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A Meta-Analysis of Cognitive Behavior Therapy and Medication for Child Obsessive Compulsive Disorder: Moderators of Treatment Efficacy, Response, and Remission

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Abstract

Background—Individual randomized controlled trials (RCTs) have demonstrated the efficacy of cognitive behavioral therapy (CBT) and serotonin reuptake inhibitors (SRIs) for the treatment of youth with obsessive-compulsive disorder (OCD). While meta-analyses have confirmed these results, there has been minimal examination of treatment moderators or an examination of treatment response and symptom/diagnostic remission for these two treatment types. The present report examined the treatment efficacy, treatment response, and symptom/diagnostic remission for

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youth with OCD receiving either CBT or SRIs relative to comparison conditions, and examined treatment moderators.

Method—A comprehensive literature search identified 20 RCTs that met inclusion criteria, and produced a sample size of 507 CBT participants and 789 SRI participants.

Results—Random effects meta-analyses of CBT trials found large treatment effects for treatment efficacy (*g*=1.21), treatment response [relative risk (RR)=3.93], and symptom/diagnostic remission (RR=5.40). Greater co-occurring anxiety disorders, therapeutic contact, and lower treatment attrition were associated with greater CBT effects. The number needed to treat (NNT) was three for treatment response and symptom/diagnostic remission. Random effects meta-analyses of SRI trials found a moderate treatment effect for treatment efficacy (*g*=0.50), treatment response (RR=1.80), and symptom/diagnostic remission (RR=2.06). Greater methodological quality was associated with a lower treatment response for SRI trials. The NNT was five for treatment response and symptom/diagnostic remission.

Conclusions—Findings demonstrate the treatment effects for CBT and SRIs across three important outcome metrics, and provide evidence for moderators of CBT across trials.

Keywords

obsessive compulsive disorder; cognitive behavior therapy; clomipramine; selective serotonin reuptake inhibitors; treatment outcome; treatment response; diagnostic remission

Introduction

Obsessive compulsive disorder (OCD) is characterized by the presence of obsessions and/or compulsions, and affects approximately 1–2% of youth.[1; 2] Although OCD may develop in adulthood,[3] a majority of cases report symptom onset during childhood.[4] Youth with OCD frequently experience co-occurring psychiatric conditions including anxiety disorders, attention deficit hyperactivity disorders (ADHD), major depressive disorders (MDD), chronic tic disorders (CTDs) and oppositional defiant disorder (ODD).[5; 6] Youth with OCD experience functional impairment,[7] disrupted family functioning,[8] and a poor quality of life.[9] As OCD symptoms rarely remit without treatment,[10] effective and efficient treatments are essential.

The two first-line empirically-supported treatment recommended for youth with OCD include cognitive behavioral therapy (CBT) and serotonin reuptake inhibitors (SRIs).[11] Cognitive behavioral therapy is a psychological treatment that includes psychoeducation, cognitive training, symptom hierarchy development, and exposure with response prevention (ERP).[12; 13] Several randomized controlled trials (RCTs) have evaluated the efficacy of CBT for youth with OCD using manualized treatment protocols that emphasize either cognitive or behavioral components, with most treatments involving both aspects. Irrespective of these distinctions, CBT significantly reduces obsessive-compulsive symptom severity relative to waitlist,[14–18] placebo,[19] treatment-as-usual,[20] and relaxation training (RT) comparison conditions,[21–23] with maintenance up to 7 years after acute treatment.[24] Indeed, CBT is a highly preferred treatment option for parents of children with OCD,[25] and

is recommended as a first-line monotherapy for youth with mild-to-moderate OCD symptom severity and together with SRIs for more severe cases.[11]

Medication management with SRIs presents another empirically-supported treatment option for youth with OCD. The SRIs that have been evaluated in RCTs for youth with OCD include clomipramine (CMI),[26–28] sertraline (SERT),[19; 29] fluoxetine (FLUX),[30–32] paroxetine (PAX),[33] and fluvoxamine (FLUV).[34] These medications significantly reduce obsessive-compulsive symptom severity relative to placebo and waitlist control conditions, with some evidence suggesting that CMI is superior to selective SRIs (SERT, FLUX, PAX, FLUV).[35] Long-term benefit from acute SRI treatment has been observed for up to 12 months with maintenance medication,[36] however symptom reemergence can occur with discontinued use.[37; 38] While appropriate safety and tolerability monitoring are needed due to side-effect concerns,[39; 40] SRI medications are recommended as first-line interventions for youth with moderately severe OCD.[11]

When making treatment recommendations, it is important to synthesize empirical evidence to guide clinical decisions.[41] Meta-analyses provide a quantitative synthesis of treatment trials, and provide for a more powerful examination of outcome moderators than individual treatment trials.[38; 42–46] To date, there have been seven published meta-analyses examining the efficacy of CBT,[47–49] SRIs,[35] or both interventions[50–52] for the treatment of pediatric OCD. Findings from these meta-analyses have demonstrated large treatment effects for CBT (1.45–1.98) and moderate effects for SRIs (0.46–0.48) for reducing symptom severity. While these meta-analyses are noteworthy contributions to the literature, they have several limitations, including: small sample size;[48] inclusion of open-label trials that may have inflated treatment effects;[47; 50] combined treatment effects across multiple OCD measures some which have poor treatment sensitivity in youth;[35; 52; 53] limited examination of treatment moderators;[35; 47–51] combined treatment effects across individual and group therapy formats that may have influenced moderator analyses;[51; 52] and inferred values from other placebo-controlled trials for comparison conditions.[52] Additionally, prior meta-analyses did not examine treatment response (i.e., when a patient exhibits a clinically meaningful reduction in obsessive-compulsive severity) and symptoms/diagnostic remission (i.e., when a patient no longer meets syndromal criteria and/or has no more than minimal symptoms),[54; 55] which are two clinically meaningful metrics that are informative to treatment providers.[35; 47–52]

In an effort to address these limitations, this report examined RCTs of individually-delivered empirically supported treatments (SRI or CBT) to determine their efficacy in reducing obsessive-compulsive symptom severity and to identify the risk ratios (RR) of experiencing a clinically meaningful response to treatment and symptom/diagnostic remission. Analyses across these three outcomes can provide clinicians with important probabilistic treatment response and symptom/diagnostic remission rates to aid parents and clinicians in the selection of empirically-supported monotherapies. Based on factors purported to impact treatment efficacy, treatment response, and symptom/diagnostic remission among CBT and SRI trials,[38; 42–45] this report examined the following putative treatment moderators: participant age; comorbidity (CTD, ADHD, depressive disorders, and anxiety disorders); baseline OCD symptom severity; medication status (for CBT trials); therapeutic contact (for

