CBT = Cognitive behavior therapy; CI = confidence interval; CoRe = coping and relaxation; CR = cognitive restructuring; ERP = exposure and Response Therapy; FAS-P = Family Accommodation Scale-parent version; MD = mean difference; N= sample size; NMD = net mean difference; NR = not reported; NS = not specified; PE = psychoeducation; PFIT= Positive Family Interaction Therapy; PMID = PubMed ID

Bold font has no independent meaning; it highlights statistical significance.

[a]Adjusted mean difference between groups at post-treatment.

Quality of Life

Six RCTs and one NRCS, enrolling a total of 1642 participants measured quality of life at baseline and end of intervention using different tools; Child Health Utility 9D (CHU9D), Manchester Short Assessment of Quality of Life (MANSA), Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire (PQ-LES-Q), Pediatric Quality of life Inventory (PEDSQL), EQ-5D.

CHU9D is a self-reported measure of quality of life with 9 items rated from 1 to 5, yielding a total score of 9-45, with higher scores indicating greater quality of life.[39] MANSA a brief and modified version of LQLP (Lancashire Quality of Life Profile). Like in the LQLP, satisfaction is rated on 7-point rating scales (1 = negative extreme, 7 = positive extreme). ,[33]; PQ-LES-Q is a 15-item rating scale with items scored from 1 (very poor) to (very good); the first 14 items are summed based on the original Q-LES-Q, with higher scores reflecting greater enjoyment and satisfaction, Freeman, 2014 #71; Franklin 2023. PedsQLTM 4.0, Generic Core Scales. Physical functioning consists of eight questions. Emotional functioning and social functioning consist of 5 questions each. Each question ranges from 0 to 4 on a Likert scale. Higher scores show worse conditions. EQ-5D is a widely used measure in health economic evaluations and consists of five dimensions measuring health-related functioning and quality of life, that is, pain/discomfort, anxiety/depression, self-care, mobility and usual activities. It also consists of a 0–100 visual analogue scale (VAS) used to measure subjective ratings of health.

Six studies assessed the comparative effect of CBT (basically ERP) alone and one study assessed the comparative effect of a combination of pharmacological agents. ERP differed across these studies in regard to setting (remote vs. in-person, home vs. hospital). Two studies compared ERP to no active treatment,[33, 36] three studies compared remote ERP to either no active treatment[56] or ERP.[39, 60] One study compared home-intensive ERP to hospital-intensive ERP Selles, 2021 #138}and one study compared a combination of N-Acetylcysteine (NAC) plus ERP to placebo plus ERP.

Three studies were rated as moderate risk of bias overall, primarily for lack of blinding or concealment. Three studies were rated as low risk of bias overall,[16, 28, 36] and the NRCS[60] was rated as high risk of bias overall primarily for lack of blinding and possible confounding based on baseline differences between arms.

Child Health Utility 9D

Behavioral Interventions

Behavioral Intervention Versus Behavioral Intervention

Remote ERP Versus ERP

One RCT assessed quality of life using CHU9D in participants assigned to internet-delivered ERP compared to traditional ERP (in-person ERP).[39] The study found no significant difference in quality of life on CHU9D between internet-delivered ERP and traditional ERP.

Table E-KQ2-24. Quality of life on CHU9D: Remote ERP versus ERP

Study, Year, PMID, Study Name	Arm	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)[a]	NMD (95% CI)
Aspvall, 2021, 33974020 RCT	Remote ERP	PE/ERP	CHU9D	74: 19.9 (5.7)	74: -3 (5.7)	0.3 (-1.54, 2.14)
	ERP	PE/ERP	.	78: 20.0 (5.5)	78: -3.3 (5.88)	.

Abbreviations: CHU9D = Child Health Utility 9D, CI = Confidence interval; ERP = Exposure and Response Prevention; meanCFB = Mean from baseline; N= Sample size; NMD = Net mean difference; PE = Psychoeducation; PMID = PubMed ID; RCT = Randomized Controlled Trial; Remote ERP = Remote ERP (internet-delivered ERP); SD = Standard deviation.

[a]Calculated by research team

MANSA (Manchester Short Assessment of Quality of Life)

Behavioral Interventions

Behavioral Versus No Active Treatment

ERP Versus Control

One three arm RCT for this outcome compared full and brief ERP each to no active treatment (Control).[33] The study found a significant difference in quality of life between full ERP and Control. Quality of life did not significantly differ between brief ERP and noAcitveRx.

Table E-KQ2-25. Quality of life on MANSA: ERP versus control

Study, Year, PMID, Study Name	Arm	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)[a]	NMD (95% CI)
Bolton, 2011, 21644984 RCT	ERP	General ERP/NS	MANSA	36: 37.3 (9.2)	36: 7.3 (8.66)	4.8 (0.67. 8.92)
	Control	None	.	24: 35.0 (8.0)	24: 2.5 (7.51)	.
Bolton, 2011, 21644984 RCT	Brief ERP	Brief ERP/NS	MANSA	36: 36.6 (9.4)	36: 2.8 (9.61)	0.3 (-4.05, 4.65)
	Control	None	.	24: 35.0 (8.0)	24: 2.5 (7.51)	.

Abbreviations: CI = Confidence interval; ERP = Exposure and Response Prevention; MANSA = Manchester Short Assessment of Quality of Life; meanCFB = Mean change from baseline; N= Sample size; NMD = Net mean difference; Control = No active treatment; NS= Not specified; PMID = PubMed ID; RCT = Randomized Controlled Trial; SD = Standard deviation.

[a]Calculated by research team

PQ-LES-Q (Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire)

Behavioral Interventions

Behavioral Intervention Versus No Active Treatment

ERP Versus Control

One RCT for this outcome compared family-based ERP to noActiveRx (no active treatment).[36] The study did not report this outcome at baseline, but only reported mean score for each arm at post-intervention. There was no significant difference on PQ-LES-Q at post-intervention between ERP and Control.

Table E-KQ2-26. Quality of life on PQ-LES-Q: ERP versus control

Study, Year, PMID, Study Name	Arm	Arm Description	Scale	Baseline N: Mean (SD)	N: Mean (SD)	MD[a] (95% CI)
Freeman, 2014, 24759852 RCT POTS Jr	ERP	Family- PE/CoRe/CR/ERP	PQ-LES-Q	63: NR	63: 4.16 (0.55)	0.14 (-0.05, 0.33)
	Control	behavCntrl	.	64: NR	64: 4.02 (0.55)	.

Abbreviations: behavCntrl = Behavioral control; CI = Confidence interval; CoRe = Coping and Relaxation; CR= Cognitive Restructuring; ERP = Exposure and Response Prevention; MD = Mean difference; N= Sample size; Control = No active treatment; NR = Not reported; PE = Psychoeducation; PMID = PubMed ID; POTS = Pediatric OCD Treatment Study; PQ-LES-Q = Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire; RCT = Randomized Controlled Trial; SD = Standard deviation.

[a]Calculated by research team

Behavioral Intervention Versus Behavioral Intervention

Remote ERP Versus ERP

One NRCS assessed quality of life in participants received either internet-delivered ERP or in-person ERP. The study found no significant difference in quality of life on PQ-LES-Q between internet-delivered ERP and in-person ERP.

Table E-KQ2-27. Quality of life on PQ-LES-Q: Remote ERP versus ERP

Study, Year, PMID, Study Name	Arm	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)[a]	NMD[a] (95% CI)
Franklin, 2023, NR NRCS	Remote ERP	Internet ERP	PQ-LES-Q	590: 57.56 (15.84)	590: 9.34 (15.94)	-1.24 (-3.11, 0.63)
	ERP	ERP	.	591: 57.11 (16.17)	591: 10.58 (16.85)	.

Abbreviations: CI = Confidence interval; ERP = Exposure and Response Prevention; meanCFB = Mean from baseline; N= Sample size; NMD = Net mean difference; NRCS = Non-Randomized Controlled Study; PMID = PubMed ID; PQ-LES-Q = Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire; Remote ERP = Remote ERP (internet-delivered ERP); SD = Standard deviation.

[a]Calculated by research team

Home-Intensive ERP Versus Hospital-Intensive ERP

One RCT assessed quality of life using PQ-LES-Q in participants assigned to either home-intensive ERP or hospital-intensive ERP.[16] Analysis of Quality of life reported on PQ-LES-Q showed no significant difference between home-intensive ERP and hospital-intensive ERP.

