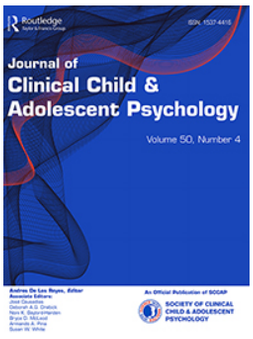

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Moderators of Psychosocial Treatment for Pediatric Obsessive-Compulsive Disorder: Summary and Recommendations for Future Directions

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ABSTRACT

This brief report examines the evidence for moderators of psychosocial treatment for youth with obsessive-compulsive disorder (OCD). Understanding treatment moderators can help clinicians select the most appropriate intervention for a particular patient and consequently increase the likelihood of initial response. A systematic search of the literature was conducted to identify randomized trials and meta-analyses reporting on moderators of psychosocial treatment for pediatric OCD. All studies included a comparison of cognitive-behavioral therapy (CBT) to active or control conditions. Few studies have evaluated moderators of psychosocial treatment for youth with OCD, and among those studies, few variables have demonstrated a differential effect on treatment response. Moderator analyses require large samples to garner the statistical power necessary to adequately evaluate differential responding in subgroups, and unfortunately, most reports of moderators in this review are post-hoc investigations of datasets from trials with relatively small sample sizes. Given the overwhelming number of CBT treatment variants and potential moderators, it would be impossible to conduct all the necessary head-to-head trials with sufficient sample sizes to develop helpful clinical guidelines. The best option for advancing the moderator literature is to utilize advanced statistical approaches for pooling existing data sets. Recommendations for leveraging emerging techniques in individual participant data meta-analysis (IPD-MA) are briefly discussed.

Reviews and meta-analyses have consistently found cognitive-behavioral therapy (CBT) to be the most efficacious treatment for pediatric obsessive-compulsive disorder (OCD) (Freeman et al., 2018, 2014; Öst et al., 2016). Despite being the frontline treatment for pediatric OCD, CBT is not a panacea and the rate of symptom remission is only about 40% following a full course of treatment (Pediatric OCD Treatment Study Team [POTS], 2004). As a result, researchers have tested a number of differing CBT formats (e.g., individual, group, family, technology-based) and augmentation strategies (e.g., SRI medication, DCS), but little is known about the differential efficacy of these CBT variants based on patient characteristics. Identifying "what works best for whom" has been identified as the next important step in the pediatric OCD treatment literature (Freeman et al., 2018, 2014). Exploring treatment moderators can help clinicians select the most appropriate intervention for a particular patient, and increase the likelihood of initial response. The goal of this brief report is to summarize the existing moderator evidence for common pediatric OCD treatments and to provide guidance for further exploring factors associated with differential responding. The focus of this report is on psychosocial intervention, specifically CBT and its variants, but medication is the most common active comparator in past clinical trials and will be discussed to the extent that it is part of the comparative evidence for CBT.

A comprehensive synthesis of the evidence base for pediatric OCD treatment was first assembled by Barrett et al. (2008) and has been updated twice (Freeman et al., 2018, 2014). Based on consistent differences in the content and focus of CBT interventions in their sample of trials, Barrett and colleagues elected to categorize the CBT interventions by individual, group, or family-focused format. Additional changes to the categorization of CBT by delivery method, augmentation strategy, and central research question were made in each of the subsequent reviews (Freeman et al., 2018, 2014). This evolution in organizing strategy is an indication of the persistent splintering of CBT into many variants. Unfortunately, the proliferation of these new interventions has far outpaced

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the evidence to clarify their differential effects and guide clinical decision-making.

Working toward Personalized Treatment

While predictors establish who is more or less likely to respond to treatment in general, moderators delineate who is likely to have a differential response to a particular treatment (Kraemer et al., 2006). Ideally, information about predictors and moderators could be used to build clinical decision-making tools to select the most appropriate treatment for a given patient. Not only could evidence for predictors and moderators enhance the likelihood of positive initial responding, but it could help prevent the use of unhelpful or even harmful interventions with certain subpopulations. Before such tools can be realized there must be a comprehensive set of validated predictors and moderators to inform the decision process. The focus of this report is on the evidence for moderator variables. The literature was reviewed for both individual studies and meta-analyses investigating moderators of treatment response to CBT for pediatric OCD.

Search Strategy

PsychINFO and PubMed were searched from the start of the database to April 1st 2020 with the following search terms: (Obsessive-compulsive Disorder OR OCD) AND (Child OR Children OR Adolescents OR teenager OR youth) AND (Moderator OR Moderators OR Moderating effect). A hand search of Google Scholar and the reference sections of relevant systematic reviews were also conducted. The search yielded a total of 147 abstracts, which was reduced to 106 after duplicates were removed. Clinical trials were included if they (1) involved a randomized controlled treatment trial (RCT) for youth (<18 years) with a primary OCD diagnosis, (2) tested a CBT treatment arm against an active comparator, and (3) included moderator analyses. Meta-analyses were included if they evaluated the efficacy of a CBT treatment arm against controls, and (2) reported moderator analyses. The search yielded a total of nine clinical trials and six meta-analyses.