CBT trials); attrition; treatment subtype; and methodological quality. Based on findings from individual RCTs, we had several hypotheses. First, we hypothesized that CBT would outperform comparison conditions. Second we hypothesized that SRIs would outperform comparison conditions. Finally, given the variable findings across moderators in individual RCTs, the association between purported moderators and treatment effects were explored across interventions. Although the efficacy of combined treatment (e.g., CBT+SRI) for pediatric OCD has some empirical support,[19; 56; 57] this treatment modality was considered too preliminary for inclusion in the current meta-analyses due to the limited number of published RCTs. Direct comparison trials of CBT and SRIs were also not examined due to their recent meta-analytic evaluation.[58] In this meta-analysis, Romanelli and colleagues[58] found that CBT outperformed SRIs across RCTs of youth and adults (effect size=0.37), but found no significant difference between CBT and CBT+SRI conditions.

Method

Search Strategy

PubMED, PsycInfo, and ProQuest Dissertations and Theses Online were searched using key search terms (i.e., “obsessive compulsive disorder” AND “children” with either “cognitive behavioral therapy” or “exposure response prevention” for CBT trials and either “selective serotonin reuptake inhibitors” OR “clomipramine” for medication trials). Identified abstracts were reviewed independently by two raters for appropriateness. The references of eligible treatment trials, and review articles were also searched. Identified abstracts/citations were evaluated for the following inclusion criteria: (1) a RCT that included an individually delivered treatment that could include family members, but was not a group-based intervention; (2) evaluated the efficacy of CBT or a SRI in treating OCD symptom severity relative to a non-evidence based comparison condition (e.g., placebo, desipramine, waitlist, relaxation training, treatment-as-usual) ; (3) included only participants under the age of 18 with a diagnosis of OCD; (4) available in English; (5) included an adequate dose/duration of CBT (5 session minimum) or SRI medication (5 week minimum); and (6) provided sufficient data to allow calculation of either treatment efficacy, treatment response, or symptom/diagnostic remission.

Procedures

A hierarchy of preferred rating scales for the primary outcome measure was established *a priori* to limit possible investigator reporting bias. In order of preference, these OCD ratings scales for treatment efficacy included the CY-BOCS,[59] and the National Institute of Mental Health Global OCD Scale (NIMH-GOCS).[60] For classification of treatment response, preference was placed on the Clinical Global Impression of Improvement (CGI-Improvement),[61] with treatment response considered a rating of “much improved” or “very much improved” consistent with extant RCTs. When the CGI-Improvement was unavailable, a reduction of 25% or greater on the CY-BOCS was used as it corresponds with a treatment response on the CGI-Improvement.[55] For classification of symptom/diagnostic remission, preference was placed on CY-BOCS 14 as it corresponds with a Clinical Global Impression-Severity (CGI-Severity) rating of “no illness” or “mild illness”.[55] If CY-BOCS remission cut-off scores were not reported and/or unavailable, diagnostic remission on the

ADIS-P was preferred.[62] Finally, a CY-BOCS reduction of 40–50% was considered to be permissible in the absence of the other two measures, as it corresponds well to CGI-Severity ratings of "no illness" or "mild illness".[55]

Study Coding

Trials were coded for the following characteristics: (1) participant mean age; (2) percentage of comorbid TS/CTD, ADHD, depressive disorders (major depressive disorder, dysthymia), and anxiety disorders (social phobia, generalized anxiety disorder, separation anxiety disorder, panic disorder); (3) baseline OCD severity; (4) number of 1-hour therapy sessions (for CBT trials); (5) percentage of SRI medication at baseline (for CBT trials); (6) active treatment attrition; (7) measure of treatment efficacy, response, and remission; (8) effect size (Hedges' *g*), treatment response, and symptom/diagnostic remission; (9) treatment subtype (ERP or CT for CBT trials; CMI or SSRI for SRI trials); (10) comparison condition; and (11) study methodological quality. Comorbid disorders were selected due to their potential impact on treatment outcome.[42–45] Comparison conditions were classified into two categories: non-active interventions (e.g., waitlist, placebo, treatment-as-usual); and active interventions (e.g., desipramine, relaxation training). Study methodology was assessed using a 23-item scale that has been used in other meta-analyses.[63–65] Possible scores range from 0 to 46, with higher values corresponding with greater methodological rigor. Study investigators were contacted to request the above information if it was not available in published form. Trials were coded by two raters to ascertain reliability. Rater disagreement was resolved through discussion and consensus.

Effect size (ES) calculation

Hedges' *g* was chosen as the treatment ES statistic for treatment efficacy since it controls for different sample sizes across studies, and was calculated in Comprehensive Meta-Analysis (CMA)Version 2.[66] Effect sizes were calculated using change scores because this increases the precision of ES estimators by controlling for pretreatment group differences of obsessive-compulsive symptom severity. Pre-and-post treatment means and standard deviations were entered into CMA, and were divided by the pooled post-treatment standard deviation. Effect sizes were standardized so that a positive result indicated that the active treatment (CBT or SRI) performed better than comparison conditions. For treatment response and symptom/diagnostic remission, the RR was selected to serve as the ES. The RR is the ratio of patients exhibiting response or remission in the active treatment condition divided by the probability of patients exhibiting response or remission in the comparison condition.[67] A RR of 1 suggests that response or remission outcomes did not differ between the two treatment conditions, whereas a RR of 4 indicates that the active treatment condition had a fourfold greater probability than the comparison condition of exhibiting response or remission. The number of treatment responders/non-responders and participants experiencing symptom remittance/non-remittance were entered into CMA, which calculated the RR for treatment response and symptom/diagnostic remittance.

