



Published in final edited form as:

J Am Acad Child Adolesc Psychiatry. 2010 October ; 49(10): 1024–1033. doi:10.1016/j.jaac.2010.06.013.

Predictors and Moderators of Treatment Outcome in the Pediatric Obsessive Compulsive Treatment Study (POTS I)

Dr. Abbe Marrs Garcia, Ph.D,
The Alpert Medical School of Brown University

Dr. Jeffrey J. Sapyta, Ph.D,
Duke University Medical Center

Dr. Phoebe S. Moore, Ph.D,
Duke University Medical Center

Dr. Jennifer B. Freeman, Ph.D,
The Alpert Medical School of Brown University

Dr. Martin E. Franklin, Ph.D,
University of Pennsylvania School of Medicine

Dr. John S. March, M.D., M.P.H, and
Duke University Medical Center

Dr. Edna B. Foa, Ph.D
University of Pennsylvania School of Medicine

Abstract

Objective—To identify predictors and moderators of outcome in the first Pediatric OCD Treatment Study (POTS I) among youth (N=112) randomly assigned to sertraline, cognitive behavioral therapy (CBT), both sertraline and CBT (COMB), or a pill placebo.

Method—Potential baseline predictors and moderators were identified by literature review. The outcome measure was an adjusted week 12 predicted score for the Children's Yale Brown Obsessive Compulsive Scale (CY-BOCS). Main and interactive effects of treatment condition and each

Correspondence to: Dr. Abbe Garcia, Bradley/Hasbro Children's Research Center, 1 Hoppin St, Providence, RI 02903; Abbe_Garcia@Brown.edu.

Disclosure: Dr. Garcia receives research support from the National Institute of Mental Health. Dr. Freeman receives research support from the National Institute of Mental Health. Dr. Franklin receives research support from the National Institute of Mental Health. Dr. March receives research support from Eli Lilly and Co., Pfizer, the National Institute of Mental Health, and the National Alliance for Research on Schizophrenia and Depression. He has served as a consultant or scientific advisory for Bristol-Myers Squibb, Eli Lilly and Co., Johnson and Johnson, MedAvent, Pfizer, Scion, Psymetrix, and Vivus. He is a stockholder of MedAvante. He receives royalties from MultiHealth Systems, Guilford Press, and Oxford University Press. Dr. Foa receives research support from Pfizer, Solvay, Eli Lilly and Co., SmithKline Beecham, GlaxoSmithKline, Cephalon, Bristol-Myers Squibb, Forest, Ciba Geigy, Kalo-Duphar, and the American Psychiatric Association. She has served as a speaker for Pfizer, GlaxoSmithKline, Forest Pharmaceuticals, the American Psychiatric Association, and Jazz Pharmaceuticals. She has served as a consultant for Acetelion Pharmaceuticals. Drs. Sapyta and Moore report no biomedical financial interests or potential conflicts of interest.

Clinical Trials Registration Information – Treatment of Obsessive Compulsive Disorder (OCD) in Children, <http://www.clinicaltrials.gov>, NCT00000384.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

candidate predictor or moderator variable were examined using GLM on the adjusted predicted week 12 CY-BOCS scores.

Results—Youth with lower OCD severity, less OCD-related functional impairment, greater insight, fewer comorbid externalizing symptoms, and lower levels of family accommodation showed greater improvement across treatment conditions than their counterparts after acute POTS treatment. Those with a family history of OCD had a six-fold decrease in effect size in CBT monotherapy relative to their counterparts in CBT without a family history of OCD.

Conclusions—Greater attention is needed to build optimized intervention strategies for more complex youth with OCD. Youth with a family history of OCD are not likely to benefit from CBT unless offered in combination with an SSRI.

Keywords

OCD; moderators; predictors; sertraline; cognitive-behavioral therapy

“What treatment, by whom, is most effective for this individual with that specific problem, and under which set of circumstance?”¹ Through the search for predictors and moderators of treatment outcome, this question frames the ultimate goal for treatment outcome research. Thus, the endeavor of randomized controlled trials research is brought full circle as aspects of the individual seeking treatment and associated contextual factors are incorporated into the task of understanding treatment outcome. This provides a more clinically-informed and clinically-relevant knowledge base than one can achieve by simply knowing whether treatments are efficacious at the group level. This question is particularly relevant for pediatric Obsessive Compulsive Disorder (OCD) treatment because although there is growing consensus that the ideal initial treatment for OCD in youth is exposure with response prevention (EX/RP) based cognitive behavioral treatment (CBT) alone or in combination with a selective serotonin reuptake inhibitor (SRI)²⁻⁴ there is little knowledge about which treatment to recommend to particular patients.

The need for judicious allocation of treatment resources is made all the more salient because of the scarcity of CBT for OCD in the community. CBT for OCD is often only available at clinics that are affiliated with academic medical centers. If the field were able to make empirically informed triaging decisions, patients’ could receive appropriate treatment more efficiently.

Predictors and moderators are variables that are present at pre-treatment and are not associated with treatment assignment. A predictor variable has a main effect on outcome, meaning that its impact is not specific to a particular treatment condition. Predictors indicate which patients are likely to benefit from any of the treatments studied. In contrast, the impact of a moderator variable on treatment outcome is dependent on which treatment condition is considered. Moderators answer the question of which patients in which treatment conditions are likely to benefit.⁵ Identifying predictors and moderators of treatment outcome is difficult because it requires large sample sizes, larger than those that are typically recruited for efficacy studies.⁵ Therefore, the number of studies that have been able to investigate predictors or moderators of treatment outcome in *pediatric* OCD is small. A recent review of 21 treatment studies in pediatric OCD published between 1985 and 2007, found that a total of nine predictors were examined in more than one study.⁶ These predictors were gender, age, duration of illness/age at onset, baseline severity of obsessive compulsive symptoms, type of OC symptoms, comorbid disorders/symptoms, psychophysiological factors, neuropsychological factors, and family factors. The authors concluded that neither gender, age, nor duration of illness (age at onset) was associated with treatment response. Baseline severity of obsessive compulsive symptoms and family dysfunction were associated with poorer response to CBT, and comorbid tics and

comorbid oppositional defiant disorder/aggression predicted poorer response to medication-only treatment.