Below is a summary of existing evidence on moderators of CBT for pediatric OCD. The current report builds on a recent comprehensive review of treatment moderators in CBT for pediatric OCD by Turner et al. (2018). This report expands on findings from Turner et al. by including four additional RCTs, reviewing moderator analyses in recent meta-analyses, and providing guidance on strategies for leveraging modern statistics and methodologies to evaluate treatment moderators by optimizing the use of existing datasets. Moderator variable is organized into four major categories (Demographics, Symptoms and Impairment, Comorbidity, and Family Factors), and relevant findings from individual RCTs and meta-analyses are briefly summarized. Additional details about each RCT and meta-analysis are presented in Tables 1 and 2, respectively.

Patient Demographics

Individual Trials

Age and gender have been the most researched moderator variables in CBT trials, but all trials have failed to detect a significant difference across comparators. A noted limitation of the moderator literature has been a lack of focus on ethnicity and race, which is driven by a lack of diversity in past OCD treatment trials. However, recent findings from a comparison of standard family-based CBT and an enhanced version of family-based CBT which placed added focus on family discord found that individuals coded as meeting racial or ethnic minority status (based on the U.S. Census Standards for Race and Ethnicity) demonstrated significantly more symptom reduction in the enhanced family-based CBT condition (Peris et al., 2020).

Meta-analyses

Few demographic variables were evaluated with consistency across meta-analyses. The most commonly tested variable was patient age, which yielded a non-significant relationship with effect size in all but one report (Öst et al., 2016). Öst and colleagues found that the effect of CBT increased with younger patient age; however, in a secondary analysis, they removed three studies that enrolled a subset of the youngest participants (ages 3–8) and found that the effect of age on outcome was no longer significant in the remaining sample. Of note, the three studies that were removed in the secondary analysis (Freeman et al., 2008, 2014; Lewin et al., 2014) tested variants of CBT with especially high levels of family involvement. It is possible the age-related effect is attributable to differences in treatment approach (i.e., high family involvement); it is also possible that other developmental or cognitive factors (e.g., increased neuroplasticity) are responsible. All other demographic variables, including gender, previous treatment, and medication status failed to demonstrate a significant effect on treatment efficacy.

Symptoms and Impairment

Individual Trials

Several variables related to symptom severity and functional impairment have been investigated as treatment moderators; however, none of these variables have demonstrated differential effects in trials comparing CBT to such

Table 1. Results of individual RCTs evaluating moderators of psychosocial treatment efficacy.

			Moderator Categories			
Study	Comparators	Sig/ NS	Demographics	Symptoms nd Impairment	Comorbidity	Family Factors
Barrett et al. (2004)	CBT, G-CBT	**Sig**	–	–	–	–
		NS	Age, Med Status (Yes/No)	–	–	–
March et al. (2007) [POTS I]	CBT, COMB, SRT, PBO	**Sig**	–	–	**Tics (ADIS)**: COMB > CBT > SRT = PBO	–
		NS	–	–	–	–
Garcia et al. (2010) [POTS I]	CBT, COMB, SRT, PBO	**Sig**	–	–	–	**Family History of OCD**: Effect was 6.5 times smaller in CBT monotherapy for those with a family history of OCD
		NS	Age, Gender, Income	Baseline OCD Severity (CY-BOCS), Functional Impairment (COIS-C/P), Insight (FBQ)	Internalizing conditions (ADIS), Externalizing conditions (ADIS), Anxiety symptoms (MASC)	Parent Psychopathology (BSI), Family functioning (FAM-III), Accommodation (FAS-PR)
Bolton et al. (2011)	CBT, Brief CBT	**Sig**	–	–	–	–
		NS	Age	–	–	–
Conelea et al. (2014) [POTS II]	MM, MM +CBT, MM +CBT info	**Sig**	–	–	–	–
		NS	–	–	Tics (YGTSS)	–
Skarphedinsson et al. (2014)	Cont'd CBT, SRT	**Sig**	–	–	**Tics (K-SADS-PL)**: SRT > Cont'd CBT	–
		NS	–	–	–	–
Wilhelm et al. (2018)	CBT+DCS, CBT+PBO	**Sig**	–	–	–	–
		NS	Age, Gender	–	Tics (K-SADS-PL), Anxiety Symptoms (K-SADS-PL), Mood Symptoms (K-SADS-PL)	–
Nair et al. (2019)	CBT, TeleCBT	**Sig**	–	–	**Interpersonal difficulties (SDQ-peer problems)**: TeleCBT = more effective with more peer problems	–
		NS	Age, Gender	Baseline OCD Severity (CY-BOCS), Age of Onset (Continuous-months)	Internalizing conditions (SDQ-emotion), Externalizing conditions (SDQ-behavior), Mood Symptoms (BDI-Y), ADHD (SDQ-hyperactivity)	Parent Psychopathology (DASS), Family History of OCD (Yes/No biological relative), Accommodation (FAS-PR)
Peris et al. (2020)	FCBT, Enhanced FCBT	**Sig**	**Minority Status**: Enhanced > FCBT among minority youth	–	–	–
		NS	Age, Gender	Impairment (COIS-R)	–	Parental Psychopathology (BSI), Family Environment (FES-cohesion, conflict), Accommodation (FAS)