Statistical Analyses

Inter-rater agreement of study characteristics and quality ratings was assessed using descriptive statistics and intra-class correlation coefficient (ICC). A random effects model using inverse variance weights examined the ES of CBT and SRIs in CMA.[66] A random effects model was chosen because the true ES were expected to vary across trials due to different study characteristics.[68] Heterogeneity of ES was assessed using the forest plot, *Q* statistic, and I^2 statistic. Publication bias was assessed by visual inspection of the funnel plot and Egger's test for bias. When publication bias was present, Duval and Tweedie's trim-and-fill method was used to account for publication bias by producing an adjusted summary effect that takes into account potential within the field.[68] An analog to the analysis of variance (ANOVA) examined the heterogeneity of ES across comparison conditions (non-active versus active comparison conditions). Separate random effect models examined the RR of CBT and SRI in CMA for treatment response and symptom/diagnostic remission. The same procedures noted above assessed for publication bias and sensitivity analyses. The number needed to treat (NNT) was calculated for treatment response and symptom/diagnostic remission for each treatment. The NNT is the number of youth with OCD that would need to be treated with the active intervention for one patient to respond who would not have responded to the comparison intervention. Finally, hypothesized moderator variables were analyzed using either method-of-moments meta-regression or an analog to ANOVA.

Results

Included Studies

Initial search strategies produced 920 potential abstracts/citations, with 34 abstracts citations being retrieved for detailed review (see Figure 1). Table 1 displays the 20 RCTs that met all inclusion criteria, which produced a total sample size of 507 CBT participants and 789 SRI participants. Table 2 presents the ES and outcome measure of treatment efficacy, treatment response and symptom/diagnostic remission across trials.

Reliability of Coding Study Characteristics

There was excellent inter-rater agreement between the two raters on categorical and continuous study characteristics (100% agreement), as well as overall study methodological quality (ICC=0.90, 95% CI=0.76, 0.96).

Efficacy of CBT, Publication Bias, and Sensitivity Analyses

The random effects meta-analysis identified a large effect for CBT relative to comparison conditions (g=1.21, 95% CI: 0.83, 1.59, z=6.17, p<0.001) (Figure 2). Visual inspection of the forest plot, *Q* statistic, and I^2 statistic identified the presence of significant heterogeneity [$Q(9)$=33.37 p<0.001, I^2=73.03%]. Although visual inspection of the funnel plot suggested that publication bias may exist, Egger's test for bias indicated that publication bias was not significant (t=1.03, p=0.33). The analog-to-ANOVA revealed that a significant difference between active comparison trials and non-active comparison trials [$Q(1)$=4.56, p=0.03]. Given the significant difference between control comparison conditions, the summary effect

was recalculated with active comparison trials excluded. Results identified a larger treatment effect (g=1.48, 95% CI: 1.04, 1.92, z=6.58, p<0.001) with less heterogeneity [Q(6)=15.19, p=0.02, I^2=60.50%] among non-active comparison trials. For active comparison trials, a moderate-to-large effect was observed (g=0.71, 95% CI: 0.16, 1.26, z=2.54, p=0.01), with significant heterogeneity [Q(2)=7.60 p=0.02, I^2=73.69%] (Figure 2). Visual inspection of the funnel plot and Egger's test (t=1.89, p=0.31) for bias indicated that publication bias was not significant.

Treatment Response with CBT

The average response rate across trials (n=10) for CBT, non-active comparison conditions, and active comparison conditions were 68%, 13%, and 36% respectively. A random effects meta-analysis identified a large effect for CBT relative to comparison conditions (RR=2.72, 95% CI: 1.83, 4.04, z=4.94, p<0.001) with significant heterogeneity [Q(9)=17.56, p=0.04, I^2=44.79%] (Figure 3). The NNT for CBT treatment response was three. Visual inspection of the funnel plot and Egger's test for bias indicated that publication bias was present (t=3.99, p=0.004). When Duval and Tweedie's trim-and-fill method was applied, four studies were trimmed and CBT still exhibited a large significant effect (RR=2.13, 95%CI: 1.39, 3.27). The analog-to-ANOVA revealed a significant difference between active comparison trials (RR=1.71) and non-active comparison trials (RR=3.93) [Q(1)=9.74, p<0.002]. Given the significant difference between comparison conditions, the summary effect was recalculated with active comparison trials removed. Results identified a large effect (RR=3.93, 95% CI: 2.52, 6.14, z=6.02, p<0.001) with minimal heterogeneity [Q(6)=6.50, p=0.37, I^2=7.51%] among non-active comparison trials. For active comparison trials, a moderate effect was observed (RR=1.71, 95% CI: 1.29, 2.25, z=3.77, p<0.001), with minimal heterogeneity [Q(2)=1.14 p=0.57, I^2=0%]. Visual inspection of the funnel plot and Egger's test (t=0.24, p=0.85) for bias indicated that publication bias was not present.

Symptom/Diagnostic Remission with CBT

The average remission rate across trials (n=10) for CBT, non-active comparison conditions, and active comparison conditions were 57%, 9%, and 23% respectively. A random effects meta-analysis identified a large effect for CBT relative to comparison conditions (RR=3.42, 95% CI: 2.11, 5.53, z=5.00, p<0.001) with little heterogeneity [Q(9)=13.96, p=0.12, I^2=35.52%] (Figure 4). The NNT for CBT remission was three. Visual inspection of the funnel plot and Egger's test for bias indicated that publication bias was present (t=3.10, p=0.01). When Duval and Tweedie's trim-and-fill method was applied, six studies were trimmed and CBT still exhibited a large significant effect (RR=2.15, 95%CI: 1.31, 3.54). The analog-to-ANOVA revealed a significant difference between active comparison trials (RR=2.05) and non-active comparison trials (RR=5.40) [Q(1)=6.93, p=0.008]. Given the significant difference between comparison conditions, the summary effect was recalculated with active comparison trials removed. Results identified a large effect (RR=5.40, 95% CI: 2.86, 10.22, z=5.18, p<0.001) with minimal heterogeneity [Q(6)=6.43, p=0.38, I^2=6.63%] among non-active comparison trials. For active comparison trials, a large effect was observed (RR=2.05, 95% CI: 1.46, 2.88, z=4.16, p<0.001), with minimal heterogeneity [Q(2)=0.39 p=0.83, I^2=0%]. Visual inspection of the funnel plot and Egger's test for bias indicated that publication bias may be present (t=11.25, p=0.06). When Duval and

Tweedie's trim-and-fill method was applied, two studies were trimmed and CBT still exhibited a moderate significant effect (RR=1.94, 95%CI: 1.43, 2.64).