With the exception of one paper⁷ from the same sample as the current paper, there have been no studies examining moderators of treatment outcome in pediatric OCD. Questions about moderation require study designs with more than one treatment condition,⁵ which is rare in the pediatric OCD literature. The Pediatric OCD Treatment Study (POTS) offers a unique opportunity within the pediatric OCD field to examine possible predictors and moderators of treatment outcome because it includes 3 active treatment conditions and a placebo condition. In addition, the methodological rigors of the POTS I design (treatment manuals with fidelity checks, random assignment, and independent evaluators to assess treatment outcome) make it ideal to test hypotheses about predictors and moderators of treatment outcome.

To generate a list of potential moderators and predictors, we started with the nine categories of predictors identified in the review by Ginsburg and colleagues. We then considered predictors or moderators of treatment outcome found in adult OCD studies. Beyond the variables already identified in the pediatric OCD literature, this review resulted in one additional variable, initial insight into OCD symptoms. Foa and colleagues⁸ found that poor initial insight into OCD symptoms was associated with worse outcome in CBT. Poor insight has also been associated with poor response to drug treatment.^{9, 10}

Because similar variables might moderate other interventions across diagnoses in youth, we included moderators identified in the largest randomized controlled combined treatment trials for youth that have reported results about predictors and moderators of outcome^{11–13} Because no results about predictors or moderators have yet been reported for the Child-Adolescent Anxiety Multimodal Study,¹⁴ we included variables that had been predictors in separate studies - the largest medication trial for other anxiety disorders¹⁵ and a report of predictors of outcome in CBT.¹⁶

The list of candidates generated by this process was then reduced to those for which a POTS variable with sufficient data was available. Variables within the same conceptual grouping (e.g., severity of illness markers) and baseline intercorrelations of >0.50 were removed to reduce potential redundancy. The resulting set of variables was organized into four categories: demographics, severity of illness markers, comorbid disorders/symptoms, and family factors. Given the POTS sample size and the desire to balance hypothesis generation with avoiding spurious results, we limited the total number of variables for further investigation to 15. Because the POTS sample was 92% white, we were unable to include race/ethnicity as a variable. Because the role of comorbid tics as a moderator of outcome was previously reported,¹² and a separate paper has already addressed the impact of the cognitive and neuropsychological variables in this sample,¹⁷ neither of these factors were included in the current analyses. Table 1 includes the final 14 constructs that we examined as potential moderators.

Method

Participants

Participants were 112 patients aged 7 to 17 years with a primary diagnosis of OCD and a CY-BOCS score of 16 or higher before treatment. The sample's demographic and clinical characteristics have been previously described in detail,³ but to summarize, roughly equal numbers of males and females, as well as younger (ages 7–11) and older (ages 12–17) youth participated. Youth with major depression, bipolar illness, psychosis, any pervasive developmental disorder, or a principal diagnosis of Tourette disorder, were excluded from the study. Other exclusions were concurrent psychiatric treatment (medication or therapy) outside of the study, or evidence of 2 previous failed SRI trials or a failed CBT trial for OCD.

Procedures

The present work consists of secondary analyses of data obtained from participants who were randomly assigned to one of the four treatment conditions: CBT + sertraline (COMB; n= 28), sertraline (SER, n=28), CBT (n=28), pill placebo (PBO, n=28). Care provided in each treatment condition as well as assessment procedures used have been described elsewhere.^{4, 18} The majority of parent-report data were provided by mothers, but for some patients fathers or another guardian provided the information. The provider of this information remained the same across time points.

Measures

Child demographic characteristics: Sex, Age, Household Income—Age was measured in years. Gross family income over the past year was obtained by parent response to an item on the Conners-March Developmental Questionnaire (CMDQ).¹⁹ Income groupings were collapsed into three categories: <\$50,000; \$50,000–\$100,000; >\$100,000.

Severity of Illness Markers: Baseline OCD Symptoms, Functional Impairment, Insight

Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS).²⁰ The CY-BOCS is a semi-structured clinical interview assessing OCD severity for obsessions and compulsions. The baseline total and obsession and compulsion subscale scores were used as clinician-rated indicators of OCD symptom severity at baseline. Adequate convergent and divergent validity have been reported.^{21, 22} In this study, inter-rater reliability at baseline was good ($r=.81$, $p=.001$).⁴

Child OCD Impact Scale (COIS-C, COIS-P).²³ The COIS is a child/parent-report of the impact that OCD symptoms have on children's psychosocial functioning. The total score from each version was used as parent- and child-report indices of OCD-related functional impairment; higher scores indicated more impairment. The COIS has excellent internal consistency and preliminary evidence suggests the measure has adequate concurrent validity.²³

Fixity of Beliefs Questionnaire (FBQ).²⁴ The FBQ consisted of five interview questions designed to assess the degree to which individuals recognized that their obsessive fears and compulsions were unreasonable. For this study, only the item assessing patient's level of insight was used ("Do you think your problems or behaviors are reasonable - i.e., make sense?" Rated from 0=excellent insight, fully rational to 4=lacks insight, delusional; definitely convinced that concerns and behavior are reasonable, unresponsive to contrary evidence.) Satisfactory inter-rater reliability has been reported previously (86% agreement; ICC=.54).²⁴

Comorbid Disorders/Symptoms: Internalizing or Externalizing Diagnoses or Symptoms—*Anxiety Disorders Interview Schedule for Children (ADIS-C)*²⁵ is a structured diagnostic interview assessing DSM-IV childhood anxiety disorders and related disorders. The DSM-III-R version of the ADIS-C was widely used and has good psychometric properties.^{26–28} The DSM-IV version also has concurrent validity.²⁹ The diagnosis with the highest clinical-level Clinician Severity Rating (CSR, defined as 6 out of 10 or higher) was deemed primary; when there was a tie, co-primary status was assigned. In all cases, OCD was deemed primary or co-primary. Given that the rates of individual comorbid conditions were low, all of the mood (i.e., dysthymia; major depression) and anxiety disorders (i.e., separation anxiety disorder; social phobia, specific phobia, panic disorder with or without agoraphobia, generalized anxiety disorder, post traumatic stress disorder) were combined into a dichotomous internalizing disorder comorbidity variable (present/absent). Similarly, ADHD, ODD and CD

were combined to form an externalizing comorbidity variable that was coded dichotomously (present/absent).