Table E-KQ2-28. Quality of life on PQ-LES-Q: Home-intensive ERP versus hospital-intensive ERP

Study, Year, PMID, Study name	Arm	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)a	NMDa (95% CI)
Selles, 2021, 34079488 RCT	Home-intensive ERP	PE/CoRe/ERP	PQ-LES-Q	12: 52.09 (9.66)	12: -1.09 (9.99)	-1.65 (-8.92, 5.62)
	Intensive ERP	PE/CoRe/ERPb	.	14: 48.29 (9.15)	14: 0.56 (8.76)	.

Abbreviations: CI = Confidence interval; CoRe = Coping and Relaxation; ERP = Exposure and Response Prevention; meanCFB = Mean change from baseline; N= Sample size; NMD = Net mean difference; PE = Psychoeducation; PMID = PubMed ID; PQ-LES-Q = Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire; RCT = Randomized Controlled Trial; SD = standard deviation.

[a]Calculated by research team.

[b]Hospital-intensive ERP.

PedsQL (Pediatric Quality of Life Inventory)

Behavioral Interventions

No studies for this outcome assigned participants to behavioral interventions.

Pharmacological Interventions

Combination With Pharmacological Interventions

NAC Plus SSRI Versus SSRI

One RCT[28] assessed different quality of life domains, at baseline and post-treatment, in participants assigned to either a combination of N-Acetylcysteine (NAC) plus citalopram or placebo plus citalopram. NAC group had a non-significant net improvement in Quality-of-life domains (Physical and Social functions) compared to placebo. Analysis of emotional function showed a significant net improvement favoring NAC.

Table E-KQ2-29. Quality of life domains on PedsQL: NAC plus SSRI versus placebo plus SSRI

Study, Year, PMID, Study Name	Arm	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)[a]	NMD[a] (95% CI)
Ghanizadeh, 2017, 28659986 RCT	NAC + SSRI	NAC + Citalopram	Physical Function on PedsQL	18: 11.1 (5.1)	18: -4.3 (5.15)	-3.8 (-8.89, 1.29)
	SSRI	Citalopram	.	11: 10.4 (7)	11: -0.5 (7.61)	.
Ghanizadeh, 2017, 28659986 RCT	NAC + SSRI	NAC + Citalopram	Emotional Function on PedsQL	18: 9.3 (4.5)	18: -5.1 (4.36)	**-7.1 (-13.43, -0.77)**
	SSRI	Citalopram	.	11: 17 (11.5)	11: 2 (10.15)	.
Ghanizadeh, 2017, 28659986 RCT	NAC + SSRI	NAC + Citalopram	Social Function on PedsQL	18: 7.7 (4.8)	18: -4.4 (4.36)	-2.1 (-5.67, 1.47)
	SSRI	Citalopram	.	11: 7.7 (5.6)	11: -2.3 (5.0)	.

Abbreviations: CI = Confidence interval; meanCFB = Mean change from baseline; N= Sample size; NAC = N-Acetylcysteine; NMD = Net mean difference; PedsQL = Pediatric Quality of Life Inventory; PMID = PubMed ID; RCT = Randomized Controlled Trial; SD = Standard deviation; SSRI = Selective Serotonin Reuptake Inhibitors.

Bold font has no independent meaning; it highlights statistical significance.

[a]Calculated by research team.

EQ-5D-Y VAS (Five Dimensions Questionnaire Youth Version Visual Analogue Scale)

Behavioral Interventions

Behavioral Intervention Versus Control

Remote ERP Versus Control

One RCT assessed quality of life using EQ-5D-Y VAS in participants randomized to either Therapist-Guided, Internet-Delivered ERP or no active treatment (Control).[56] The study showed no significant net difference in EQ-5D-Y VAS score between internet-delivered ERP and noActieRx.

Table E-KQ2-30. Quality of Life domains on EQ-5D-Y VAS: Remote ERP versus control

Study, Year, PMID, Study Name	Arm	Arm Description	Scale	Baseline N: Mean (SD)	N: meanCFB (SD)[a]	NMD (95% CI)
Lenhard, 2017, 27993223 RCT	Remote ERP	PE/ERP	EQ-5D-Y VAS	33: 66.11 (22)	33: 0.0007 (0.051)	0.0041 (-0.018, 0.026)
	Control	None	.	34: 66.2 (22)	34: -0.0034 (0.041)	.

Abbreviations: CI = Confidence interval; ERP = Exposure and Response Prevention; EQ-5D-Y VAS = Five Dimensions Questionnaire Youth version Visual Analogue Scale (VAS); meanCFB = Mean change from baseline; N= Sample size; NMD = net mean difference; Control = No active treatment; PE= Psychoeducation; PMID = PubMed ID; RCT = Randomized Controlled Trial; Remote ERP = Remote ERP (internet-delivered ERP); SD = Standard deviation.

[a]Calculated by research team.

Parent Satisfaction With Services

Three RCTs [39, 40, 57] enrolling a total of 192 participants measured parent satisfaction with services using The Client Satisfaction Questionnaire (CSQ-8) or the 7-Item inventory at the end of intervention. CSQ-8 is an 8-item scale that is used to measure satisfaction with the treatment, each item is rated from 1 to 4, yielding a total score of 9-36 where higher scores indicate greater satisfaction.[39] The 7-item inventory includes items such as, “To what extent has this program met your needs?” and “If a friend's child were in similar need, would you recommend the program?” Items were rated on a 4-point Likert scale with 0=not at all and 4=very much (maximum score= 28).[57]

The three studies assessed the comparative effect of CBT (basically ERP) alone or as a combination with family intervention. No study assessed the comparative effect of pharmacological agents. Two studies compared remote ERP (internet-delivered ERP) to traditional ERP (in-person ERP).[39, 40] One study compared a combination of ERP plus family intervention to traditional ERP.[57]

One study was rated as moderate risk of bias overall, [39] primarily for lack of blinding or concealment. Two studies were rated as low risk of bias overall.[40, 57]

CSQ-8 (Client Satisfaction Questionnaire)

Behavioral Interventions

Behavioral Intervention Versus Behavioral Intervention

Remote ERP versus ERP

Two studies assessed parent satisfaction with internet-delivered ERP compared to traditional ERP (in-person ERP).[39, 40] One study[39] found that parents were significantly less satisfied with internet-delivered ERP than traditional ERP. Another[40] found no significant difference in satisfaction rated by mother between internet-delivered ERP and traditional ERP.

Table E-KQ2-31. Parent satisfaction on CSQ-8: Remote ERP versus ERP

Study, Year, PMID, Study Name	Arm	Arm Description	Scale	Baseline N: Mean (SD)	N: Mean (SD)	MD[a] (95% CI)
Aspvall, 2021, 33974020 RCT	Remote ERP	PE/ERP	CSQ-8 Parent rated	-	74: 25.25 (5.06)	**-2.62 (-4.14, -1.1)**
	ERP	PE/ERP	.	-	78: 27.87 (4.47)	.
Comer, 2017, 278694 RCT	Remote ERP	ERP	CSQ-8 Mother rated	-	10: 28.55 (4.5)	-1.95 (-5.00, 1.10)
	ERP	ERP	.	-	10: 30.5 (2)	.

Abbreviations: CI = Confidence interval; CSQ-8 = The Client Satisfaction Questionnaire; ERP = Exposure and Response Prevention; MD = Mean difference; N= sample size; PE = psychoeducation; PMID = PubMed ID; Remote ERP = Internet-delivered ERP; RCT = Randomized Controlled Trial; SD = Standard deviation.

Bold font has no independent meaning; it highlights statistical significance.

[a]Assessed at post-treatment only, as this assessment was not applicable at baseline.

The 7-Item Inventory

Behavioral Intervention

Combination With Behavioral Intervention

PFI Plus ERP Versus ERP

Only One RCT for this outcome compared a combination of ERP plus a family intervention with traditional ERP alone.[57] The study found no significant difference in satisfaction rated by mother between ERP plus family intervention and traditional ERP. Fathers in the same study were more satisfied with ERP plus family intervention than traditional ERP. Significance could not be known due to missing data.