Moderators of CBT Across Treatment Efficacy, Treatment Response, and Symptom Remission

Given the significant difference between comparison interventions, moderator analyses were conducted separately on CBT trials using non-active and active comparison conditions. Table 3 presents the results of moderator analyses across all three outcome types. For non-active comparison conditions, there was a positive association between the percentage of youth with co-occurring anxiety disorders and ES for treatment efficacy and response, with trials that had participants with more co-occurring anxiety disorders exhibiting larger ES. Additionally, for treatment efficacy and symptom remission, there was a positive association between the number of therapeutic hours and ES, with trials that had greater therapeutic contact exhibiting larger ES. Furthermore, there was an association between active treatment attrition and ES for treatment efficacy, with trials exhibiting greater attrition yielding lower ES. There was no significant difference between non-active comparison CBT trials that emphasized ERP relative to CT for treatment efficacy (g=1.52 vs. 1.41), treatment response (RR=5.50 vs. 3.67), or symptom diagnostic/remission (RR=6.69 vs. 4.47). There were no other significant moderators of treatment efficacy, treatment response, or symptom/diagnostic remission among non-active comparison trials. Table 3 also presents moderator analyses for active-comparison trials across all three outcome types. For treatment efficacy, a positive association was found between comorbid TS/CTD and ES, with trials that had a greater percentage of TS/CTD exhibited larger ES. Otherwise, there were no significant moderators of treatment efficacy, treatment response, or symptom/diagnostic remission among active-comparison trials.

Efficacy of SRIs

A random effects meta-analysis identified a moderate effect of SRIs compared to all control conditions (g=0.50, 95% CI: 0.37, 0.63, z=7.33, p<0.001) (Figure 2). Visual inspection of the forest plot, Q statistic, and I^2 statistic identified minimal heterogeneity across SRI trials [$Q(10)$=5.70 p=0.94, I^2=0%]. Visual inspection of the funnel plot and Egger's test for bias indicated that publication bias was not significant (t=0.98, p=0.35). The analog-to-ANOVA revealed no significant difference between active comparison trials (g=0.78) and non-active comparison trials (g=0.48) [$Q(1)$=0.94, p=0.33].

SRI Treatment Response

The average response rate across trials (n=7) for SRI and non-active comparison conditions were 50% and 25%, respectively. A random effects meta-analysis identified a moderate effect for SRIs relative to comparison conditions (RR=1.80, 95% CI: 1.43, 2.26, z=5.06 p<0.001) with minimal heterogeneity [$Q(6)$=6.89, p=0.33, I^2=12.88%] (Figure 3). The NNT for SRI treatment response was five. Visual inspection of the funnel plot and Egger's test for bias indicated that publication bias was present (t=4.46, p=0.006). When Duval and Tweedie's trim-and-fill method was applied, four studies were trimmed and SRIs still

exhibited a moderate effect (RR=1.52, 95%CI: 1.18, 1.95). All trials with treatment response data used a placebo control condition.

SRI Symptom/Diagnostic Remission

The average remission rate across trials (n=3) for SRI and non-active comparison conditions were 47% and 22%, respectively. A random effects meta-analysis identified a moderate effect for SRIs relative to comparison conditions (RR=2.06, 95% CI: 1.03, 4.13, z=2.05 p=0.04) with minimal heterogeneity [$Q(2)$=3.66, p=0.16, I^2=45.35%] (Figure 4). The NNT for SRI symptom remission was five. Visual inspection of the funnel plot and Egger's test for bias indicated that publication bias was not present (t=2.25, p=0.27). All trials with treatment response data used a placebo control condition.

Moderators of SRIs Across Treatment Efficacy, Treatment Response, and Symptom Remission

Given that there was no significant difference between active and non-active comparison conditions, all comparison conditions were included in moderator analyses. Table 3 presents the results of moderator analyses across all three outcome types. Although there was a non-significant trend for larger treatment effects in CMI trials relative to SSRI trials, there were no significant differences in treatment efficacy (g=0.73 vs. 0.45) or treatment response (RR=3.56 vs. 1.68). There was a small negative association between methodological quality and ES for treatment response (p=0.04), with trials that had greater methodological rigor exhibiting smaller ES. There were no other significant moderators of treatment efficacy, treatment response, or symptom/diagnostic remission among SRI trials.

Discussion

Prior meta-analyses of childhood OCD treatments have focused primarily on treatment efficacy, with minimal to no attention dedicated to treatment response or symptom/diagnostic remission. This is the first meta-analysis to collectively examine the treatment efficacy, treatment response, and symptom/diagnostic remission of evidence-based treatments for youth with OCD. Findings suggest that CBT has a large treatment effect for treatment efficacy (g=1.21), and an excellent RR for both treatment response (RR=2.72) and symptom/diagnostic remission (RR=3.42). Interestingly, there was little difference between treatment response and remission rates for CBT, which may suggest that youth who respond to CBT likely experience marked reductions in symptom severity that typically reach symptom/diagnostic remission. Several CBT treatment moderators in non-active comparison trials were identified that included the percentage of co-occurring anxiety disorders (treatment efficacy and treatment response), the number of therapeutic contact hours (treatment efficacy and symptom/diagnostic remission), and active treatment attrition (treatment efficacy). Additionally, TS/CTD was found to moderate treatment outcome in active comparison trials. The finding that CBT trials that had a greater incidence of co-occurring anxiety disorders exhibited larger treatment effects may suggest that OCD comorbid with other anxiety disorders could be driven by a more fear-based psychopathology which then leads to a more robust CBT response. The relationship between a greater number of CBT contact hours and larger treatment effects is consistent with

psychosocial interventions for related disorders.[64; 65] Similarly, CBT trials that had higher treatment dropout rates were associated with lower therapeutic benefit. Taken together, these findings suggest that youth who persist in treatment and receive a full-course of CBT may likely experience optimal therapeutic benefit. While trials that emphasized ERP exhibited larger effects relative to CT, the difference was not statistically significant. Notably, the power to detect this statistical difference was largely constrained by the small number of trials that emphasized CT, as well as the possible overlap between "behavioral experiments" used in CT trials and "exposures" in ERP trials. Finally, the association between greater ES and a greater incidence of TS/CTD in active comparison trials is consistent with recent findings highlighting the benefit of CBT for tic-related OCD.[69]

Findings across SRI trials suggest that SRIs have a moderate-to-large treatment effect for treatment efficacy (g=0.50), and a moderate effect for treatment response (RR=1.80) and remission (RR=2.06). When examining treatment moderators of SRI trials, only methodological quality moderated treatment response. Thus, SRI trials with greater methodological rigor exhibited lower treatment response rates, which is likely attributed to reduced error variance in well-controlled medication trials. Interestingly, the difference between SSRI and CMI trended toward significance for both treatment efficacy (p=0.11) and treatment response (p=0.09) favoring CMI. Contrary to findings from individual SRI trials,[38; 44] TS/CTD and ADHD were not significant moderators of treatment efficacy, treatment response, or symptom/diagnostic remission. Although further examination is still warranted, this suggests that youth with TS/CTD or ADHD may still benefit from SRIs to treat their obsessive-compulsive symptoms.