ADIS = Anxiety Disorders Interview Schedule; BDI-Y = Beck Depression Inventory – Youth; BriefCBT = 5 instead of 12 weeks of therapist contact; BSI = Brief Symptom Inventory; CBT = Individual format; COMB = CBT+Sertraline; COIS – C/P = Child OCD Impact Scale – Child and Parent report; Cont'd CBT = ongoing individual format despite initial non-response; CY-BOCS = Children's Yale-Brown Obsessive Compulsive Scale; DASS = Depression Anxiety Stress Scale; FAM-III = Family Assessment Measure – Third Edition; FAS-PR = Family Accommodation Scale-Parent Report; FBQ = Fixity of Beliefs Questionnaire; FCBT = Family-based CBT; G-CBT = Group format; MASC = Multidimensional Anxiety Scale; PBO = Pill Placebo; SRT = Sertraline; *SDQ* = Strengths and Difficulties Questionnaire – Parent Report; TeleCBT = Services delivered via telephone; YGTSS = Yale Global Tic Severity Scale

active comparators as medication-alone, combined CBT and medication, or telephone-delivered CBT (Garcia et al., 2010; Nair et al., 2019). The early and consistent finding that individuals with more severe symptoms do not respond as well (or as quickly) to CBT alone led to the recommendation that CBT be combined with SRI medication as the clinical standard for patients presenting with moderate to severe symptoms (Geller & March, 2012); however, this practice recommendation has not been supported in subsequent empirical evaluations (Ivarsson et al., 2015; Öst et al., 2016).

Meta-analyses

Only two reports investigated the influence of symptoms severity or impairment on treatment efficacy, and both tested the same variable: baseline OCD severity (McGuire et al., 2015; Öst et al., 2016). Neither meta-analysis detected a significant effect of baseline OCD symptoms on the efficacy of CBT.

Comorbidity

Individual Trials

Among the many comorbid conditions assessed, only the presence of tics has received support for a differential effect on treatment response. Based on data from the first POTS trial, March et al. (2007) found CBT remained effective among individuals with tics, but Sertraline monotherapy was no more effective than placebo. Tic status has also been evaluated as a moderator of

Table 2. Results of meta-analyses evaluating moderators of psychosocial treatment efficacy.

Study *Goals*	Sample and Comparisons	Sig/ NS	Moderators Patient Variables	Moderators Treatment Variables
Sanchez-Meca et al. (2014) *Examine efficacy of CBT, Med, and Combo*	RCTs only CBT vs Control	**Sig** NS	– *Demographics* – Age, Gender, Any previous treatment	**Study protocol, Total treatment hours (+)** Inclusion of ERP, Parental involvement, Treatment focus (Child vs Family), Weeks of treatment, Hours per week, Rate of attrition, type of control comparator
Rosa-Alcazar et al. (2015) *Compare efficacy of differing CBT techniques*	RCTs and UCTs CBT vs pooled control	**Sig** NS	– *Demographics* **–** Age, Gender, Age of onset, Any previous treatment (≥ 50% of study sample) *Comorbidity* **–** Presence of comorbidity (≥ 50% sample with comorbidity)	**Relapse prevention, Parental Involvement (+), Study protocol** Inclusion of ERP, Cognitive Restructuring, Behavioral Experiments, Problem Solving, Treatment focus (Child vs Family), Treatment mode (Ind, Group, Mix), Weeks of treatment, Hours per week, Total hours, Rate of attrition
McGuire et al. (2015) *Examine efficacy of CBT and medication*	RCTs only CBT vs Control	**Sig** NS	***Comorbidity* – % Co-occurring anxiety disorders (+)†, % Tics (+)‡** *Demographics* – Age, % on Medication*Symptoms & Impairment* – Baseline OCD symptoms*Comorbidity* – % ADHD, % Depressive disorders	**Total hours (+)†, Attrition rate (-)†** Emphasis of ERP vs CT
Öst et al. (2016) *Examine efficacy of CBT and medication*	RCTs only CBT vs Active Treatment or Control	**Sig** NS	***Demographics* – Age (-)**, ***Symptom Severity & Impairment* – Baseline OCD severity (-)** ***Comorbidity* – Anxiety comorbidity (+)** Gender, % any comorbidity, % on Medication	**Type of control**: higher ES for passive control relative to active control Treatment format, Parental involvement
Iniesta-Sepulveda et al. (2017) *Examine efficacy of cognitive-behavioral family treatment*	RCTs and UCTs CBT vs pooled control	**Sig** NS	***Comorbidity* – % Autism spectrum disorders (-)** *Demographics* – Age, gender, ethnicity, years with OCD, previous treatment *Comorbidity* – % with 2 or more comorbid conditions, anxiety disorders, depressive disorders, ADHD, Tics, Conduct disorders, Eating disorders	**Treatment mode (Individual > Group)** Treatment technique, Family involvement, Treatment protocol, Treatment duration (Weeks), Treatment intensity (Weekly hours)
McGrath and Abbott (2019) *Efficacy of parent involvement techniques*	RCTs and UCTs CBT vs pooled control	**Sig** NS	– –	– Hours of family intervention, Hours of parent-only intervention, Number of family factors targeted in treatment[a]