Table E-KQ2-32. Parent satisfaction on the 7-Item Inventory: PFI plus ERP versus ERP

Study, Year, PMID, Study Name	Arm	Arm Description	Scale	Baseline N: Mean (SD)	N: Mean (SD)	MD[a] (95% CI)
Peris, 2013, 22548378 RCT	PFIT + ERP	PE/CR/ERP	Mother Rated	-	10: 24.9 (4.61)	0.8 (-2.78, 4.38)
	ERP	PE/CR/ERP	.	-	10: 24.1 (3.47)	.
Peris, 2013, 22548378 RCT	PFI + ERP	PE/CR/ERP	Father Rated	-	NR: 26.71 (1.5)	7.11[b]
	ERP	PE/CR/ERP	.	-	NR: 19.6 (1.34)	.

Abbreviations: CI = Confidence interval; CR = Cognitive Restructuring; ERP = Exposure and Response Prevention; MD = Mean difference; N= Sample size; NR = Not reported; PE = Psychoeducation; PFIT = Positive Family Interaction Therapy; PMID = PubMed ID; RCT = Randomized Controlled Trial; SD = Standard deviation.

[a]Assessed at post-treatment only, as this assessment was not applicable at baseline.

[b]Confidence interval could not be calculated, as the N for each arm was not reported, however, total number of fathers was 12 per reported.

Other Scales

One study reported on parental satisfaction using a questionnaire developed by the researchers. No significant effect on parental satisfaction was observed when comparing telephone CBT versus in-person CBT.

Table E-KQ2-33. Parental satisfaction

Study, Year, PMID	Timepoint	Intervention Arms	Intervention Description	n/N (%)	RR (95% CI)	P Value
Turner, 2014, 25457928	Study Period	CBT	Telephone CBT	33/36 (93.1)	1.00 (0.85, 1.18)	1.000
	Study Period	CBT	In-person CBT	32/36 (88.9)	.	.

Abbreviations: % = percent, CBT = cognitive behavioral therapy, CI = confidence interval, n = event, N = total sample analyzed, PMID = PubMed identifier, RR = relative risk, wk = week.

One study reported on patient satisfaction using a questionnaire developed by the researchers. No significant effect on parental satisfaction was observed when comparing telephone CBT versus in-person CBT.

Table E-KQ2-34. Patient satisfaction

Study, Year, PMID	Timepoint	Intervention Arms	Intervention Description	n/N (%)	RR (95% CI)	P Value
Turner, 2014, 25457928	Study Period	CBT	Telephone CBT	35/36 (96.3)	1.06 (0.95, 1.19)	0.311
	Study Period	CBT	In-person CBT	33/36 (92.6)	.	.

Abbreviations: % = percent, CBT = cognitive behavioral therapy, CI = confidence interval, n = event, N = total sample analyzed, PMID = PubMed identifier, RR = relative risk, wk = week.

Adverse Events Leading to Withdrawal or Discontinuation

Seven studies reported on adverse events leading to withdrawal or discontinuation.[25, 34, 41, 45, 61-63] Three studies reported on the comparison of TCA versus Placebo,[45, 61, 62] two on CBT versus SSRI,[34, 63] one compared different TCAs,[25] one on CBT versus TCA.[41]

Paroxetine showed higher risk of reporting adverse events leading to withdrawal after study period (RR 3.57; 95%CI 1.01-12.60)[62] and Sertraline after 12 weeks follow-up (RR 4.13, 95%CI 1.20, 14.16).[45] No other study reported significant adverse events leading to withdrawal related to intervention.

Table E-KQ2-35. Adverse events leading to withdrawal or discontinuation

Study, Year, PMID	Timepoint	Intervention Arms	Intervention Description	n/N (%)	RR (95% CI)	P Value
Geller, 2004, 15502598	Study period	TCA	Paroxetine	10/98 (10.2)	**3.57 (1.01, 12.60)**	**0.048**
	Study period	Placebo	Placebo	3/105 (2.9)	.	.
POTS, 2004, 15507582	12wk	CBT	ERP	0/28 (0)	NA	NA
	12wk	SSRI	Sertraline	1/28 (3.6)	.	..
Leonard, 1989, 2686576	Study period	TCA	Clomipramine	1/45 (2.2)	NA	NA
	Study period	TCA	Desipramine	0/45 (0)	.	.
March, 1998, 9842950	12wk	TCA	Sertraline	12/92 (13)	**4.13 (1.20, 14.16)**	**0.024**
	12wk	Placebo	Placebo	3/95 (3.2)	.	.
Geller, 2003, 12880497	16wk	TCA	Paroxetine	8/95 (8.4)	0.75 (0.32, 1.78)	0.511
	16wk	Placebo	Placebo	11/98 (11.2)	.	.

Study, Year, PMID	Timepoint	Intervention Arms	Intervention Description	n/N (%)	RR (95% CI)	P Value
Franklin, 2011, 21934055	Study period	Remote CBT + SSRI	Remote CBT + SSRI	5/42 (11.9)	1.59 (0.41, 6.21)	0.504
	Study period	SSRI	SSRI	3/40 (7.5)	.	.
Asbahr, 2005, 16239861	Study period	CBT	ERP	0/20 (0)	NA	NA
	Study period	TCA	Sertraline	1/20 (5)	.	.

Abbreviations: % = percent, CBT = cognitive behavioral therapy, CI = confidence interval, ERP = exposure and response prevention, n = event, N = total sample analyzed, PMID = PubMed identifier, POTS = Pediatric OCD Treatment Study, RR = relative risk, SSRI = slow serotonin reuptake inhibitor, TCA = tricyclic antidepressant, wk = week.

Bold font has no independent meaning; it highlights statistical significance.

Adverse Events, Serious/Severe

Four studies reported on serious/severe adverse events.[34, 49, 50, 61] One study reported on the comparison of TCA versus Placebo,[61] one on NMDA versus CBT,[49] one on CBT versus SSRI,[34] and one on regular versus slow titration of an SSRI.[50] No significant risk rations of serious/severe adverse events were observed.

Table E-KQ2-36. Adverse events, serious (grade 3 or 4)

Study, Year, PMID	Timepoint	Intervention Arms	Intervention Description	n/N (%)	RR (95% CI)	P Value
Geller, 2003, 12880497	12wk	TCA	Paroxetine	2/95 (2.1)	1.03 (0.15, 7.18)	0.976
	12wk	Placebo	Placebo	2/98 (2)	.	.
Storch, 2016, 27367832	10wk	CBT + NMDA agonist	CBT + D-cycloserine	0/70 (0)	NA	NA
	10wk	CBT	CBT + Placebo	0/72 (0)	.	.
Franklin, 2011, 21934055	Study period	SSRI + iCBT	SSRI + internet CBT	1/40 (2.5)	1.05 (0.07, 16.23)	0.972
	Study period	SSRI	SSRI	1/42 (2.4)	.	.
Storch, 2013, 24184429	Study period	SSRI + CBT	Regular Sertraline + CBT	1/14 (7.1)	1.21 (0.08, 17.71)	0.887
	Study period	SSRI + CBT	Slow Sertraline + CBT	1/17 (5.9)	.	.

Abbreviations: % = percent, CBT = cognitive behavioral therapy, CI = confidence interval, n = event, N = total sample analyzed, NMDA = N-methyl-D-aspartate, PMID = PubMed identifier , RR = relative risk, SSRI = slow serotonin reuptake inhibitor, TCA = tricyclic antidepressant, wk = week.

Adverse Events, Total

Ten studies reported on total adverse events.[31, 34, 39, 43, 48, 64-67] One study reported on the comparison of different TCAs,[64] two on NMDA versus placebo,[48, 65] one on CBM-I versus waitlist,[67] one on TCA versus placebo, one on antipsychotic drug versus TCA,[31] one on SSRI versus placebo,[43] one on SSRI versus CBT,[34] one on internet CBT versus in-person CBT,[39] and one on SSRI versus TCA.[66]

One study reported a reduced risk of total adverse events using fluvoxamine versus clomipramine (RR 0.48, 95%CI 0.27-0.83).[64] Another study comparing SSRI and TCA reported that participants treated with Sertraline reported reduced adverse events than those

treated with clomipramine (RR 0.42, 95%CI 0.24-0.72).[66] No other study reported significant adverse events leading to withdrawal related to intervention.