Multidimensional Anxiety Scale for Children (MASC).³⁰: The MASC is a self-report measure of anxiety symptoms. The MASC has excellent test-retest reliability, internal consistency, and validity and broad-based normative data are available.³¹ The total score was used.

Conners' Parent Report Scale-Revised – Long Version (CPRS-R-L).³²: The CPRS-R-L is a parent-report measure of attention-deficit/hyperactivity disorder and related problem behaviors. It has excellent test-retest reliability, internal consistency and norms from a sample of over 8000 cases.³² The Global Index score was used.

Family Factors: Parental Psychopathology, Family History of OCD, Family Functioning

Brief Symptom Inventory (BSI).³³: The BSI is a self-report measure of psychological symptoms for adults. The measure yields global severity scores indicating the total number of symptoms and distress severity, as well as nine primary symptom subscales. The mean item score for the Global Symptom Index was used in this study. The BSI has good internal consistency, test-retest reliability over two weeks, and convergent validity.³³

Family History of OCD: During the intake assessment, parents were asked if they or anyone in their families had ever been diagnosed with OCD. For the present study, a positive family history of OCD means that either parent and/or a sibling of the identified patient had been diagnosed with OCD.

Family Assessment Measure III- General Scale (FAM-III).^{34, 35}: The General Scale, completed by parents, includes 50 statements about general family relationships and interactions. The scale includes seven clinical subscales and two response-style subscales (Social Desirability and Defensiveness). T-scores were computed for each of the seven clinical subscales and averaged to generate an Overall Rating T-score.³⁵

Family Accommodation Scale-Parent Report (FAS-PR): The FAS-PR is a 13-item parent-report instrument derived from the original FAS,³⁶ which is a clinician-rated instrument that assesses OCD-accommodating behaviors and associated distress and impairment. The FAS-PR is identical in scoring and content to the original FAS. Each item is rated on a 5-point Likert-type scale ranging from 0 to 4. A parent-report version of the FAS has been used extensively by other researchers.^{37–39} Because some studies have used a 9-item total and others have used a 13-item total, we used the item mean, computed from all 13 items, as an index of accommodation. The FAS has demonstrated good psychometric properties in previous use with adults⁴⁰ and children.³⁸

Statistical Method

The primary outcome for the predictor/moderator analyses is an adjusted week 12 predicted score on the CY-BOCS derived from a longitudinal random coefficients regression model.^{5, 41–44} The adjusted week 12 predicted score is an estimated score generated through random-coefficients regression that is adjusted for the fixed (treatment, time, treatment x time) and random (patient, patient x time) effects. Based on superior model fit, we used a square root transformation rather than the natural log of days from baseline, which was employed in the initial outcome paper.³ This model yielded results that were consistent with the primary findings of the original study (i.e., COMB > CBT, SER > PBO). We used analysis of variance or χ^2 to test for pre-randomization differences in the treatment arms on any of the proposed

predictors. No group differences on any of these variables were found. Variables from summed total scores were scaled by the item-mean if they had an acceptable level of missing data (< 20 % items missing). For the purposes of this paper, we used the general linear model (GLM) approach to examine the main and interaction effects of treatment and candidate predictors on the adjusted week 12 predicted scores. A candidate variable was considered a moderator if it demonstrated a significant (candidate X treatment) interaction on outcome. Candidate variables that demonstrated a significant main effect on outcome without a significant (candidate X treatment) interaction was considered a predictor. Predictors were further analyzed by creating subgroups based either on meaningful cut scores (e.g., clinical cutoff for T-scores) or by generating subgroups that contained approximately balanced numbers of participants per subgroup (e.g., median splits). The GLM procedure was repeated, omitting the interaction term, with the week 12 scores as the dependent variable and the predictor as the grouping variable. Moderators were further analyzed using the same method of creating subgroups; these subgroups were used in subsequent analyses using GLM to examine the effects of treatment on the adjusted predicted week 12 CY-BOCS scores within each subgroup of the moderator. If there was a significant treatment effect within a subgroup, Tukey posthoc tests were used to examine pairwise differences among the treatment conditions. Patients were omitted from analyses for specific measures if they had more than 20% missing data on that particular measure. No pattern was detected in the missing data, and as such, they are considered missing at random. Given the sample size and associated power, our analyses are exploratory rather than conclusive and therefore alpha was set at 0.05.

Although these analyses were largely exploratory, based on previous research there were several specific hypotheses. We expected baseline severity of OCD symptoms and family dysfunction to be associated with poorer treatment response, perhaps especially in CBT. We also expected that comorbid externalizing symptoms would be associated with poorer treatment response.

Results

Patient Disposition and Characteristics

As was previously reported,⁴ 112 patients were randomized to one of four treatment groups. Ninety-seven of the 112 patients (87%) completed the full 12 weeks of treatment. The sample was representative of youth with OCD seen in general clinical practice. On average, patient's OCD severity was in the moderate to moderately severe range prior to treatment. The mean (SD) age was 11.7 (2.7) years (range 7–17 years). Males and females were equally represented. Eighty percent of the sample had at least 1 comorbid psychiatric disorder. Forty-five of the patients (40%) had a parent and/or a sibling with OCD (n=43 parent; n=8 sibling; n=6 parent plus sibling).