(±) = direction of relationship with effect size; † Non-active control; ‡ Active control; [a] = Family factors demonstrated a significant effect on accommodation but not symptom reduction; RCT = Randomized Controlled Trial, UCT = Uncontrolled Trial

outcome among patients who failed to respond to an initial course of CBT (Skarphedinsson et al., 2014). In this sample, the initiation of medication led to better responding among those with tics than did continued CBT. Using POTS II data, Conelea et al. (2014) also evaluated tics as a moderator of outcome in a sample of medication refractory patients and found no support for a differential response to continued medication management (MM), MM+CBT, or MM+ information about CBT provided by their prescriber. In all, the evidence for tics as a moderator of responding to CBT relative to sertraline has yielded mixed findings, which are difficult to reconcile in light of key differences in sample characteristics and the measurement of tics across studies (see Table 1 for details). Another symptom variable that has demonstrated a statistically significant differential effect on treatments is the presence of peer problems among individuals randomized to in-person versus telephone-delivered CBT (Nair et al., 2019). Specifically, more parent-reported peer problems at baseline were associated with more symptom reduction in the teleCBT group, whereas peer problems were not associated with response in the face-to-face condition.

Meta-analyses

In most instances, meta-analyses have approached comorbidity as a single categorical variable of either present or absent in a study based on percentage of participants with comorbidity (>50%). All reports that used a single categorical variable for comorbidity failed to detect a significant effect of comorbidity on treatment efficacy. There were three studies that evaluated specific diagnostic categories, two of which found that the percentage of patients with a co-occurring anxiety diagnosis was positively associated with treatment efficacy (McGuire et al., 2015; Öst et al., 2016). There was some support for the increased efficacy of CBT with an increase in the percentage of individuals with tics (McGuire et al., 2015), and a decrease in the efficacy of CBT with an increase in the percentage of individuals with Autism Spectrum Disorders (ASD) (Iniesta-Sepúlveda et al., 2017).

Family Factors

Individual Trials

Although several family factors have been evaluated as potential moderators of treatment, only the presence of

OCD in a first-degree relative has demonstrated a significant differential effect on treatment responding. In a secondary analysis of POTS I data, Garcia et al. (2010) found a six-fold reduction in effect size for CBT when individuals had a family history of OCD, such that CBT alone was no longer efficacious for this group whereas CBT+sertraline remained efficacious. However, the presence of OCD in a relative was not a significant moderator of outcome in a comparison of two forms of CBT that differed by delivery format (i.e., face-to-face and telephone-delivered CBT; Nair et al., 2019).

Meta-analyses

No meta-analysis reported on parent and family variables at the level of sample characteristics, but most reported on parent and family involvement at the treatment level. Only one out of the five studies that evaluated the relationship between parent involvement and efficacy found a significant effect (Rosa-Alcázar et al., 2015), which indicated increased parental involvement was associated with increased treatment efficacy. McGrath and Abbott (2019) took a closer look at specific family intervention strategies employed across family-focused CBT packages. Treatments were coded based on whether they targeted each of the following factors: family accommodation, problem-solving skills, conflict, blame/criticism, and communication. They found that the number of factors targeted by a treatment was related to reductions in family accommodation but was not related to treatment efficacy.