Table E-KQ2-37. Adverse events, total

Study, Year, PMID	Timepoint	Intervention Arms	Intervention Description	n/N (%)	RR (95% CI)	P Value
Wolters, 2021	Study period	CBM-I + CBT	Internet Cognitive Bias Modification + CBT	0/40 (0)	NA	NA
	Study period	Waitlist + CBT	CBT	0/39 (0)	.	.
NCT01933919, 2017,	Study period	TCA	Fluvoxamine	13/19 (68.4)	0.87 (0.59, 1.27	0.476
	Study period	Placebo	Placebo	15/19 (78.9)	.	.
He, 2007	Study period	TCA	Fluvoxamine	10/30 (33.3)	**0.48 (0.27, 0.83)**	**0.010**
	Study period	TCA	Clormipramine	21/30 (70)	.	.
Liu, 2012	Study period	TCA + antipsychotic	Fluvoxamine + Risperidone	3/44 (6.8)	1.00 (0.21, 4.69)	1.000
	Study period	TCA	Fluvoxamine	3/44 (6.8)	.	.
Mataix-Cols, 2014, 24262813	Study period	CBT + NMDA agonist	CBT + D-cycloserine	0/13 (0)	NA	NA
	Study period	CBT + Placebo	CBT + Placebo	0/14 (0)	.	.
Storch, 2010, 20817153	Study period	CBT + NMDA agonist	CBT + D-cycloserine	0/15 (0)	NA	NA
	Study period	CBT + Placebo	CBT + Placebo	0/15 (0)	.	.
Franklin, 2011, 21934055	Study period	SSRI + iCBT	SSRI + internet CBT	33/40 (82.5)	0.94 (0.78, 1.12)	0.503
	Study period	SSRI	SSRI	37/42 (88.1)	.	.
Geller, 2001, 11437015	Study period	SSRI	Fluoxetine	53/71 (74.6)	0.88 (0.72, 1.08)	0.217
	Study period	Placebo	Placebo	27/32 (84.4)	.	.
Aspvall, 2021, 33974020	Study period	iCBT	Internet CBT	47/74 (63.5)	0.95 (0.75, 1.20)	0.669
	Study period	CBT	In-person CBT	52/78 (66.7)	.	.
Nai, 2009,	Study period	SSRI	Sertraline	10/32 (31.3)	**0.42 (0.24, 0.72)**	**0.002**
	Study period	TCA	Clomipramine	24/32 (75)	.	.

Abbreviations: % = percent, CBT = cognitive behavioral therapy, CI = confidence interval, n = event, N = total sample analyzed, NMDA = N-methyl-D-aspartate, PMID = PubMed identifier, RR = relative risk, SSRI = slow serotonin reuptake inhibitor, TCA = tricyclic antidepressant, wk = week.

Bold font has no independent meaning; it highlights statistical significance.

Suicidal Thoughts and Behavior

One study reported on suicidal thoughts and behavior using a questionnaire developed by the researchers.[62] No cases were reported in both regular sertraline plus CBT and slow sertraline plus CBT groups.

Table E-KQ2-38. Suicidal thoughts and behavior

Study, Year, PMID	Timepoint	Intervention Arms	Intervention Description	n/N (%)	RR (95% CI)	P Value
Geller, 2004, 15502598	Study Period	SSRI	Paroxetine	1/98 (1)	NA	NA
	Study period	Placebo	Placebo	0/105 (0)	.	.

Abbreviations: % = percent, CI = confidence interval, n = event, N = total sample analyzed, PMID = PubMed identifier, RR = relative risk, SSRI = slow serotonin reuptake inhibitor, wk = week.

Withdrawals/Discontinuation

Eleven studies reported on withdrawals and discontinuation.[7, 30, 34, 43, 45, 49, 50, 56, 61, 62, 68] One study reported on the comparison of CBT versus SSRI,[34] one on different TCAs,[61] two on TCA versus placebo,[45, 62] one on iCBT versus placebo,[56] one on CBT versus TCA,[68] one on ACT versus CBT,[7] one on SSRI versus placebo,[43] and one on different SSRIs.[50] No study reported significant effect of intervention on the risk of withdrawal or discontinuation.

Table E-KQ2-39. Withdrawals/discontinuation

Study, Year, PMID	Timepoint	Intervention Arms	Intervention Description	n/N (%)	RR (95% CI)	P Value
March, 1998, 9842950	Study Period	TCA	Sertraline	18/92 (19.6)	1.43 (0.74, 2.75)	0.283
	Study Period	Placebo	Placebo	13/95 (13.7)	.	.
Franklin, 2011, 21934055	Study Period	SSRI + iCBT	SSRI + internet CBT	5/40 (12.5)	0.48 (0.18, 1.25)	0.133
	Study Period	SSRI	SSRI	11/42 (26.2)	.	.
Lenhard, 2017, 27993223	Study Period	iCBT	CBT	1/33 (3)	0.52 (0.05, 5.41)	0.584
	Study Period	Waitlist	Placebo	2/34 (5.9)	.	.
Shabani, 2019	Study Period	ACT + SSRI	CBT + SSRI	2/22 (9.1)	0.67 (0.12, 3.61)	0.645
	Study Period	CBT + SSRI	CBT + SSRI	3/22 (13.6)	.	.
Geller, 2003, 12880497	Study Period	TCA	Paroxetine	53/95 (55.8)	0.84 (0.67, 1.06)	0.137
	Study Period	TCA	Placebo	65/98 (66.3)	.	.
Geller, 2004, 15502598	Study Period	TCA	Paroxetine	33/98 (33.7)	1.41 (0.91, 2.20)	0.123
	Study Period	Placebo	Placebo	25/105 (23.8)	.	.
Skarphedinsson, 2015, 25239489	Study Period	TCA	Sertraline	7/22 (32)	1.27 (0.52, 3.09)	0.599
	Study Period	CBT	CBT	7/28 (25)	.	.
Grant, 2014, 24356715	Study Period	Glutamate inhibitor	Riluzole	7/30 (23.3)	7.00 (0.92, 53.47)	0.060
	Study Period	Placebo	Placebo	1/30 (3.3)	.	.
Storch, 2016, 27367832	Study Period	CBT + NMDA agonist	CBT + D-cycloserine	3/70 (4.3)	NA	NA
	Study Period	CBT + Placebo	CBT + Placebo	0/72 (0)	.	.
Storch, 2013, 24184429	Study Period	SSRI + CBT	Regular Sertraline + CBT	6/14 (42.9)	1.46 (0.56, 3.78)	0.439
	Study Period	SSRI + CBT	Slow Sertraline + CBT	5/17 (29.4)	.	.
	Study Period	SSRI	Fluoxetine	22/71 (31.0)	0.83 (0.47, 1.46)	0.509

Study, Year, PMID	Timepoint	Intervention Arms	Intervention Description	n/N (%)	RR (95% CI)	P Value
Geller, 2001, 11437015	Study Period	Placebo	Placebo	12/32 (37.5)	.	.

Abbreviations: % = percent, ACT = acceptance and commitment therapy, CBT = cognitive behavioral therapy, CI = confidence interval, n = event, N = total sample analyzed, NMDA = N-methyl-D-aspartate, PMID = PubMed identifier, POTS = pediatric OCD (Obsessive compulsive disorder) treatment study, RR = relative risk, SSRI = slow serotonin reuptake inhibitor, TCA = tricyclic antidepressant, wk = week.

Predictors/Mediators of Effect

Full extractions for the single-arm predictor studies are in Appendix H. The following tables summarize the results.

Table E-KQ2-40. RCT predictors/mediators

Study	Comparison (n)	Behavioral Intervention, Components	Outcome	Age	Gender	Comorbidity*	CY-BOCS (Baseline)	FAS (Base-line)	FAD (Base-line)
Barrett, 2005, 16175105	Individual CBFT (24) vs. group CBFT (29) or waitlist (24)	Psychoeducation, Cognitive restructuring, ERP	CY-BOCS (lower post-treatment score)	NS	.	.	.	.	.
Wilhelm, 2018, 30149332	CBT + DCS (70) vs. CBT + placebo (72)	Psychoeducation, Cognitive restructuring, ERP	CY-BOCS (lower post-treatment score)	NS	NS	NS	.	.	.
Barrett, 2005, 16175105	Individual CBFT (24) vs. group CBFT (29) or waitlist (24)	Psychoeducation, Cognitive restructuring, ERP	NIMH GOCS (% reduction)	NS	.	NS	+	.	–
Wilhelm, 2018, 30149332 (Storch 2016)	CBT + DCS (70) vs. CBT + placebo (72)	Psychoeducation, Cognitive restructuring, ERP	CY-BOCS <12	NS	NS	NS	.	.	.

Cell coloring applied for visual emphasis only; it does not provide unique information.