Several limitations should be considered. First, there was inconsistent reporting of variables needed to calculate treatment efficacy, treatment response, and symptom/diagnostic remission across RCTs. Although study investigators were contacted to obtain these data, this resulted in a limited number of RCTs included in treatment response and symptom/diagnostic remission analyses and may have influenced findings. Second, most of these RCTs focused on acute outcomes and were not designed with the goal of symptom/diagnostic remission. Thus, it may be that longer treatment durations and/or higher doses may yield improved symptoms/diagnostic remission rates for CBT and SRIs. Third, some moderator analyses had appropriate power to detect effects, but others had less power. Borenstein and colleagues [68] recommend 10 studies for moderator analyses. Thus, non-significant moderator findings should not be interpreted as a conclusive lack of association. Moreover, an examination of patient-level data may yield different moderator results, however such data are unavailable at this time.[46] Finally, there were limited characteristics available for extraction across RCTs. Although theoretically driven moderators were selected, there may be unexamined factors (e.g., homework compliance, medication adherence) omitted from these reports that influence treatment effects.

In summary, findings suggest that CBT produces large treatment effects for treatment efficacy, treatment response, and symptom/diagnostic remission. The presence of greater comorbid anxiety disorders and TS/CTD, greater therapeutic contact, and decreased treatment attrition were found to be associated with greater CBT treatment effects. Meanwhile, SRIs produce moderate treatment effects for treatment efficacy, treatment

response, and symptom/diagnostic remission. Although methodological quality was associated with smaller treatment effects, no other characteristics influenced treatment effects across trials. Although we encourage the future examination of patient-level moderator analyses from these combined RCTs, in their absence, these findings provide some guidance to practicing clinicians. From a clinical perspective, these findings provide three practical implications. First, these findings provide clinicians with probabilistic treatment response and symptom/diagnostic remission rates in response to empirically-supported monotherapies, which can be useful to inform families in the treatment selection process and aid patient/parent expectations. Second, these findings suggest that youth with either comorbid anxiety disorders or TS/CTD are good candidates for CBT. Third, these findings indicate that improved CBT therapeutic outcomes were associated with greater therapeutic contact and lower attrition rates. Thus, practicing clinicians should encourage families who wish to discontinue treatment early to stay the course for a full CBT trial.

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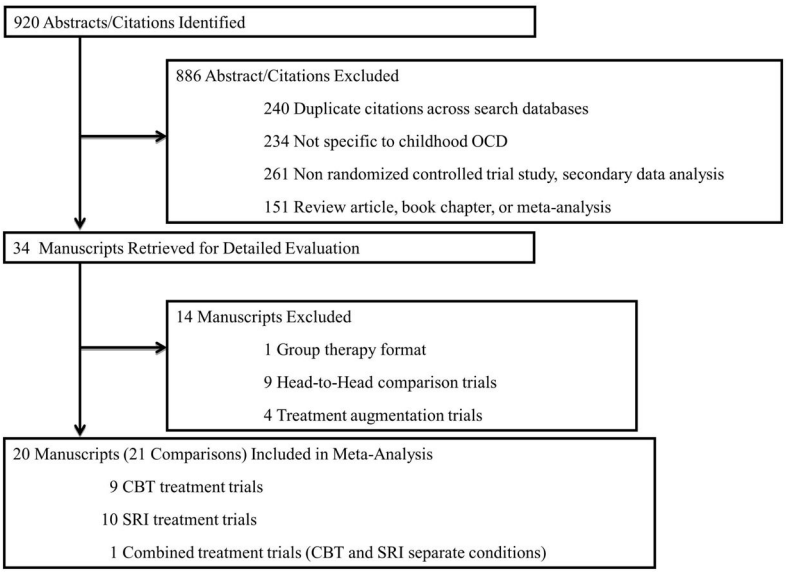

Figure 1.
Study Selection and Rationale For Exclusion.

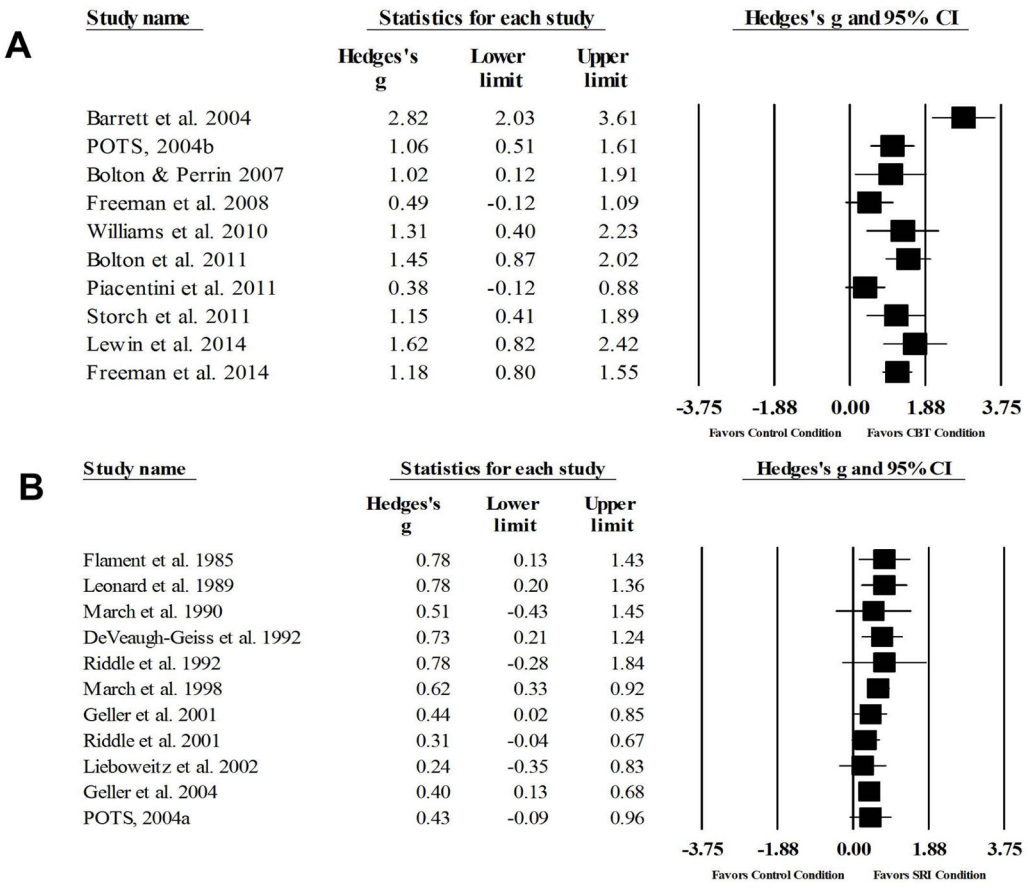

Figure 2.
Forest plots of treatment efficacy in CBT trials (A) and SRI trials (B)