Summary of Treatment Moderators

Clinical Implications

Few studies have reported moderators of treatment for pediatric OCD, and among these studies, only a narrow range of treatment options have been compared. Additionally, there are marked between-trial differences in sample characteristics (e.g., responder status, range of included age, race, and ethnicity) that complicate the generalizability of the findings. The most frequently tested comparators were CBT and Sertraline, either alone or in combination; these findings have come from only two study samples (Pediatric OCD Treatment Study Team (POTS), 2004; Torp et al., 2015). The analyses of moderator variables have yielded little evidence of differential responding among these comparators. Much less is known about moderators among variants of CBT format and delivery approach. The limited moderator literature makes it difficult to draw any evidence-based decisions about how to augment or individualize CBT based on patient characteristics. Evidence from individual trials yielded preliminary support for the moderating effects of four variables: minority status, peer dynamics, comorbid tics, and presence of OCD in a first-degree relative. Meta-analytic reports rarely evaluate specific categories of comorbid conditions, and did not evaluate family variables at the level of sample characteristics; consequently, meta-analytic findings did not converge on the same set of moderator variables identified in the individual trial literature. Meta-analytic findings provide additional clinical information from the inclusion of treatment-level variables in their moderation analyses. In sum, the meta-analytic literature provided mixed support for patient age, the presence of comorbid anxiety disorders, treatment mode (individual vs. group), and total hours of treatment as moderators of CBT efficacy. While several reports investigated the influence of specific treatment components (ERP and CT) and family involvement on treatment efficacy, the relationship consistently failed to reach statistical significance.

Future investigations of psychosocial treatment moderators for pediatric OCD should consider variables with support as treatment predictors that have yet to be evaluated as moderators. Evaluating specific OCD symptom domains, functional impairment, and the presence of such family factors as family conflict, blame, cohesion, communication, and parental distress tolerance are all candidates for future moderator analyses. Recent findings also support neurocognitive variables such as executive functioning as predictors of outcome (Flessner et al., 2010; Hybel et al., 2017), and there is emerging evidence for learning variables (i.e., fear extinction learning (Geller et al., 2019)) and treatment process variables such as homework completion as predictors of CBT outcome as well (Olatunji et al., 2015).

Limitations of the Moderator Literature and Next Steps

Moderator studies are challenging with this population, the low base rate of OCD has led to smaller sample sizes in existing RCTs, which are often too small to test moderation with adequate power. The main issues with the methodology of current moderator studies include the post-hoc, exploratory design of most investigations, small cell sizes in some analyses (i.e., presence of tic disorder), lack of reporting effect sizes for non-significant interactions, and confounding with sample characteristics and treatment approach. It is not surprising, given these limitations, that few treatment modifiers have been identified. The sample characteristics and exclusion criteria from the past trials pose unique limitations on the generalizability of moderator findings. Specifically, past trials have primarily consisted of non-

Hispanic, Caucasian patients (POTS I: 92% White), and co-morbid diagnoses have been limited such that individuals with ASD are often excluded despite a considerable rate of comorbidity with OCD.

Conclusions across meta-analyses are difficult to reconcile due to the studies that make up the CBT comparator in each report varying based on the specific research question and associated inclusion criteria employed. To illustrate, investigations of CBT with high parental involvement by Iniesta-Sepúlveda et al. (2017) and McGrath and Abbott (2019) found conflicting findings with regard to treatment effects on measures of family accommodation, which may be explained by the low degree of overlap (40%) in the studies that comprised these analyses despite a similar research focus. This inconsistency also applies to how control conditions are defined which contributes to variability in findings both in terms of the estimated treatment effects and the estimated influence of moderators. Inconsistency in included trials, how treatments are classified, and the absence of head-to-head comparisons among the many CBT variants, along with between-trial differences in recruited samples (Dahabreh et al., 2020), means current meta-analyses struggle to answer the question of "what works for whom?" To answer this question requires estimating average treatment effects for all comparisons among CBT variants within each subgroup thought to modify treatment response (i.e., conditional average treatment effects). Ideally, these estimates would be generated through a large number of randomized controlled trials. Given all the possible CBT variants and the many potential moderator variables, it would be impossible to run all the necessary trials to generate the required estimates for developing guidelines. A more practical approach is to pair existing data with advanced statistical approaches to obtain the required estimates.

Leveraging Modern Statistics and Methodology

Conventional meta-analytic methods aim to summarize aggregate statistics (e.g., published effect sizes) from multiple-related studies to answer specific clinical questions. This approach, often referred to as aggregate data meta-analysis (AD-MA), can summarize findings but struggles to provide unbiased estimates of conditional average treatment effects required to answer the "what works for whom" question. To produce unbiased estimates using conventional AD-MA approaches requires that the estimates for each subgroup be generated for each trial and requires strong and often untenable assumptions about the equivalence of samples among trials (Borenstein & Higgins, 2013). A more comprehensive approach to evaluating moderators is through individual participant data meta-analysis (IPD-MA). Rather than extracting mean effects from published studies, IPD-MA involves obtaining and synthesizing the raw individual data from available studies and is considered the gold-standard for meta-analysis (Stewart & Parmar, 1993).