Abbreviations: + = increase in predictor/predictor (or noted predictor) present predicts statistically significant increase in outcome; – = decrease in predictor/predictor present predicts statistically significant increase in outcome; . = study did not evaluate predictor; NS no significant relationship; ? = significant relationship but direction unclear (not used in this table); CBT = cognitive behavioral therapy, CBFT = cognitive behavioral family therapy, CY-BOCS = Children's Yale-Brown Obsessive Compulsive Scale, DCS = D-cycloserine, ERP = exposure and response therapy, FAS = Family Accommodation Scale, FAD = Family Assessment Device, OCD = Obsessive Compulsive Disorder, TCBT = telephone cognitive behavioral therapy,

* The comorbidities assessed by studies were anxiety, depression, and tics.

Table E-KQ2-41. Single-arm study predictor/mediators

Study; Study Name/Site	N; Age, Baseline CY-BOCS Score, Mean (SD)	Intervention, Components	Regression Quality	Outcome	Age	Age at Onset/Duration	Gender	Comorbidity	CY-BOCS (Base-line)	Insurance	Medication	Minoritized Group	Treatment	COIS (base-line)	FAS (Base-line)	Symptoms (Base-line)	Other
Riise, 2019, 31134420; Haukeland University hospital, Norway	N=63; Age =14.4 (1.9); Baseline CY-BOCS Score=26.52 (3.99)	Psychoeducation, ERP	Adequate	CY-BOCS (lower post-treatment score)	.	.	.	.	+*	.	.	.	.	NS	NS	.	.
Nakatani, 2011, 21726224; Maudsley Hospital (London, UK) 1996-2007	N=109; Age =NR; Baseline CY-BOCS Score=NR	Psychoeducation, Cognitive restructuring, ERP	Inadequate	CY-BOCS (lower post-treatment score)	.	NS	NS	NS	–	.	–	.	.	.	.	.	.
Brown, 2015, 25301176; Maudsley Hospital (London, UK) 2007-2012	N=98; Age =NR; Baseline CY-BOCS Score=NR	Psychoeducation, ERP	Adequate	CY-BOCS (lower post-treatment score)	NS	.	.	NS	–	.	NS	.	.	.	.	.	.
Torp, 2015, 25721185; NordLOTS, stage 1	N=269; Age =12.8 (2.7); Baseline CY-BOCS Score=24.6 (5.1)	ERP	Adequate	CY-BOCS (lower post-treatment score)	–	NS	NS	NS	.	.	.	.	.	.	NS	.	.
Højgaard , 2020, 31203735; OCD Center at he Rogers Memorial Hospital in Oconomowoc, Wisconsin	N=314; Age =15.56 (1.20); Baseline CY-BOCS Score=25.65 (5.63)	Cognitive restructuring, ERP	Adequate	CY-BOCS (lower post-treatment score)	NS	.	NS	NS	–	.	.	.	NS	.	.	.	.
Rudy, 2014, 25193378; University of Florida OCD Program	N=78; Age =13.2 (2.72); Baseline CY-BOCS Score=NR	Psychoeducation, Cognitive restructuring, ERP	Adequate	CY-BOCS (lower post-treatment score)	NS	.	NS	.	–	.	.	.	.	NS	NS	.	.

Study; Study Name/Site	N; Age, Baseline CY-BOCS Score, Mean (SD)	Intervention, Components	Regression Quality	Outcome	Age	Age at Onset/Duration	Gender	Comorbidity	CY-BOCS (Base-line)	Insurance	Medication	Minoritized Group	Treatment	COIS (base-line)	FAS (Base-line)	Symptoms (Base-line)	Other
Garcia, 2023, none; Bradley Hospital Pediatric Anxiety Research Center, 2013-2022	N=185; Age =12.2 (3.3); Baseline CY-BOCS Score=28.9 (4.6)	ERP	Adequate	CY-BOCS (reduction)	NS	.	NS	+ (Anxiety Mood ADHD ASD Tics)	+	NS	NS	–‖	–†	.	.	.	.
Storch, 2008, 17986317 University of Florida OCD Program	N=92; Age =13.6 (3.3); Baseline CY-BOCS Score=NR	Psychoeducation, Cognitive restructuring, ERP	Inadequate	CGI-S (reduction)	.	.	.	.	.	.	.	.	.	.	.	+¶	
Farrell, 2020, 37669531; Griffith U, Queensland AU	N=63; Age =12.2 (2.8); Baseline CY-BOCS Score=25.7 (5.3)	CBT/not specified	Adequate	CY-BOCS (reduction)	NS	.	?	– (ADHD)	.	.	.	.	.	.	.	.	.
Selles, 2018, 29179016; British Columbia Children's Hospital Provincial OCD Program	N=85; Age =13.9 (2.49); Baseline CY-BOCS Score=23.36 (4.98)	Psychoeducation, Cognitive restructuring, ERP	Inadequate	CY-BOCS (reduction)	.	.	.	.	NS	.	.	.	.	.	.	.	.
Jassi, 2023, 34914003; Maudsley Hospital (London, UK) 2005-2018	N=323; Age =14.6 (2.2); Baseline CY-BOCS Score=NR	Psychoeducation, ERP	Adequate	CY-BOCS (reduction)	.	.	.	– (ASD)	.	.	.	.	.	.	.	.	.
Duholm, 2022, 33861384; NordLOTS, stage 1	N=269; Age =12.8 (2.7); Baseline CY-BOCS Score=24.6 (5.1)	ERP	Inadequate	CY-BOCS (reduction)	.	.	.	.	.	.	.	.	.	.	.	NS	.

Study; Study Name/Site	N; Age, Baseline CY-BOCS Score, Mean (SD)	Intervention, Components	Regression Quality	Outcome	Age	Age at Onset/Duration	Gender	Comorbidity	CY-BOCS (Base-line)	Insurance	Medication	Minoritized Group	Treatment	COIS (base-line)	FAS (Base-line)	Symptoms (Base-line)	Other
McGuire , 2013, 23623154; Storch 2008, standard clinic	N=144; Age =12.62 (2.81); Baseline CY-BOCS Score=26.24(4.65)	Psychoeducation , Cognitive restructuring, ERP	Adequate	CY-BOCS (reduction)	.	.	.	NS	.	.	.	.	.	.	NS	.	.
Storch, 2008, 17986317; University of Florida OCD Program	N=92; Age =13.6 (3.3); Baseline CY-BOCS Score=NR	Psychoeducation , Cognitive restructuring, ERP	Inadequate	CY-BOCS (reduction)	.	.	.	.	.	.	.	.	.	.	.	NS	.
Hybel, 2017, 28881220; NordLOTS, stage 1	N=50; Age = NR; Baseline CY-BOCS Score = 25.34 (5.26)	ERP	Inadequate	CY-BOCS (reduction)	.	.	.	.	.	.	.	.	.	.	.	.	–§
Wolters, 2021, 2022-96874-001; Wolters Study 1	N=59; Age =15.3 (2.4); Baseline CY-BOCS Score=25.4 (5.3)	CBT/not specified	Adequate	CY-BOCS (reduction)	NS	.	NS	.	NS	.	.	.	.	.	.	.	.
Højgaard , 2019, 30656432; NordLOTS, stage 1	N=269; Age =12.8 (2.7); Baseline CY-BOCS Score=24.6 (5.1)	ERP	Adequate	CY-BOCS <16	?	NS	NS	.	.	.	.	.	.	NS	NS	NS	.
Højgaard , 2020, 31203735; OCD Center at he Rogers Memorial Hospital in Oconomowoc, Wisconsin	N=314; Age =15.56 (1.20); Baseline CY-BOCS Score=25.65 (5.63)	Cognitive restructuring, ERP	Adequate	CY-BOCS <16	NS	.	NS	NS	NS	.	.	.	NS	.	.	.	.
Torp, 2019, 31622874; NordLOTS, stage 1	N=248; Age =NR; Baseline CY-BOCS Score=24.6 (5.1)	ERP	Adequate	CY-BOCS <16	+	NS	NS	NS	.	.	.	.	.	NS	NS	.	.