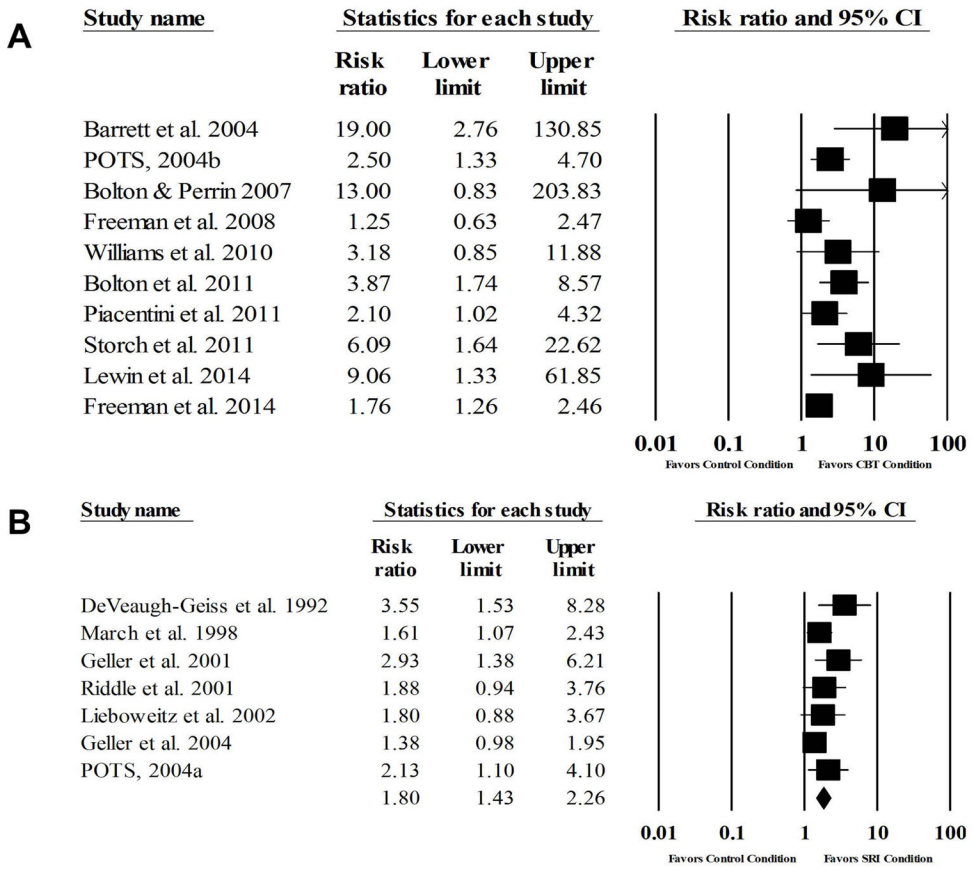

Figure 3.
Forest plots of treatment response in CBT trials (A) and SRI trials (B)

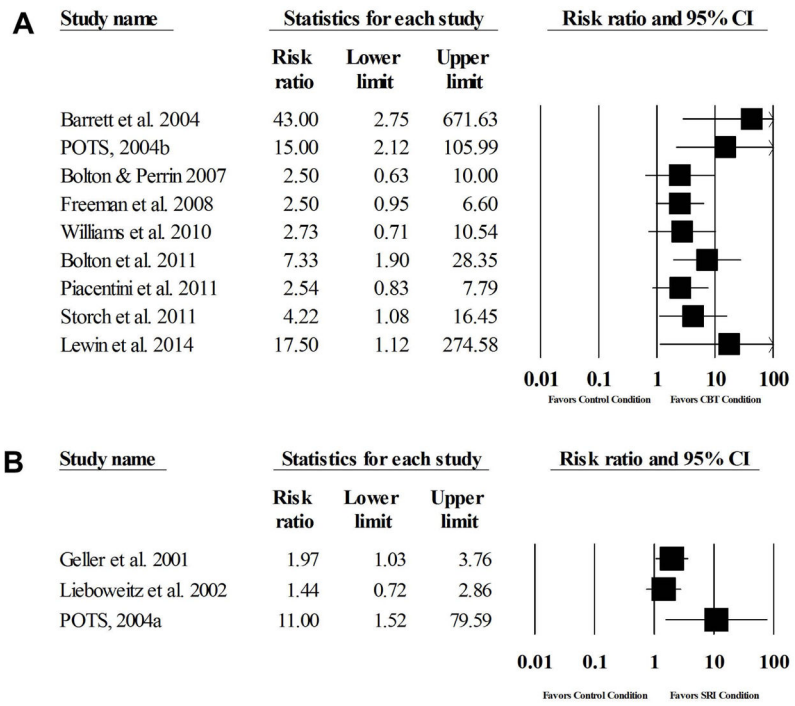

Figure 4.
Forest plots of symptom/diagnostic remission in CBT trials (A) and SRI trials (B)

Table 1

Characteristics of Randomized Controlled Trials of Cognitive Behavioral Therapy (CBT) and Serotonin Reuptake Inhibitores (SRIs) Included in Meta-analysis