Primary outcomes

The interpretation of the results regarding predictors or moderators of treatment is informed by an understanding of the primary treatment outcome results. Using the continuous measure of outcome (CY-BOCS score at week 12), combined treatment was superior to CBT ($p = .008$), to sertraline ($p = .006$), and to placebo ($p < .001$). CBT alone and sertraline alone did not differ from each other ($p = .80$), and both were superior to placebo (CBT, $p = .003$; sertraline $p = .007$).

Predictors—Results of the omnibus tests are summarized in Table 2. From the 14 candidate constructs, 15 separate variables were tested. Five variables were identified as predictors of outcome and one variable was identified as a moderator. For variables identified as predictors of outcome (column 4 of Table 2), results of subgroup analyses are presented in Table 3. For variables with more than 2 levels, Tukey posthoc tests were used to determine significance for

the pairwise comparisons. The strategy for handling missing data yielded different sample sizes for each of the analyses in Table 3.

Youth with higher baseline OCD symptom severity continued to have the higher severity scores by week 12 than did those with lower baseline symptom severity. Specifically, those with higher baseline CY-BOCS scores (CY-BOCS ≥ 24) did worse in all treatment conditions than those with lower baseline CY-BOCS scores. Similarly, participants with higher levels of OCD-related functional impairment as rated by their parent (COIS-P) did worse across all treatment conditions than did those with lower levels of OCD-related functional impairment. Patients with higher levels of comorbid externalizing symptoms (CPRS-L Global Index T ≥ 65) did worse across treatment conditions than did those with lower levels of comorbid externalizing symptoms. Patients with higher levels of family accommodation did worse across all treatment conditions than did those with lower levels of family accommodation. Although a main effect of insight was found, posthoc testing failed to find pairwise group differences among the levels of the insight variable.

Moderators—Table 2 showed that one variable, family history of OCD, moderated the effect of treatment condition. Follow up testing demonstrated that among those without a family history, COMB was superior to PBO and SER, and CBT was superior to PBO (See Table 4). Among those with a family history of OCD, there were no significant differences in outcome across the treatment conditions when each condition was examined separately.

Effect sizes associated with active treatments as compared to placebo at different levels of the moderator are presented in Table 5. In all instances effect sizes were smaller for those with a family history of OCD, but for CBT monotherapy this reduction in effect size was marked – the effect size for those with a family history was 6 and a half times smaller than for those without a family history. To examine whether differences in family accommodation could underlie this reduction in effect size, a t-test was performed using the FAS as the dependent variable. Patients with and without a family history of OCD did not differ in the amount of family accommodation reported ($t(94) = 0.56, p = .58$).

Discussion

This is the first study to investigate possible predictors and moderators of outcome among the three most commonly employed treatment approaches for pediatric OCD: CBT alone, an SSRI (sertraline) alone, and their combination. Youth entering treatment with lower OCD severity, less OCD-related functional impairment, greater insight, fewer comorbid externalizing symptoms, and lower level of family accommodation showed greater improvement regardless of treatment assignment. Family history of OCD in a first-degree relative functioned as a moderator of treatment outcome.

All measures related to OCD severity were predictors of outcome. When conceptualized in terms of OCD-related functional impairment, our result replicates the findings of Piacentini and colleagues⁴⁵ who reported that school-based functional impairment was a predictor of outcome in a CBT open trial. Although it differs from many previous controlled medication trials with children^{46–49} and CBT trials with medicated and unmedicated adults,⁵⁰ in the present study, baseline OCD symptom severity predicted worse outcome across all treatment conditions in our study. In two adult trials that also found this relationship,^{51, 52} they were able to demonstrate that people continued to benefit from exposure sessions during a follow-up phase. Therefore, our findings suggest that patients with more severe OCD may need additional sessions relative to their peers with more mild or moderate symptoms, either via a longer course of treatment than the 12 weeks (14 sessions) of therapy under investigation in this study, or via more sessions delivered within the 12-week period (e.g., twice-weekly).

Patients with higher levels of externalizing symptoms fared worse across all treatment conditions relative to their peers with lower levels of externalizing symptoms. Previous studies have reported similar findings.^{53,54} The lack of significant findings for diagnosis-level data is attributed to a lack of statistical power. A relatively small number of POTS patients met the threshold for an externalizing disorder (n=25 total, of which n=17 ADHD, n=7 ODD, and n=1 CD). Therefore, it is also not surprising that the two methods of examining the impact of externalizing problems in the present study (diagnosis versus symptoms) produced different results. When the Conners Global Index score was broken down into more narrow-band externalizing subscales, all subscales produced results consistent with the “omnibus” finding for the broad-band measure. These results suggest that the presence of elevated levels of externalizing symptoms interferes with the efficacy of the treatments in targeting OCD symptoms. This interpretation may indicate that children with comorbid externalizing issues require additional treatment components that address these issues. Future research should not only examine the efficacy of these additional treatment components but also in what sequence these additional components should be presented for youth with comorbid externalizing issues and OCD.

The negative findings for all of the demographics variables indicate that the effects of treatment are consistent and that these treatments can be used with a broad array of youth with OCD. We were unable to examine race and ethnicity as a predictor or moderator due to the low rate (8%) of non-Caucasian subjects enrolled. Therefore, caution is needed in generalizing the findings to diverse racial and ethnic groups, which is an important area for future research.

The absence of findings for the demographic variables is consistent with the majority of studies in pediatric OCD, and is reflected in Ginsburg and colleagues conclusion that gender and age are not associated with treatment response.⁶ However, it is different from results of moderator analyses of the MTA and TADS studies, both of which found socioeconomic status variables to be related to outcome. In the MTA study, those with more educated parents did better in combined treatment than in medication management alone.⁵⁵ In the TADS study, youth from high-income families, which also tended to be more highly educated, fared relatively better in CBT-containing conditions.¹³ These results point to the need to examine parental education level as a potential moderator of treatment outcome in future studies of pediatric OCD.