Compared to AD-MA, IPD-MA approaches are able to utilize the same analytic approach across trials, run analyses for subgroups not reported in the published literature, and address between-trial differences in participant characteristics (Cooper & Patall, 2009; Debray et al., 2015; Smith et al., 2016). IPD-MA also enables the use of cutting-edge causal inference techniques that enable unbiased estimates of conditional average treatment effects in target populations (Dahabreh et al., 2020). Although a full description of such techniques is beyond the scope of this brief report, a causal interpretation of IPD-MA enables accurate transportation of treatment effects to a defined target population, comparison of interventions not compared in head-to-head trials, and estimation of conditional average treatment effects for predefined subgroups. IPD-MA requires that investigators obtain well-documented individual-level data for each trial with the documentation including description of the treatment, trial implementation, and data dictionary. These data must then be understood by the analytic team and harmonized to a common template. Harmonization can be time-consuming as trials differ in which variables were assessed, how they were assessed (e.g., the measures used), and how the responses were recorded. Obtaining and harmonizing data continues to be a prominent barrier to implementing IPD-MA (Polanin & Williams, 2016), but this burden can be mitigated to the extent that common data elements are used across trials.

Fortunately, the field of pediatric OCD treatment is especially well suited to take advantage of IPD-MA given the relatively small sample of clinical trialists who have conducted many of the existing RCTs. Pooling trial data among several of these researchers would generate a representative sample of the treatment literature. Moreover, pediatric OCD trialists have consistently used the same symptom measure for assessing treatment response across trials (i.e., CY-BOCS). Conducting an IPD-MA with data from previous trials of CBT for pediatric OCD has the potential to greatly enhance the current knowledge base and move toward a better understanding of what works for whom.

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References

Barrett, P., Farrell, L., Pina, A., Peris, T., & Piacentini, J. (2008). Evidence-based psychosocial treatments for child and adolescent obsessive-compulsive disorder. *Journal of Clinical Child and Adolescent Psychology*, *37*(1), 131–155. https://doi.org/10.1080/15374410701817956

*Barrett, P., Healy-Farrell, L., & March, J. (2004). Cognitive-behavioral family treatment of childhood obsessive-compulsive disorder: A controlled trial. *Journal of the American Academy of Child and Adolescent Psychiatry*, *43*(1), 46–62. https://doi.org/10.1097/00004583-200401000-00014

*Bolton, D., Williams, T., Perrin, S., Atkinson, L., Gallop, C., Waite, P., & Salkovskis, P. (2011). Randomized controlled trial of full and brief cognitive-behaviour therapy and wait-list for paediatric obsessive-compulsive disorder. *Journal of Child Psychology and Psychiatry 52*(12), 1269–1278. https://doi.org/10.1111/j.1469-7610.2011.02419.x

Borenstein, M., & Higgins, J. P. (2013). Meta-analysis and subgroups. *Prevention Science*, *14*(2), 134–143. https://doi.org/10.1007/s11121-013-0377-7

*Conelea, C., Walther, M., Freeman, J., Garcia, A., Sapyta, J., Khanna, M., & Franklin, M. (2014). Tic-related obsessive-compulsive disorder (OCD): Phenomenology and treatment outcome in the pediatric OCD treatment study II. *Journal of the American Academy of Child and Adolescent Psychiatry*, *53*(12), 1308–1316. https://doi.org/10.1016/j.jaac.2014.09.014

Cooper, H., & Patall, E. A. (2009). The relative benefits of meta-analysis conducted with individual participant data versus aggregated data. *Psychological Methods*, *14*(2), 165–176. https://doi.org/10.1037/a0015565

Dahabreh, I. J., Petito, L. C., Robertson, S. E., Hernán, M. A., & Steingrimsson, J. A. (2020). Toward causally interpretable meta-analysis: Transporting inferences from multiple randomized trials to a new target population. *Epidemiology*, *31*(3), 334–344. https://doi.org/10.1097/EDE.0000000000001177

Debray, T. P., Riley, R. D., Rovers, M. M., Reitsma, J. B., & Moons, K. G. (2015). Individual participant data (IPD) meta-analyses of diagnostic and prognostic modeling studies: Guidance on their use. *PLoS Medicine*, *12*(10), e1001886. https://doi.org/10.1371/journal.pmed.1001886

Flessner, C. A., Allgair, A., Garcia, A., Freeman, J., Sapyta, J., Franklin, M. E., … March, J. (2010). The impact of neuropsychological functioning on treatment outcome in pediatric obsessive–compulsive disorder. *Depression and Anxiety*, *27*(4), 365–371. https://doi.org/10.1002/da.20626

Freeman, J., Benito, K., Herren, J., Kemp, J., Sung, J., Georgiadis, C., … Garcia, A. (2018). Evidence base update of psychosocial treatments for pediatric obsessive-compulsive disorder: Evaluating, improving, and transporting what works. *Journal of Clinical Child & Adolescent Psychology*, *47*(5), 669–698. https://doi.org/10.1080/15374416.2018.1496443