	N	Treatment Subtype	Control Tx	Mean Age	% Comorbid TS/CTD	% Comorbid ADHD	% Comorbid Depressive Disorder	% Comorbid Anxiety Disorder	Baseline OCD Severity on CY-BOCS	% on SRI Med at Baseline	# of 1hr Therapy Sessions	% Active Tx Dropout	Method Quality
CBT Trials													
Barrett et al. 2004	48	ERP	WL	11.3	23	0	2	77	23.3	17	14	0	29
POTS, 2004[a]	56	ERP	PLBO	11.9	14	16	7	29	25.6	0	14	11	38
Bolton & Perrin, 2007	20	ERP	WL	13.2	5	5	10	50	23.0	0	9	20	30
Freeman et al. 2008	42	ERP	RT	7.1	10	19	NR	NR	22.4	14	12	27	32
Williams et al. 2010	21	CT	WL	13.6	NR	10	5	NR	22.1	33	10	9	31
Bolton et al. 2011	60	CT	WL	14.6	3	8	15	38	23.1	15	12	6	31
Piacentini et al. 2011	71	ERP	RT	12.2	11	14	4	47	24.9	9	12	16	38
Storch et al. 2011	31	ERP	WL	11.1	3	7	10	45	23.4	55	14	13	31
Lewin et al. 2014	31	ERP	TAU	5.8	0	42	0	71	24.5	0	12	0	32
Freeman et al. 2014	127	ERP	RT	7.2	18	14	2	47	25.6	2	12	13	41
SRI Trials													
Flament et al. 1985[b]	19	CMI	WL	14.5	NR	NR	NR	NR	NR	0	NA	0	33
Leonard et al. 1989[b]	49	CMI	DES	13.9	NR	NR	NR	NR	NR	0	NA	2	28
March et al. 1990[c]	16	CMI	PLBO	15.0	0	NR	NR	NR	26.0	0	NA	25	26
DeVeaugh-Geiss et al. 1992[c]	60	CMI	PLBO	14.3	0	0	NR	NR	27.7	0	NA	13	31
Riddle et al. 1992	13	FLUX	PLBO	11.7	15	8	15	54	22.4	0	NA	14	36
March et al. 1998	107	SERT	PLBO	12.6	4	5	2	4	22.8	0	NA	20	34
Geller et al. 2001[c]	103	FLUX	PLBO	11.4	0	0	NR	NR	25.0	0	NA	31	37
Riddle et al. 2001	120	FLUV	PLBO	13.0	NR	2	1	2	24.2	0	NA	33	33
Liebowietz et al. 2002[c]	43	FLUX	PLBO	12.7	0	7	21	47	23.2	0	NA	5	39
Geller et al. 2004	203	PARX	PLBO	11.3	NR	9	NR	7	24.8	0	NA	34	39
POTS, 2004[a]	56	SERT	PLBO	12.0	18	16	7	34	23.4	0	NA	7	29

[a] placebo group used in both comparisons,

[b] used a cross-over trial design,

[c] Tourette Syndrome in exclusion criteria

NOTE: NR = Not Reported, NA = Not Available/Applicable

Table 2

Effect sizes and Outcome Measures for Treatment Efficacy, Treatment Response and Symptom/Diagnostic Remission Across Included Trials

	Treatment Efficacy Measure	Effect size (Hedges' g)	Treatment Response Measure	Relative Risk of Treatment Resposne	Symptom /Diagnostic Remission Measure	Relative Risk of Symptom/ Diagnostic Remission
CBT Trials						
Barrett et al. 2004	CYBOCS	2.82	25% CYBOCS Reduction	19.00	ADIS-P	43.00
POTS, 2004[a]	CYBOCS	1.06	25% CYBOCS Reduction	2.50	CYBOCS ≤10	15.00
Bolton & Perrin, 2007	CYBOCS	1.02	25% CYBOCS Reduction	13.00	CYBOCS ≤14	2.50
Freeman et al. 2008	CYBOCS	0.49	CGI-I	1.25	CYBOCS ≤12	2.50
Williams et al. 2010	CYBOCS	1.31	25% CYBOCS Reduction	3.18	CYBOCS ≤14	2.73
Bolton et al. 2011	CYBOCS	1.45	25% CYBOCS Reduction	3.87	ADIS-C/P	7.33
Piacentini et al. 2011	CYBOCS	0.38	CGI-I	2.10	CYBOCS ≤10	2.54
Storch et al. 2011	CYBOCS	1.15	CGI-I	6.09	CYBOCS ≤10	4.22
Lewin et al. 2014	CYBOCS	1.62	CGI-I	9.06	CYBOCS ≤12	17.50
Freeman et al. 2014	CYBOCS	1.18	CGI-I	1.76	CYBOCS ≤14	1.94
SRI Trials						
Flament et al. 1985[b]	NIMH-GOCS	0.78	NA	---	NA	---
Leonard et al. 1989[b]	NIMH-GOCS	0.78	NA	---	NA	---
March et al. 1990[c]	CYBOCS	0.51	NA	---	NA	---
DeVeaugh-Geiss et al. 1992	CYBOCS	0.73	CGI-I	3.56	NA	---
Riddle et al. 1992	CYBOCS	0.78	NA	---	NA	---
March et al. 1998	CYBOCS	0.62	CGI-I	1.61	NA	---
Geller et al. 2001	CYBOCS	0.44	CGI-I	2.93	40% CYBOCS Reduction	1.97
Riddle et al. 2001	CYBOCS	0.31	CGI-I	1.88	NA	---
Liebowietz et al. 2002	CYBOCS	0.24	CGI-I	1.80	CYBOCS ≤14	1.44
Geller et al. 2004	CYBOCS	0.40	CGI-I	1.38	NA	---
POTS, 2004[a]	CYBOCS	0.44	25% CYBOCS Reduction	2.13	CYBOCS ≤10	11.00

[a] placebo group used in both,

[b] used a cross-over trial design

NOTE: CY-BOCS = Children's Yale-Brown Obsessive-Compulsive Scale, NIMH-GOCS = National Institute of Mental Health Global Obsessive Compulsive Disorder Scale, NA = Not Available/Applicable, CGI-I = Clinical Global Impression of Improvement, ADIS-C/P = Anxiety Disorder Interview Schedule-Child and Parent report

Table 3

Regression Analyses and Analog to ANOVA Examining Moderators of Treatment Efficacy, Treatment Response, and Remission for CBT and SRI Trials