Study; Study Name/Site	N; Age, Baseline CY-BOCS Score, Mean (SD)	Intervention, Components	Regression Quality	Outcome	Age	Age at Onset/Duration	Gender	Comorbidity	CY-BOCS (Base-line)	Insurance	Medication	Minoritized Group	Treatment	COIS (base-line)	FAS (Base-line)	Symptoms (Base-line)	Other
Selles, 2020, 31228561; UBC-POP, NordLOTS, stage 1; DCS-CBT, Griffith,	N=573; Age =12.67 (2.87); Baseline CY-BOCS Score=24.95 (5.24)	Psychoeducation, Cognitive restructuring, ERP	Adequate	35% reduction in CY-BOCS score	+	.	.	.	+	.	.	.	.		.	.	–‡
Rudy, 2014, 25193378; University of Florida OCD Program	N=78; Age =13.2 (2.72); Baseline CY-BOCS Score=NR	Psychoeducation, Cognitive restructuring, ERP	Adequate	ADIS CSR<4 and/or CY-BOCS<10	NS	.	NS	.	NS	.	.	.	.	NS	.	.	.
Farrell, 2020, 37669531; Griffith U, Queensland AU	N=63; Age =12.2 (2.8); Baseline CY-BOCS Score=25.7 (5.3)	CBT/not specified	Adequate	FAS (post-treatment score)	NS	.	NS	– (ADHD)	.	.	.	.	.	.	.	.	.
Weidle, 2015, 25527002; NordLOTS, stage 1	N=269; Age =12.8 (2.7); Baseline CY-BOCS Score=24.6 (5.1)	ERP	Inadequate	QOL: KINDL - child report (change)	.	.	.	NS	.	.	.	.	.	NS	NS	.	.
Weidle, 2015, 25527002; NordLOTS, stage 1	N=269; Age =12.8 (2.7); Baseline CY-BOCS Score=24.6 (5.1)	ERP	Inadequate	QOL: KINDL - parent report (change)	.	.	.	NS	.	.	.	.	.	NS	NS	.	.

+ = increase in predictor/predictor present predicts statistically significant increase in outcome; – = decrease in predictor/predictor present predicts statistically significant increase in outcome; NS no significant relationship; ? = significant relationship but direction unclear; CBT = cognitive behavioral therapy, COIS = Child Obsessive Compulsive Impact Scale, CY-BOCS = Children's Yale-Brown Obsessive Compulsive Scale, ERP = exposure and response therapy, FAS = family accommodation scale, OCD = Obsessive Compulsive Disorder, QOL = quality of life

Color is for emphasis only and does not convey meaning

* Not significant at post treatment; lower score predicted higher score at 6 months.

|| youth identifying as Black, Asian, other, more than one race, or Latinx Ethnicity.

† 4hr/day treatment predicted greater symptom reduction than 6hr/day.

¶ symptoms included symmetry/ordering, contamination/cleaning, sexual/religious obsessions, aggressive/checking, hoarding.

‡ Limited child recognition of impairment and greater baseline avoidance predicted reduced likelihood of achieving response to CBT.

§ Executive function: baseline LVEF high performers = lower response to CBT; baseline BRIEF = NS.

Appendix F. Appendix References

1. Sampson M, Nama N, O'Hearn K, et al. Creating enriched training sets of eligible studies for large systematic reviews: the utility of PubMed's Best Match algorithm. Int J Technol Assess Health Care. 2020 Dec 18;37:e7. doi: 10.1017/S0266462320002159. PMID: 33336640.

2. Farhat LC, Vattimo EFQ, Ramakrishnan D, et al. Systematic Review and Meta-analysis: An Empirical Approach to Defining Treatment Response and Remission in Pediatric Obsessive-Compulsive Disorder. J Am Acad Child Adolesc Psychiatry. 2022 Apr;61(4):495-507. doi: 10.1016/j.jaac.2021.05.027. PMID: 34597773.

3. Balk EM, Earley A, Patel K, et al. Empirical Assessment of Within-Arm Correlation Imputation in Trials of Continuous Outcomes Agency for Healthcare Research and Quality. Rockville, MD: 2012.

4. Huwaldt J. Plot Digitizer. 2.6.9 ed; 2020.

5. Scahill L, Riddle MA, McSwiggin-Hardin M, et al. Children's Yale-Brown Obsessive Compulsive Scale: reliability and validity. J Am Acad Child Adolesc Psychiatry. 1997 Jun;36(6):844-52. doi: 10.1097/00004583-199706000-00023. PMID: 9183141.

6. Novara C, Pardini S, Cardona F, et al. Comparing Models of the Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS) in an Italian Clinical Sample. Front Psychiatry. 2020;11:615. doi: 10.3389/fpsyt.2020.00615. PMID: 32848897.

7. Shabani MJ, Mohsenabadi H, Zanjani Z, et al. Psychometric evaluation of the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS) in Iranian clinical and non-clinical samples. Journal of Obsessive-Compulsive and Related Disorders. 2019;22. doi: 10.1016/j.jocrd.2019.100450. PMID: 2019-80248-001.

8. Stewart SE, Ceranoglu TA, O'Hanley T, et al. Performance of clinician versus self-report measures to identify obsessive-compulsive disorder in children and adolescents. J Child Adolesc Psychopharmacol. 2005 Dec;15(6):956-63. doi: 10.1089/cap.2005.15.956. PMID: 16379516.

9. Adamowska S, Adamowski T, Frydecka D, et al. Diagnostic validity Polish language version of the questionnaire MINI-KID (Mini International Neuropsychiatry Interview for Children and Adolescent). Compr Psychiatry. 2014 Oct;55(7):1744-50. doi: 10.1016/j.comppsych.2014.05.019. PMID: 25023384.

10. Fisher PW, Shaffer D, Piacentini JC, et al. Sensitivity of the Diagnostic Interview Schedule for Children, 2nd edition (DISC-2.1) for specific diagnoses of children and adolescents. J Am Acad Child Adolesc Psychiatry. 1993 May;32(3):666-73. doi: 10.1097/00004583-199305000-00026. PMID: 8496131.

11. Högberg C, Billstedt E, Björck C, et al. Diagnostic validity of the MINI-KID disorder classifications in specialized child and adolescent psychiatric outpatient clinics in Sweden. BMC Psychiatry. 2019 May 9;19(1):142. doi: 10.1186/s12888-019-2121-8. PMID: 31072319.

12. Krebs G, Liang H, Hilton K, et al. Computer-assisted assessment of obsessive-compulsive disorder in young people: A preliminary evaluation of the development and well-being assessment. Child and Adolescent Mental Health. 2012;17(4):246-51. doi: 10.1111/j.1475-3588.2012.00651.x. PMID: 2012-28430-008.

13. Sheehan DV, Sheehan KH, Shytle RD, et al. Reliability and validity of the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID). J Clin Psychiatry. 2010 Mar;71(3):313-26. doi: 10.4088/JCP.09m05305whi. PMID: 20331933.

14. Lewin AB, Park JM, Jones AM, et al. Family-based exposure and response prevention therapy for preschool-aged children with obsessive-compulsive disorder: a pilot randomized controlled trial. Behav Res Ther. 2014 May;56:30-8. doi: 10.1016/j.brat.2014.02.001. PMID: 24657310.

15. Storch EA, Geffken GR, Merlo LJ, et al. Family-based cognitive-behavioral therapy for pediatric obsessive-compulsive disorder: comparison of intensive and weekly approaches. J Am Acad Child Adolesc Psychiatry. 2007 Apr;46(4):469-78. doi: 10.1097/chi.0b013e31803062e7. PMID: 17420681.

16. Selles RR, Naqqash Z, Best JR, et al. Effects of Treatment Setting on Outcomes of Flexibly-Dosed Intensive Cognitive Behavioral Therapy for Pediatric OCD: A Randomized Controlled Pilot Trial. Front Psychiatry. 2021;12:669494. doi: 10.3389/fpsyt.2021.669494. PMID: 34079488.

17. Rosa-Alcázar Á, Rosa-Alcázar AI, Olivares-Olivares PJ, et al. Family involvement and treatment for young children with Obsessive-Compulsive Disorder: Randomized control study. Int J Clin Health Psychol. 2019 Sep;19(3):218-27. doi: 10.1016/j.ijchp.2019.06.001. PMID: 31516500.

18. Merlo LJ, Storch EA, Lehmkuhl HD, et al. Cognitive behavioral therapy plus motivational interviewing improves outcome for pediatric obsessive-compulsive disorder: a preliminary study. Cogn Behav Ther. 2010;39(1):24-7. doi: 10.1080/16506070902831773. PMID: 19675960.

19. Tuerk PW, McGuire JF, Piacentini J. A Randomized Controlled Trial of OC-Go for Childhood Obsessive–Compulsive Disorder: Augmenting Homework Compliance in Exposure With Response Prevention Treatment. Behavior Therapy. 2023. PMID: 38418042.