Findings regarding family factors were perhaps the most intriguing to emerge from these analyses. Two of the four family factors variables were associated with outcome. Family history of OCD moderated outcome. The six-fold difference in effect size for monotherapy CBT for those with and without a family history is particularly striking. A family history of OCD could attenuate CBT due to the fact that treatment involving EX/RP may require more family support than medication compliance. For example, parents and other families are often asked to assist the child at home with CBT tasks such as symptom monitoring and EX/RP homework. For parents who have OCD or have immediate family members with OCD, these activities are likely more difficult than simply monitoring medication compliance. It appears that COMB was more robust to these issues in that there was a less marked difference in effect size (2.5-fold). The clinical implications of these findings are that *perhaps* those with a family history of OCD should be offered CBT only in combination with medication. Replication of these results would be necessary before such a recommendation should be codified.

Although there was no evidence of a relationship between broad-based family dysfunction or parental psychopathology and treatment outcome, a more specific measure of family functioning was associated with outcome. Higher levels of family accommodation were associated with poorer treatment outcome across treatment conditions. Complementary findings have been reported elsewhere in that decreases in family accommodation predicted improvement in family-based CBT that targeted accommodation.⁵⁶ The CBT delivered in this

study allowed other family members to participate in sessions as needed, but it was not conceptualized as a family-based treatment. These results suggest that when levels of accommodation are high, more family work and explicit focus on reducing accommodation may be warranted. It is possible that there is a link between accommodation and family history. Although the present study was underpowered to identify moderation controlling for covariates, it is possible that there is a functional influence between family history of OCD and accommodation of OCD.

These results must be understood in the context of several limitations. First, although one of the largest randomized samples pediatric OCD, the study was not powered adequately to examine questions of moderators across 4 treatment conditions. Therefore, the absence of findings should not be taken as findings of absence. We consider this work exploratory and hypothesis generating.

With one exception, nothing in the present report invalidates the conclusion of the primary paper³ that patients with OCD should start treatment with either CBT or CBT + medication. Specifically for those with a family history of OCD, CBT with E/RP appears to be dramatically hindered unless augmented with SSRI treatment. The present results also suggest specific groups of patients for whom the standard treatment approaches may be less efficacious. Specifically, the present results suggest the need for further examination of the following: longer duration than 12 weeks of treatment or more intensive visit schedule for those with more severe symptoms, augmentation strategies (either pharmacological or psychotherapies) that target externalizing symptoms, and family-based treatment strategies that address the fact that more than one family member may be affected by OCD and can address high levels of family accommodation. Future work will be able to address whether the specific predictors and moderator identified in the present study convey to other samples of youth with OCD.

Acknowledgments

The Pediatric OCD Treatment Study was supported by NIMH grants R01 MH55126 (PI: Edna B. Foa) and R01 MH55121 (PI: John S. March). Sertraline and matching placebo were provided to the POTS under an independent educational grant from Pfizer Inc to Dr. March.

The authors would like to thank the many research assistants that have supported the coordination and acquisition of data for this study. The authors would like to dedicate this paper to the memory of Henrietta Leonard, M.D.

References

1. Paul GL. Strategy of outcome research in psychotherapy. *J Consult Psychol* 1967;31:109–118. [PubMed: 5342732]
2. Practice Parameters for the Assessment and Treatment of Children and Adolescents With Obsessive-Compulsive Disorder. *J Am Acad Child Adolesc Psychiatry* 1998;37(10, Supplement 1):27S–45S. [PubMed: 9785727]
3. March JS, Frances A, Carpenter D, et al. Treatment of obsessive-compulsive disorder. *J Clin Psychiatry* 1997;58(suppl 4):2–72. [PubMed: 9183300]
4. Pediatric OCD Treatment Study Team [POTS]. Cognitive-behavior therapy, sertraline, and their combination with children and adolescents with Obsessive-Compulsive Disorder: The Pediatric OCD Treatment Study (POTS) randomized controlled trial. *JAMA* 2004;292(16):1969–1976. [PubMed: 15507582]
5. Kraemer HC, Wilson GT, Fairburn CG, Agras WS. Mediators and moderators of treatment effects in randomized clinical trials. *Arch Gen Psychiatry* 2002;59(10):877–883. [PubMed: 12365874]
6. Ginsburg GS, Kingery JN, Drake KL, Grados MA. Predictors of Treatment Response in Pediatric Obsessive-Compulsive Disorder. *J Am Acad Child Adolesc Psychiatry* 2008;47(8):868–878. 810.1097/CHI.1090b1013e3181799ebd. [PubMed: 18596553]