Freeman, J., Garcia, A., Coyne, L., Ale, C., Przeworski, A., Himle, M., … Leonard, H. (2008). Early childhood OCD: Preliminary findings from a family-based cognitive-behavioral approach. *Journal of the American Academy of Child & Adolescent Psychiatry*, *47*(5), 593–602. https://doi.org/10.1097/CHI.0b013e31816765f9

Freeman, J., Garcia, A., Frank, H., Benito, K., Conelea, C., Walther, M., & Edmunds, J. (2014). Evidence base update for psychosocial treatments for pediatric obsessive-compulsive disorder. *Journal of Clinical Child & Adolescent Psychology*, *43*(1), 7–26. https://doi.org/10.1080/15374416.2013.804386

*Garcia, A., Sapyta, J., Moore, P., Freeman, J., Franklin, M., March, J., & Foa, E. (2010). Predictors and moderators of treatment outcome in the pediatric obsessive compulsive treatment study (POTS I). *Journal of the American Academy of Child and Adolescent Psychiatry*, *49*(10), 1024–1033. https://doi.org/10.1016/j.jaac.2010.06.013

Geller, D. A., & March, J. (2012). Practice parameter for the assessment and treatment of children and adolescents with obsessive-compulsive disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, *51*(1), 98–113. https://doi.org/10.1016/j.jaac.2011.09.019

Geller, D. A., McGuire, J. F., Orr, S. P., Small, B. J., Murphy, T. K., Trainor, K., … Storch, E. A. (2019). Fear extinction learning as a predictor of response to cognitive behavioral therapy for pediatric obsessive compulsive disorder. *Journal of Anxiety Disorders*, *64*, 1–8. https://doi.org/10.1016/j.janxdis.2019.02.005

Hybel, K. A., Mortensen, E. L., Lambek, R., Højgaard, D. R., & Thomsen, P. H. (2017). Executive function predicts cognitive-behavioral therapy response in childhood obsessive-compulsive disorder. *Behaviour Research and Therapy*, *99*, 11–18. https://doi.org/10.1016/j.brat.2017.08.009

*Iniesta-Sepúlveda, M., Rosa-Alcázar, A. I., Sánchez-Meca, J., Parada-Navas, J. L., & Rosa-Alcázar, Á. (2017). Cognitive-behavioral high parental involvement treatments for pediatric obsessive-compulsive disorder: A meta-analysis. *Journal of Anxiety Disorders*, *49*, 53–64. https://doi.org/10.1016/j.janxdis.2017.03.010

Ivarsson, T., Skarphedinsson, G., Kornør, H., Axelsdottir, B., Biedilæ, S., Heyman, I., … March, J. (2015). The place of and evidence for serotonin reuptake inhibitors (SRIs) for obsessive compulsive disorder (OCD) in children and adolescents: Views based on a systematic review and meta-analysis. *Psychiatry Research*, *227*(1), 93–103. https://doi.org/10.1016/j.psychres.2015.01.015

Kraemer, H. C., Frank, E., & Kupfer, D. J. (2006). Moderators of treatment outcomes: Clinical, research, and policy importance. *Journal of the American Medical Association*, *296*(10), 1286–1289. https://doi.org/10.1001/jama.296.10.1286

Lewin, A., Park, J., Jones, A., Crawford, E., De Nadai, A., Menzel, J., … Storch, E. A. (2014). Family-based exposure and response prevention therapy for preschool-aged children with obsessive-compulsive disorder: A pilot randomized controlled trial. *Behaviour Research and Therapy*, *56*, 30–38. https://doi.org/10.1016/j.brat.2014.02.001

*March, J., Franklin, M., Leonard, H., Garcia, A., Moore, P., Freeman, J., & Foa, E. (2007). Tics moderate treatment outcome with sertraline but not cognitive-behavior therapy in

pediatric obsessive-compulsive disorder. *Biological Psychiatry*, *61*(3), 344–347. https://doi.org/10.1016/j.biopsych.2006.09.035

*McGuire, J., Piacentini, J., Lewin, A., Brennan, E., Murphy, T., & Storch, E. (2015). A meta-analysis of cognitive behavior therapy and medication for child obsessive-compulsive disorder: Moderators of treatment efficacy, response, and remission. *Depression and Anxiety*, *32*(8), 580–593. https://doi.org/10.1002/da.22389

*McGrath, C. A., & Abbott, M. J. (2019). Family-based psychological treatment for obsessive compulsive disorder in children and adolescents: A meta-analysis and systematic review. *Clinical Child and Family Psychology Review*, *22*(4), 478–501. https://doi.org/10.1007/s10567-019-00296-y