20. Wolters LH, Hagen A, Beek VOD, et al. Effectiveness of an online interpretation training as a pre-treatment for cognitive behavioral therapy for obsessive-compulsive disorder in youth: a randomized controlled trial. Journal of obsessive-compulsive and related disorders. 2021;29. doi: 10.1016/j.jocrd.2021.100636. PMID: CN-02248290.

21. Rezvan S, Bahrami F, Abedi M, et al. A Preliminary Study on the Effects of Attachment-based Intervention on Pediatric Obsessive-Compulsive Disorder. Int J Prev Med. 2013 Jan;4(1):78-87. PMID: 23413047.

22. Salemink E, Wolters L, de Haan E. Augmentation of Treatment As Usual with online Cognitive Bias Modification of Interpretation training in adolescents with Obsessive Compulsive Disorder: A pilot study. J Behav Ther Exp Psychiatry. 2015 Dec;49(Pt A):112-9. doi: 10.1016/j.jbtep.2015.02.003. PMID: 25724385.

23. Nasiry S, Ameli Z, Pezeshki P. Online cognitive bias modification of interpretation for children with obsessive-compulsive disorder. Journal of Practice in Clinical Psychology. 2020 Aut 2020;8(4):325-34. doi: 10.32598/jpcp.8.4.739.1. PMID: 2021-41311-008.

24. Rempel S, Backhausen LL, McDonald M, et al. App-Based Mindfulness Meditation Training and an Audiobook Intervention Reduce Symptom Severity but Do Not Modify Backward Inhibition in Adolescent Obsessive-Compulsive Disorder: Evidence from an EEG Study. J Clin Med. 2023 Mar 24;12(7). doi: 10.3390/jcm12072486. PMID: 37048570.

25. Leonard HL, Swedo SE, Rapoport JL, et al. Treatment of obsessive-compulsive disorder with clomipramine and desipramine in children and adolescents. A double-blind crossover comparison. Arch Gen Psychiatry. 1989 Dec;46(12):1088-92. doi: 10.1001/archpsyc.1989.01810120030006. PMID: 2686576.

26. Alaghband-Rad J, Hakimshooshtary M. A randomized controlled clinical trial of citalopram versus fluoxetine in children and adolescents with obsessive-compulsive disorder (OCD). Eur Child Adolesc Psychiatry. 2009 Mar;18(3):131-5. doi: 10.1007/s00787-007-0634-z. PMID: 19190958.

27. Li F, Welling MC, Johnson JA, et al. N-Acetylcysteine for Pediatric Obsessive-Compulsive Disorder: A Small Pilot Study. J Child Adolesc Psychopharmacol. 2020 Feb;30(1):32-7. doi: 10.1089/cap.2019.0041. PMID: 31800306.

28. Ghanizadeh A, Mohammadi MR, Bahraini S, et al. Efficacy of N-Acetylcysteine Augmentation on Obsessive Compulsive Disorder: A Multicenter Randomized Double Blind Placebo Controlled Clinical Trial. Iran J Psychiatry. 2017 Apr;12(2):134-41. PMID: 28659986.

29. Noras MR, Soltanifar A, Salari R, et al. Comparing the Effects of a Herbal Drug based on Echium Amoenum With Fluvoxamine in the Treatment of Adolescents with Obsessive-compulsive Disorder. Curr Drug Discov Technol. 2022;19(5):e240622206368. doi: 10.2174/1570163819666220624093416. PMID: 35748547.

30. Grant PJ, Joseph LA, Farmer CA, et al. 12-week, placebo-controlled trial of add-on riluzole in the treatment of childhood-onset obsessive-compulsive disorder. Neuropsychopharmacology. 2014 May;39(6):1453-9. doi: 10.1038/npp.2013.343. PMID: 24356715.

31. Liu Y. Randomized controlled trial of fl uvoxoxamine combining with risperidone

in the treatment of children and adolescents with obsessive-compulsive disorder. China Journal of Health Psychology. 2012;20(10):1460-1. PMID: Liu-2012_SR-37347947.

32. Agrawal A, Agarwal V, Kumar Kar S, et al. Transcranial direct current stimulation as early augmentation in adolescent obsessive compulsive disorder: A pilot proof-of-concept randomized control trial. World Journal of Clinical Pediatrics,. 2024;13(2). doi: 10.5409/wjcp.v13.i2.93138. PMID: CN-02530420.

33. Bolton D, Williams T, Perrin S, et al. Randomized controlled trial of full and brief cognitive-behaviour therapy and wait-list for paediatric obsessive-compulsive disorder. J Child Psychol Psychiatry. 2011 Dec;52(12):1269-78. doi: 10.1111/j.1469-7610.2011.02419.x. PMID: 21644984.

34. Franklin ME, Sapyta J, Freeman JB, et al. Cognitive behavior therapy augmentation of pharmacotherapy in pediatric obsessive-compulsive disorder: the Pediatric OCD Treatment Study II (POTS II) randomized controlled trial. Jama. 2011 Sep 21;306(11):1224-32. doi: 10.1001/jama.2011.1344. PMID: 21934055.

35. Shabani MJ, Mohsenabadi H, Omidi A, et al. An Iranian study of group acceptance and commitment therapy versus group cognitive behavioral therapy for adolescents with obsessive-compulsive disorder on an optimal dose of selective serotonin reuptake inhibitors. Journal of obsessive-compulsive and related disorders. 2019;22. doi: 10.1016/j.jocrd.2019.04.003. PMID: CN-02003764.

36. Freeman J, Sapyta J, Garcia A, et al. Family-based treatment of early childhood obsessive-compulsive disorder: the Pediatric Obsessive-Compulsive Disorder Treatment Study for Young Children (POTS Jr)--a randomized clinical trial. JAMA Psychiatry. 2014 Jun;71(6):689-98. doi: 10.1001/jamapsychiatry.2014.170. PMID: 24759852.

37. Hollmann K, Hohnecker CS, Haigis A, et al. Internet-based cognitive behavioral therapy in children and adolescents with obsessive-compulsive disorder: A randomized controlled trial. Front Psychiatry. 2022;13:989550. doi: 10.3389/fpsyt.2022.989550. PMID: 36329915.

38. Storch EA, Caporino NE, Morgan JR, et al. Preliminary investigation of web-camera delivered cognitive-behavioral therapy for youth with obsessive-compulsive disorder. Psychiatry Res. 2011 Oct 30;189(3):407-12. doi: 10.1016/j.psychres.2011.05.047. PMID: 21684018.

39. Aspvall K, Andersson E, Melin K, et al. Effect of an Internet-Delivered Stepped-Care Program vs In-Person Cognitive Behavioral Therapy on Obsessive-Compulsive Disorder Symptoms in Children and Adolescents: A Randomized Clinical Trial. Jama. 2021 May 11;325(18):1863-73. doi: 10.1001/jama.2021.3839. PMID: 33974020.

40. Comer JS, Furr JM, Kerns CE, et al. Internet-delivered, family-based treatment for early-onset OCD: A pilot randomized trial. J Consult Clin Psychol. 2017 Feb;85(2):178-86. doi: 10.1037/ccp0000155. PMID: 27869451.

41. Asbahr FR, Castillo AR, Ito LM, et al. Group cognitive-behavioral therapy versus sertraline for the treatment of children and adolescents with obsessive-compulsive disorder. J Am Acad Child Adolesc Psychiatry. 2005 Nov;44(11):1128-36. doi: 10.1097/01.chi.0000177324.40005.6f. PMID: 16239861.

42. Neziroglu F, Yaryura-Tobias JA, Walz J, et al. The effect of fluvoxamine and behavior therapy on children and adolescents with obsessive-compulsive disorder. J Child Adolesc Psychopharmacol. 2000 Winter;10(4):295-306. doi: 10.1089/cap.2000.10.295. PMID: 11191690.

43. Geller DA, Hoog SL, Heiligenstein JH, et al. Fluoxetine treatment for obsessive-compulsive disorder in children and adolescents: a placebo-controlled clinical trial. J Am Acad Child Adolesc Psychiatry. 2001 Jul;40(7):773-9. doi: 10.1097/00004583-200107000-00011. PMID: 11437015.

44. Liebowitz MR, Turner SM, Piacentini J, et al. Fluoxetine in children and adolescents with OCD: a placebo-controlled trial. J Am Acad Child Adolesc Psychiatry. 2002 Dec;41(12):1431-8. doi: 10.1097/00004583-200212000-00014. PMID: 12447029.