7. March JS, Franklin M, Leonard H, et al. Tics moderate treatment outcome with sertraline but not cognitive-behavior therapy in pediatric obsessive-compulsive disorder. *Biol Psychiatry* 2007;61:344–347. [PubMed: 17241830]
8. Foa EB, Abramowitz JS, Franklin ME, Kozak MJ. Feared consequence, fixity of belief, and treatment outcome in patients with Obsessive-Compulsive Disorder. *Behavior Therapy* 1999;30:717–724.
9. Ravi Kishore V, Samar R, Janardhan Reddy YC, Chandrasekhar CR, Thennarasu K. Clinical characteristics and treatment response in poor and good insight obsessive-compulsive disorder. *European Psychiatry* 2004;19(4):202–208. [PubMed: 15196601]
10. Shetti CN, Reddy YCJ, Kandavel T, et al. Clinical Predictors of Drug Nonresponse in Obsessive-Compulsive Disorder. *J Clin Psychiatry* 2005;66(12):1517–1523. [PubMed: 16401151]
11. MTA Cooperative Group. Moderators and mediators of treatment response for children with attention-deficit/hyperactivity disorder: The multimodal treatment study of children with attention-deficit/hyperactivity disorder. *Arch Gen Psychiatry* 1999;56(12):1088–1096. [PubMed: 10591284]
12. Owens EB, Hinshaw SP, Kraemer HC, et al. Which treatment for whom for ADHD? Moderators of treatment response in the MTA. *J Consult Clin Psychol* 2003;71(3):540–552. [PubMed: 12795577]
13. Curry J, Rohde P, Simons A, et al. Predictors and Moderators of Acute Outcome in the Treatment for Adolescents With Depression Study (TADS). *J Am Acad Child Adolesc Psychiatry* 2006;45(12):1427–1439. [PubMed: 17135988]
14. Walkup JT, Albano AM, Piacentini J, et al. Cognitive Behavioral Therapy, Sertraline, or a Combination in Childhood Anxiety. *N Engl J Med* December 25;2008 359(26):2753–2766. [PubMed: 18974308]
15. Walkup JT, Labellarte MJ, Riddle MA, et al. Searching for moderators and mediators of pharmacological treatment effects in children and adolescents with anxiety disorders. *Journal of the American Academy of Child & Adolescent Psychiatry* 2003;42(1):13–21. [PubMed: 12500072]
16. Southam-Gerow MA, Kendall PC, Weersing VR. Examining outcome variability: Correlates of treatment response in a child and adolescent anxiety clinic. *J Clin Child Psychol* 2001;30(3):422–436. [PubMed: 11501258]
17. Flessner CA, Allgair A, Garcia AM, et al. The impact of neuropsychological functioning on treatment outcome in pediatric Obsessive-Compulsive Disorder. *Depress Anxiety* 2010;27(4):365–371. [PubMed: 19842168]
18. Franklin M, Foa E, March JS. The Pediatric Obsessive-Compulsive Disorder Treatment Study: Rationale, Design, and Methods. *J Child Adolesc Psychopharmacol* 2003;13(supplement 1):39–51.
19. Conners, CK. Conners-March Developmental Questionnaire. March, JS., editor. North Tonawanda, NY: Multi-Health Systems, Inc; 1994.
20. Scahill L, Riddle MA, McSwiggan-Hardin M, et al. Children's Yale-Brown Obsessive-Compulsive Scale: Reliability and validity. *J Am Acad Child Adolesc Psychiatry* 1997;36:844–852. [PubMed: 9183141]
21. Yucelen AG, Rodopman-Arman A, Topcuoglu V, Yazgan MY, Fisek G. Interrater reliability and clinical efficacy of Children's Yale-Brown Obsessive-Compulsive Scale in an outpatient setting. *Compr Psychiatry* 2006;47:48–53. [PubMed: 16324902]
22. Storch EA, Murphy TK, Adkins JW, et al. The Children's Yale-Brown Obsessive-Compulsive Scale: Psychometric properties of child-and parent-report formats. *J Anxiety Disord* 2006;20(8):1055–1070. [PubMed: 16503111]
23. Piacentini J, Bergman RL, Keller M, McCracken J. Functional impairment in children and adolescents with obsessive-compulsive disorder. *J Child Adolesc Psychopharmacol* 2003;13(Supplement 1):S61–S69. [PubMed: 12880501]
24. Foa EB, Kozak MJ. DSM-IV field trial: Obsessive-compulsive disorder. *Am J Psychiatry* 1995;152(1):90–96. [PubMed: 7802127]
25. Silverman, WK.; Albano, AM. Anxiety disorders interview schedule for DSM-IV. San Antonio: The Psychological Corporation; 1996.
26. Silverman W, Eisen A. Age differences in the reliability of parent and child reports of child anxious symptomatology using a structured interview. *J Am Acad Child Psychiatry* 1992;31(1):117–124.
27. Silverman W, Nelles W. The Anxiety Disorders Interview Schedule for Children. *J Am Acad Child Adolesc Psychiatry* 1988;27(6):772–778. [PubMed: 3198566]

28. Silverman W, Rabian B. Test-retest reliability of the DSM-III-R childhood anxiety disorders symptoms using the Anxiety Disorders Interview Schedule for Children. *J Anxiety Disord* 1995;9(2):139–150.
29. Wood JJ, Piacentini JC, Bergman RL, McCracken J, Barrios V. Concurrent validity of the anxiety disorders section of the Anxiety Disorders Interview Schedule for DSM-IV: Child and Parent Versions. *Journal of Clinical Child and Adolescent Psychology* 2002;31(3):335–342. [PubMed: 12149971]
30. March, J. *Multidimensional Anxiety Scale for Children*. North Tonawanda, NY: Multi-Health Systems Inc; 1997.
31. March JS, Parker J, Sullivan K, Stallings P, Conners K. The Multidimensional Anxiety Scale for Children MASC. *J Am Acad Child Adolesc Psychiatry* 1997;36:554–565. [PubMed: 9100431]
32. Conners, CK. *Conners' Rating Scales-Revised: Instruments for Use with Children and Adolescents*. North Tonawanda, NY: Mutli-Health Systems; 1997.
33. Derogatis L, Melisaratos N. The Brief Symptom Inventory: An Introductory Report. *Psychol Med* 1983;13(3):595–605. [PubMed: 6622612]
34. Skinner HA, Steinhauer PD, Santa-Barbara J. *The Family Assessment Measure*. *Can J Commun Ment Health* 1983;2:91–105.
35. Skinner, HA.; Steinhauer, PD.; Santa-Barbara, J. *Family Assessment Measure-III Manual*. Toronto, Canada: Multi Health Systems; 1995.
36. Calvocoressi L, Mazure C, Kasl SV, et al. Family accommodation of obsessive-compulsive symptoms. *J Nerv Ment Dis* 1999;187(10):636–642. [PubMed: 10535658]
37. Peris TS, Bergman RL, Langley A, Chang S, McCracken JT, Piacentini J. Correlates of Accommodation of Pediatric Obsessive-Compulsive Disorder: Parent, Child, and Family Characteristics. *J Am Acad Child Adolesc Psychiatry*. Aug 21;2008
38. Storch EA, Geffken GR, Merlo LJ, et al. Family accommodation in peditrict obsessive-compulsive disorder. *Journal of Clinical Child and Adolescent Psychology* 2007;36(2):207–216. [PubMed: 17484693]
39. Stewart SE, Beresin C, Haddad S, Stack DE, Fama J, Jenike M. Predictors of accommodation in obsessive-compulsive disorder. *Ann Clin Psychiatry* 2008;20(2):65–70. [PubMed: 18568577]
40. Calvocoressi L, Lweis B, Harris M, et al. Family accommodation in obsessive-compulsive disorder. *Am J Psychiatry* 1995;152:441–443. [PubMed: 7864273]
41. Brown, H.; Prescott, R. *Applied mixed models in medicine*. New York: John Wiley and Sons; 1999.
42. Gueorguieva R, Krystal JH. Move over ANOVA: Progress in analyzing repeated measures data and its reflection in papers published in the Srchives of General Psychiatry. 2004;61(3):310–317.
43. Raudenbush, SW.; Bryk, AS. *Hierarchical linear models: Applications and data analysis methods*. 2. Thousand Oaks, CA: Sage; 2002.
44. Singer, JD.; Willet, JB. *Applied longitudinal data analysis: Modeling change and event occurrence*. New York: Oxford University Press; 2003.
45. Piacentini J, Bergman L, Jacobs C, McCracken JT, Kretchman J. Open trial of cognitive behavior therapy for childhood obsessive-compulsive disorder. *J Anxiety Disord* 2002;16:207–219. [PubMed: 12194545]
46. Flament MF, Rapoport JL, Berg CJ, et al. Clomipramine treatment of childhood obsessive-compulsive disorder. *Arch Gen Psychiatry* 1985;42:977–983. [PubMed: 3899048]
47. 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;43(11):1387–1396. [PubMed: 15502598]
48. Leonard HL, Swedo SE, Rapoport JL, et al. Treatment of obsessive-compulsive disorder with clomipramine and desipramine in children and adolescents. *Arch Gen Psychiatry* 1989;46:1088–1092. [PubMed: 2686576]
49. March JS, Biederman J, Wolkow R, et al. Sertraline in children and adolescents with obsessive-compulsive disorder: A multicenter randomized controlled trial. *JAMA* 1998;280(20):1752–1756. [PubMed: 9842950]