*Nair, A., Turner, C., Heyman, I., Mataix-Cols, D., Lovell, K., Krebs, G., … O'Kearney, R. (2019). Moderators and predictors of outcomes in telephone delivered compared to face-to-face cognitive behaviour therapy for pediatric obsessive–compulsive disorder: Preliminary evidence from a non-inferiority RCT. *Cognitive Behaviour Therapy*, *48*(5), 353–368. https://doi.org/10.1080/16506073.2018.1513555

Olatunji, B. O., Rosenfield, D., Monzani, B., Krebs, G., Heyman, I., Turner, C., … Mataix-Cols, D. (2015). Effects of homework compliance on cognitive-behavioral therapy with d-cycloserine augmentation for children with obsessive compulsive disorder. *Depression and Anxiety*, *32*(12), 935–943. https://doi.org/10.1002/da.22423

*Öst, L., Riise, E., Wergeland, G., Hansen, B., & Kvale, G. (2016). Cognitive behavioral and pharmacological treatments of OCD in children: A systematic review and meta-analysis. *Journal of Anxiety Disorders*, *43*, 58–69. https://doi.org/10.1016/j.janxdis.2016.08.003

Pediatric OCD Treatment Study Team. (2004). Cognitive-behavior therapy, sertraline, and their combination for children and adolescents with obsessive-compulsive disorder: The pediatric OCD treatment study randomized controlled trial. *Journal of the American Medical Association*, *292*(16), 1969–1976. https://doi.org/10.1001/jama.292.16.1969

*Peris, T. S., Rozenman, M. S., Bai, S., Perez, J., Thamrin, H., & Piacentini, J. (2020). Ethnicity moderates outcome in family focused treatment for pediatric obsessive-compulsive disorder. *Journal of Anxiety Disorders*, 102229. *73* https://doi.org/10.1016/j.janxdis.2020.102229

Polanin, J. R., & Williams, R. T. (2016). Overcoming obstacles in obtaining individual participant data for meta-analysis. *Research Synthesis Methods*, *7*(3), 333–341. https://doi.org/10.1002/jrsm.1208

*Skarphedinsson, G., Weidle, B., Thomsen, P., Dahl, K., Torp, N., Nissen, J., … Ivarsson, T. (2014). 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. *European Child & Adolescent Psychiatry*, *24*(5), 591–602. https://doi.org/10.1007/s00787-014-0613-0

*Sánchez-Meca, J., Rosa-Alcázar, A. I., Iniesta-Sepúlveda, M., & Rosa-Alcázar, Á. (2014). Differential efficacy of cognitive-behavioral therapy and pharmacological treatments for pediatric obsessive–compulsive disorder: A meta-analysis. *Journal of Anxiety Disorders*, *28*(1), 31–44. https://doi.org/10.1016/j.janxdis.2013.10.007

*Rosa-Alcázar, A. I., Sánchez-Meca, J., Rosa-Alcázar, Á., Iniesta-Sepúlveda, M., Olivares-Rodríguez, J., & Parada-Navas, J. L. (2015). Psychological treatment of obsessive-compulsive disorder in children and adolescents: A meta-analysis. *The Spanish Journal of Psychology*, *18*, 1–22. https://doi.org/10.1017/sjp.2015.22

Smith, C. T., Marcucci, M., Nolan, S. J., Iorio, A., Sudell, M., Riley, R., … Williamson, P. R. (2016). Individual participant data meta-analyses compared with meta-analyses based on aggregate data. *Cochrane Database of Systematic Reviews*, *2016*(9), 1–48. https://doi.org/10.1002/14651858.MR000007.pub3

Stewart, L. A., & Parmar, M. K. B. (1993). Meta-analysis of the literature or of individual patient data: Is there a difference? *Lancet*, *341*(8842), 418–422. https://doi.org/10.1016/0140-6736(93)93004-K

Torp, N., Dahl, K., Skarphedinsson, G., Compton, S., Thomsen, P., Weidle, B., … Ivarsson, T. (2015). Predictors associated with improved cognitive-behavioral therapy outcome in pediatric obsessive-compulsive disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, *54*(3), 200–207. https://doi.org/10.1016/j.jaac.2014.12.007

Turner, C., O'Gorman, B., Nair, A., & O'Kearney, R. (2018). Moderators and predictors of response to cognitive behaviour therapy for pediatric obsessive-compulsive disorder: A systematic review. *Psychiatry Research*, *261*, 50–60. https://doi.org/10.1016/j.psychres.2017.12.034

*Wilhelm, S., Berman, N., Small, B. J., Porth, R., Storch, E. A., & Geller, D. (2018). D-Cycloserine augmentation of cognitive behavior therapy for pediatric OCD: Predictors and moderators of outcome. *Journal of Affective Disorders*, *241*, 454–460. https://doi.org/10.1016/j.jad.2018.07.042