45. March JS, Biederman J, Wolkow R, et al. Sertraline in children and adolescents with obsessive-compulsive disorder: a multicenter randomized controlled trial. Jama. 1998 Nov 25;280(20):1752-6. doi: 10.1001/jama.280.20.1752. PMID: 9842950.

46. Riddle MA, Scahill L, King RA, et al. Double-blind, crossover trial of fluoxetine and placebo in children and adolescents with obsessive-compulsive disorder. J Am Acad Child Adolesc Psychiatry. 1992 Nov;31(6):1062-9. doi: 10.1097/00004583-199211000-00011. PMID: 1429406.

47. Farrell LJ, Waters AM, Boschen MJ, et al. Difficult-to-treat pediatric obsessive-compulsive disorder: feasibility and preliminary results of a randomized pilot trial of D-cycloserine-augmented behavior therapy. Depress Anxiety. 2013 Aug;30(8):723-31. doi: 10.1002/da.22132. PMID: 23722990.

48. Storch EA, Murphy TK, Goodman WK, et al. A preliminary study of D-cycloserine augmentation of cognitive-behavioral therapy in pediatric obsessive-compulsive disorder. Biol Psychiatry. 2010 Dec 1;68(11):1073-6. doi: 10.1016/j.biopsych.2010.07.015. PMID: 20817153.

49. Storch EA, Wilhelm S, Sprich S, et al. Efficacy of Augmentation of Cognitive Behavior Therapy With Weight-Adjusted d-Cycloserine vs Placebo in Pediatric Obsessive-Compulsive Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2016 Aug 1;73(8):779-88. doi: 10.1001/jamapsychiatry.2016.1128. PMID: 27367832.

50. Storch EA, Bussing R, Small BJ, et al. Randomized, placebo-controlled trial of cognitive-behavioral therapy alone or combined with sertraline in the treatment of pediatric obsessive-compulsive disorder. Behav Res Ther. 2013 Dec;51(12):823-9. doi: 10.1016/j.brat.2013.09.007. PMID: 24184429.

51. Farrell LJ, Waters AM, Tiralongo E, et al. Efficacy of D-cycloserine augmented brief intensive cognitive-behavioural therapy for paediatric obsessive-compulsive disorder: A randomised clinical trial. Depress Anxiety. 2022 Jun;39(6):461-73. doi: 10.1002/da.23242. PMID: 35084071.

52. Peris TS, Rozenman MS, Sugar CA, et al. Targeted Family Intervention for Complex Cases of Pediatric Obsessive-Compulsive Disorder: A Randomized Controlled Trial. J Am Acad Child Adolesc Psychiatry. 2017 Dec;56(12):1034-42.e1. doi: 10.1016/j.jaac.2017.10.008. PMID: 29173737.

53. Piacentini J, Bergman RL, Chang S, et al. Controlled comparison of family cognitive behavioral therapy and psychoeducation/relaxation training for child obsessive-compulsive disorder. J Am Acad Child Adolesc Psychiatry. 2011 Nov;50(11):1149-61. doi: 10.1016/j.jaac.2011.08.003. PMID: 22024003.

54. Lebowitz ER. Treatment of extreme family accommodation in a youth with obsessive-compulsive disorder. Clinical handbook of obsessive-compulsive and related disorders: A case-based approach to treating pediatric and adult populations. 2016:321-35.

55. Barrett P, Healy-Farrell L, March JS. Cognitive-behavioral family treatment of childhood obsessive-compulsive disorder: a controlled trial. J Am Acad Child Adolesc Psychiatry. 2004 Jan;43(1):46-62. doi: 10.1097/00004583-200401000-00014. PMID: 14691360.

56. Lenhard F, Andersson E, Mataix-Cols D, et al. Therapist-Guided, Internet-Delivered Cognitive-Behavioral Therapy for Adolescents With Obsessive-Compulsive Disorder: A Randomized Controlled Trial. J Am Acad Child Adolesc Psychiatry. 2017 Jan;56(1):10-9.e2. doi: 10.1016/j.jaac.2016.09.515. PMID: 27993223.

57. Peris TS, Piacentini J. Optimizing treatment for complex cases of childhood obsessive compulsive disorder: a preliminary trial. J Clin Child Adolesc Psychol. 2013;42(1):1-8. doi: 10.1080/15374416.2012.673162. PMID: 22548378.

58. Schuberth DA, McMahon RJ, Best JR, et al. Parent Management Training Augmentation to Address Coercive and Disruptive Behavior in Cognitive-Behavioral Therapy for Pediatric Obsessive-Compulsive Disorder. Child Psychiatry Hum Dev. 2023 May 20. doi: 10.1007/s10578-023-01543-8. PMID: 37209194.

59. Rosa-Alcázar AI, Iniesta-Sepúlveda M, Storch EA, et al. A preliminary study of cognitive-behavioral family-based treatment versus parent training for young children with obsessive-compulsive disorder. J Affect Disord. 2017 Jan 15;208:265-71. doi: 10.1016/j.jad.2016.09.060. PMID: 27792972.

60. Franklin ME, Engelmann JM, Bulkes NZ, et al. Intensive Cognitive-Behavioral Therapy Telehealth for Pediatric Obsessive-Compulsive Disorder During the COVID-19 Pandemic: Comparison With a Matched Sample Treated in Person. JAACAP Open. 2023. doi: 10.1016/j.jaacop.2023.09.007. PMID: Franklin-2023_adhoc_TEP.

61. Geller DA, Biederman J, Stewart SE, et al. Impact of comorbidity on treatment response to paroxetine in pediatric obsessive-compulsive disorder: is the use of exclusion criteria empirically supported in randomized clinical trials? J Child Adolesc Psychopharmacol. 2003;13 Suppl 1:S19-29. doi: 10.1089/104454603322126313. PMID: 12880497.

62. Geller DA, Wagner KD, Emslie G, et al. Paroxetine treatment in children and adolescents with obsessive-compulsive disorder: a randomized, multicenter, double-blind, placebo-controlled trial. J Am Acad Child Adolesc Psychiatry. 2004 Nov;43(11):1387-96. doi: 10.1097/01.chi.0000138356.29099.f1. PMID: 15502598.

63. POTS Team. Cognitive-behavior therapy, sertraline, and their combination for children and adolescents with obsessive-compulsive disorder: the Pediatric OCD Treatment Study (POTS) randomized controlled trial. Jama. 2004 Oct 27;292(16):1969-76. doi: 10.1001/jama.292.16.1969. PMID: 15507582.

64. He Y. Control Study of Fluvoxamine and Chlormipramine in Treatment of Child-Adolescence Obsession. Medical Journal of Chinese People's Health. 2007;19(6):438-40. PMID: He-2007_SR-35121274.

65. Mataix-Cols D, Turner C, Monzani B, et al. Cognitive-behavioural therapy with post-session D-cycloserine augmentation for paediatric obsessive-compulsive disorder: pilot randomised controlled trial. Br J Psychiatry. 2014 Jan;204(1):77-8. doi: 10.1192/bjp.bp.113.126284. PMID: 24262813.

66. Nai X. A comparative study of sertraline and clomipramine in the treatment of children obsessive-compulsive disorder. Chinese Journal of Practical Nervous Diseases 2009;12(20):10-1. PMID: Nai-2009_SR-35121274.

67. Wolters LH, Ball J, Brezinka V, et al. Brief intensive cognitive behavioral therapy for children and adolescents with OCD: Two international pilot studies. Journal of Obsessive-Compulsive and Related Disorders. 2021;29:1-7. doi: 10.1016/j.jocrd.2021.100645. PMID: 2022-96874-001.

68. Skarphedinsson G, Weidle B, Thomsen PH, et al. Continued cognitive-behavior therapy versus sertraline for children and adolescents with obsessive-compulsive disorder that were non-responders to cognitive-behavior therapy: a randomized controlled trial. Eur Child Adolesc Psychiatry. 2015 May;24(5):591-602. doi: 10.1007/s00787-014-0613-0. PMID: 25239489.

Appendix G. Key Question 1 Full Extractions

The Excel file is located at https://effectivehealthcare.ahrq.gov/products/obsessive-compulsive-disorder/research.

Appendix H. Key Question 2 Predictors

The Excel file is located at https://effectivehealthcare.ahrq.gov/products/obsessive-compulsive-disorder/research.