50. Steketee G, Shapiro LJ. Predicting behavioral treatment outcome for agoraphobia and obsessive compulsive disorder. *Clin Psychol Rev* 1995;15(4):317–346.
51. Keijsers GPJ, Hoogduin CAL, Schaap CPDR. Predictors of treatment outcome in the behavioural treatment of obsessive-compulsive disorder. *Br J Psychiatry* 1994;165(6):781–786. [PubMed: 7661936]
52. de Haan E, van Oppen P, van Balkom AJLM, Spinhoven P, Hoogduin KAL, Van Dyck R. Prediction of outcome and early vs. late improvement in OCD patients treated with cognitive behaviour therapy and pharmacotherapy. *Acta Psychiatr Scand* 1997;96(5):354–361. [PubMed: 9395153]
53. Masi G, Millepiedi S, Mucci M, Bertini N, Milantoni L, Arcangeli F. A naturalistic study of referred children and adolescents with obsessive-compulsive disorder. *J Am Acad Child Adolesc Psychiatry* 2005;44(7):673–681. [PubMed: 15968236]
54. Wever C, Rey JM. Juvenile obsessive-compulsive disorder. *Aust N Z J Psychiatry* 1997;31:105–113. [PubMed: 9088493]
55. Rieppi R, Greenhill LL, Ford RE, et al. Socioeconomic Status as a Moderator of ADHD Treatment Outcomes. *J Am Acad Child Adolesc Psychiatry* 2002;41(3):269–277. [PubMed: 11886021]
56. Merlo LJ, Lehmkuhl HD, Geffken GR, Storch EA. Decreased family accommodation associated with improved therapy outcome in pediatric obsessive-compulsive disorder. *J Consult Clin Psychol* Apr; 2009 77(2):355–360. [PubMed: 19309195]
57. 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;40(2):222–229. [PubMed: 11211371]
58. Barrett P, Farrell L, Dadds M, Boulter N. Cognitive-behavioral family treatment of childhood obsessive-compulsive disorder: Long-term follow-up and predictors of outcome. *J Am Acad Child Adolesc Psychiatry* 2005;44(10):1005–1014. [PubMed: 16175105]
59. Wagner KD, Cook EH, Chung H, Messig M. Remission status after long-term sertraline treatment of pediatric obsessive-compulsive disorder. *J Child Adolesc Psychopharmacol* 2003;13(2):S53–s60. [PubMed: 12880500]
60. Kishore VR, Samar R, Janardhan Reddy YC, Chandrasekhar CR, Thennarasu K. Clinical characteristics and treatment response in poor and good insight obsessive-compulsive disorder. *European Psychiatry* 2004;19(4):202–208. [PubMed: 15196601]
61. RUPP ASG. Treatment of pediatric anxiety disorders: an open-label extension of the research units on pediatric psychopharmacology anxiety study. *J Child Adolesc Psychopharmacol* 2002;12(3):175–188. [PubMed: 12427292]
62. Leonard HL, Swedo SE, Lenane M, et al. A 2- to 7-year follow-up study of 54 obsessive-compulsive children and adolescents. *Arch Gen Psychiatry* 1993;50:429–439. [PubMed: 8498877]
63. Yaryura-Tobias JA, Grunes MS, Walz J, Neziroglu F. Parental obsessive-compulsive disorder as a prognostic factor in a year long fluvoxamine treatment in childhood and adolescent obsessive-compulsive disorder. *Int Clin Psychopharmacol* 2000;15(3):163–168. [PubMed: 10870874]

Table 1

Variables examined as potential moderators of Acute Treatment Outcome

Category/POTS Variable	Results of Previous Studies ^a	
	Previous Moderator	Previous Predictor
Demographics		
Gender		46
Age		13, 57, 16
Household Income	11, 13	
Severity of Illness Markers		
Baseline OCD Severity		58, 45, 53, 59
Functional Impairment		58
Insight		8, 60, 10
Comorbidity		
Internalizing Diagnosis	11	53, 61
Externalizing Diagnosis		53, 54
Anxiety Symptoms		58
Externalizing Symptoms		54
Family Factors		
Parental Psychopathology	12, 57	62, 63
Family History OCD		63
Family Functioning		58
Accommodation		56

Note: OCD = Obsessive Compulsive Disorder; POTS = Pediatric Obsessive Compulsive Treatment Study.