CBT Trials versus Non-active comparisons	**Treatment Efficacy (*n*=7)**				**Treatment Response (*n*=7)**				**Symptom Remission (*n*=7)**			
Study Characteristics	***B***	***SE***	***z***	***p***	***B***	***SE***	***z***	***p***	***B***	***SE***	***z***	***p***
Mean Participant Age	−0.05	0.09	−0.50	0.61	−0.09	0.12	−0.82	0.41	−0.16	0.16	−1.01	0.31
Percentage of comorbid TS or CTD	0.05	0.03	1.49	0.14	<0.01	0.05	0.01	0.99	0.09	0.06	1.47	0.14
Percentage of comorbid ADHD	−0.01	0.02	−0.40	0.69	−0.01	0.03	−0.33	0.74	0.03	0.04	0.83	0.41
Percentage of comorbid Depressive Disorders	−0.06	0.05	−1.21	0.22	−0.03	0.06	−0.58	0.56	−0.05	0.08	−0.63	0.53
Percentage of comorbid Anxiety Disorders	0.03	0.01	2.59	0.01	0.04	0.02	2.41	0.02	0.02	0.03	0.60	0.55
Baseline CY-BOCS Symptom Severity	−0.09	0.23	−0.40	0.69	−0.20	0.16	−1. 24	0.21	0.54	0.33	1.66	0.10
Percentage of participants on a SRI	−0.00	0.01	−0.06	0.95	−0.01	0.01	0.70	0.48	−0.01	0.02	−0.67	0.50
Number of 1-hour Therapy Sessions	0.13	0.05	2.75	0.005	0.08	0.10	0.84	0.40	0.23	0.11	2.01	0.04
Percentage of Active Treatment Dropout	−0.07	0.03	−2.57	0.01	−0.05	0.06	−0.97	0.33	−0.09	0.05	−1.79	0.07
Methodological Quality	−0.09	0.07	−1.29	0.20	−0.11	0.06	−1.84	0.07	0.14	0.14	0.96	0.34
		Q	***(df)***	***p***		***Q***	***(df)***	***p***		***Q***	***(df)***	***p***
Treatment Subtype (ERP vs. CT)		0.08	1	0.78		0.55	1	0.46		0.34	1	0.56
Outcome Measure		NA	NA	NA		1.04	1	0.31		1.39	1	0.24
CBT Trials versus Active Comparisons	**Treatment Efficacy (*n*=3)**				**Treatment Response (*n*=3)**				**Symptom Remission (*n*=3)**			
Study Characteristics	***B***	***SE***	***z***	***p***	***B***	***SE***	***z***	***p***	***B***	***SE***	***z***	***p***
Mean Participant Age	−0.10	0.12	−0.79	0.43	0.05	0.08	0.62	0.53	0.05	0.12	0.39	0.70
Percentage of comorbid TS or CTD	0.10	0.04	2.67	0.01	0.02	0.04	0.46	0.64	−0.03	0.05	−0.61	0.54
Percentage of comorbid ADHD	−0.06	0.15	−0.37	0.71	−0.08	0.08	−1.00	0.32	0.04	0.11	0.40	0.69
Percentage of comorbid Depressive Disorders	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Percentage of comorbid Anxiety Disorders	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Baseline CY-BOCS Symptom Severity	−0.16	0.22	0.71	0.48	0.10	0.12	0.87	0.39	−0.08	0.17	−0.51	0.61
Percentage of participants on a SRI	−0.06	0.04	−1.67	0.10	−0.02	0.03	−0.64	0.52	0.02	0.04	0.58	0.56
Number of 1-hour Therapy Sessions	−0.10	0.12	−0.82	0.41	0.05	0.08	0.60	0.55	0.05	0.12	0.40	0.69
Percentage of Active Treatment Dropout	−0.04	0.05	−0.79	0.43	−0.02	0.03	−0.85	0.40	0.02	0.04	0.52	0.61
Methodological Quality	−0.07	0.07	0.96	0.34	0.03	0.04	0.79	0.43	−0.03	0.06	−0.54	0.59

CBT Trials versus Non-active comparisons	**Treatment Efficacy (*n*=7)**				**Treatment Response (*n*=7)**				**Symptom Remission (*n*=7)**			
Study Characteristics	***B***	***SE***	***z***	***p***	***B***	***SE***	***z***	***p***	***B***	***SE***	***z***	***p***
		Q	***(df)***	***p***		***Q***	***(df)***	***p***		***Q***	***(df)***	***p***
Treatment Subtype (ERP vs. CT)		N/A	N/A	N/A		N/A	N/A	N/A		N/A	N/A	N/A
Outcome Measure		N/A	N/A	N/A		N/A	N/A	N/A		N/A	N/A	N/A
SRI Trials versus Non-Active Comparisons	**Treatment Efficacy (*n*=11)**				**Treatment Response (*n*=7)**				**Symptom Remission (*n*=3)**			
Study Characteristics	***B***	***SE***	***z***	***p***	***B***	***SE***	***Z***	***p***	***B***	***SE***	***z***	***p***
Mean Participant Age	0.08	0.06	1.26	0.21	0.18	0.12	1.44	0.15	−0.29	1.42	−0.21	0.83
Percentage of comorbid TS or CTD	< 0.01	0.02	0.03	0.97	−0.01	0.03	−0.33	0.74	0.10	0.06	1.80	0.07
Percentage of comorbid ADHD	< −0.01	0.02	−0.31	0.76	−0.03	0.02	−1.22	0.22	0.09	0.09	0.99	0.32
Percentage of comorbid Depressive Disorders	−0.01	0.02	−0.47	0.63	<0.01	0.02	0.19	0.85	−0.03	0.08	−0.34	0.73
Percentage of comorbid Anxiety Disorders	< −0.01	0.01	−0.26	0.79	0.01	0.01	0.74	0.46	NA	NA	NA	NA
Baseline CY-BOCS Symptom Severity	< 0.01	0.05	0.09	0.93	0.10	0.09	1.14	0.26	−0.20	0.96	−0.21	0.84
Percentage of Active Treatment Dropout	−0.01	0.01	−1.40	0.16	−0.01	0.01	−0.93	0.35	−0.02	0.07	−0.24	0.81
Methodological Quality	−0.02	0.02	−1.44	0.15	−0.06	0.03	−2.01	0.04	0.34	0.18	1.91	0.06
		Q	***(df)***	***p***		***Q***	***(df)***	***p***		***Q***	***(df)***	***p***
Treatment Subtype (SSRI v. CMI)		2.55	1	0.11		2.85	1	0.09		NA	NA	NA
Outcome Measure		1.79	1	0.18		0.21	1	0.64		3.66	2	0.16

Note: TS = Tourette Syndrome, CTD = Chronic Tic Disorder, CY-BOCS = Children's Yale-Brown Obsessive-Compulsive Scale, SRI = Serotonin Reuptake Inhibitor, NA = Not Applicable,