^aNumbers refer to citations in the Reference list.

Table 2

Predictors and Moderators of Acute Outcome in the First Pediatric Obsessive Compulsive Disorder Treatment Study (POTS I)

Category/Variable (measure)	Variable F (df)	Variable x Treatment F(df)	Status
Demographics			
Gender (M/F)	.03 (1, 104)	.78 (3, 104)	
Age (yrs)	.51 (1, 104)	.11 (3, 104)	
Household Income	1.10 (2, 90)	.57 (6, 90)	
Severity of Illness Markers			
Baseline OCD Severity			
(CY-BOCS)	41.12 ^{***} (1, 104)	1.01 (3, 104)	P
Functional Impairment			
(COIS-P)	17.72 ^{***} (1, 96)	1.94 [*] (3, 96)	P
(COIS-C)	2.26 (1, 89)	2.06 (3, 89)	
Insight (FBQ)	2.98 [*] (3, 79)	.69 (8, 79)	P
Comorbid Disorders or Symptoms at Baseline			
Any Internalizing Diagnosis (ADIS-C)	1.61 (1, 100)	.52 (3, 100)	
Any Externalizing Diagnosis (ADIS-C)	.12 (1, 100)	.70 (3, 100)	
Anxiety Symptoms (MASC)	.78 (1, 91)	.88 (3, 91)	
Externalizing Symptoms (CPRSL- Global Index score)	8.52 ^{**} (1, 88)	.99 (3, 88)	P
Family Factors			
Parental Psychopathology- (BSI)	3.67 (1, 92)	2.04 (3, 92)	
First-Degree Family History OCD (Y/N)	.03 (1, 104)	2.70 [*] (3, 104)	Mo
Family Functioning – Overall (FAM-III – Overall T-score)	.03 (1, 96)	.12 (3, 96)	
Accommodation (FAS-PR)	8.75 ^{**} (1, 88)	1.32 (3, 88)	P

Note: ADIS-C = Anxiety Disorders Interview Schedule for Children; BSI = Brief Symptom Inventory; COIS-C = Child OCD Impact Scale – Child report; COIS-P = Child OCD Impact Scale – Parent Report; CPRSL = Conners Parent Report Scale – Long Version; CY-BOCS = Children's Yale Brown Obsessive Compulsive Scale; df=degrees of freedom; F = female; FAM-III = Family Assessment Measure – Third Edition; FAS-PR = Family Accommodation Scale-Parent Report; FBQ = Fixity of Beliefs Scale; M = male; MASC = Multidimensional Anxiety Scale; Mo = Moderator; N = no; OCD = Obsessive Compulsive Disorder; P = Predictor; Y = yes; Yrs = years.

* p <.05,

** p <.01,

*** p <.001.

Table 3

Subgroup Estimated Means for Adjusted Week 12 Predicted Children's Yale-Brown Obsessive Compulsive Scale Scores

Predictor	Subgroup	n	Estimated Wk12	Group
			Mean (SD)	Differences
Baseline OCD Severity (CY-BOCS)	1. < 24	1. 45	1. 11.86 (5.99)	1 < 2***
	2. ≥ 24	2. 67	2. 17.73 (5.96)	
OCD-related Functional impairment (COIS-P)	1. T < 65	1. 68	1. 14.07 (6.12)	1 < 2***
	2. T ≥ 65	2. 14	2. 23.68 (6.25)	
Insight (FBQ)	1. excellent insight	1. 12	1. 19.86 (7.10)	none
	2. good insight	2. 43	2. 13.64 (6.64)	
	3. fair insight	3. 30	3. 15.77 (6.50)	
	4. poor insight	4. 9	4. 16.91 (7.09)	
Externalizing Symptoms (CPRSL-Global Index T)	1. T < 65	1. 57	1. 13.69 (6.40)	1 < 2**
	2. T ≥ 65	2. 33	2. 17.66 (6.45)	
Accommodation (FAS-PR)	1. below median (2.62)	1. 47	1. 13.76 (6.68)	1 < 2*
	2. at or above median	2. 45	2. 16.55 (6.67)	

Note: COIS-P = Child OCD Impact Scale – Parent report; CPRSL = Conners Parent Report Scale – Long Version; CY-BOCS = Children's Yale Brown Obsessive Compulsive Scale; FAS-PR = Family Accommodation Scale-Parent Report; FBQ = Fixity of Beliefs Scale; OCD= Obsessive Compulsive Disorder.

* p < .05,

** p < .01,

*** p < .001.

Table 4
 Moderator of Acute Treatment Outcome in the First Pediatric Obsessive Compulsive Disorder Treatment Study (POTS I)

Moderator	n	Treatment Condition/Estimated Means (SD)				F
		COMB	CBT	SER	PBO	
First-Degree Family History of OCD						
No Family History	67	8.67 ^a (5.30)	13.28 ^{a,b} (6.44)	16.67 ^{b,c} (8.55)	22.15 ^{b,c} (4.21)	15.29 ^{***}
Yes Family History	45	12.77 (5.54)	16.67 (8.05)	13.89 (7.16)	18.27 (4.28)	1.44

Note: Means with the same superscript are not significantly different. CBT = cognitive-behavioral therapy; COMB = combination treatment; OCD = Obsessive Compulsive Disorder; PBO = placebo; SER = sertraline.

*** p < .001.

Table 5Effect Sizes (*d*) for Active Treatments at Different Levels of Moderator

Treatment	<u>First-Degree Family History of OCD</u>	
	No (n=67)	Yes (n=45)
COMB	2.82	1.11
CBT	1.63	.25
SERT	.81	.74

Note: Effect sizes are calculated on adjusted week 12 predicted Children's Yale Brown Obsessive Compulsive Scale (CY-BOCS) scores. CBT = cognitive-behavioral therapy; COMB = combination treatment; OCD = Obsessive Compulsive Disorder; PBO = placebo; SER = sertraline.