

## Supplementary Online Content

Franklin ME, Sapyta J, Freeman J, et al. Cognitive Behavior Therapy Augmentation of Pharmacotherapy in Pediatric Obsessive Compulsive Disorder: the Pediatric OCD Treatment Study II (POTS II) Randomized, Controlled Trial. *JAMA*. 2011;306(11):1224-1232.

**eAppendix.** Post hoc Analysis of the Effect of Remaining on Initially Assigned Treatment

This supplementary material has been provided by the authors to give readers additional information about their work.

## eAppendix. Post Hoc Analysis of the Effect of Remaining on Initially Assigned Treatment

By design, participants in each treatment group who for clinical reasons such as marked increase in psychiatric symptoms, severe adverse reactions to medication, or dangerousness to self/others were considered premature terminators and were then recommended by study staff for ancillary treatment. For example, patients with a marked increase in OCD symptoms but randomized to treatment arms other than MM+CBT could then be eligible to receive open label CBT and/or adjust medications freely. Another common case was for patients to experience a marked increase of other psychiatric symptoms (e.g., depression), which led them to be prematurely terminated so these emergent symptoms could be addressed appropriately. Combined, 17 participants were considered premature terminators (see the **FIGURE** below). Of the 17, 7 who were offered ancillary treatment refused and subsequently dropped out of the study. The other 10 (MM-only = 7; MM+I-CBT = 1; MM+CBT = 2) were provided with ancillary treatment outside of the protocol, yet continued to be assessed for the duration of the study. In this secondary, post-hoc analyses, we compared mean outcomes between participants who remained in MM-only (n=30) versus those who remained in MM+I-CBT (n=34) versus those who remained in MM+CBT (n=37) for the entire duration of the acute phase of the study.

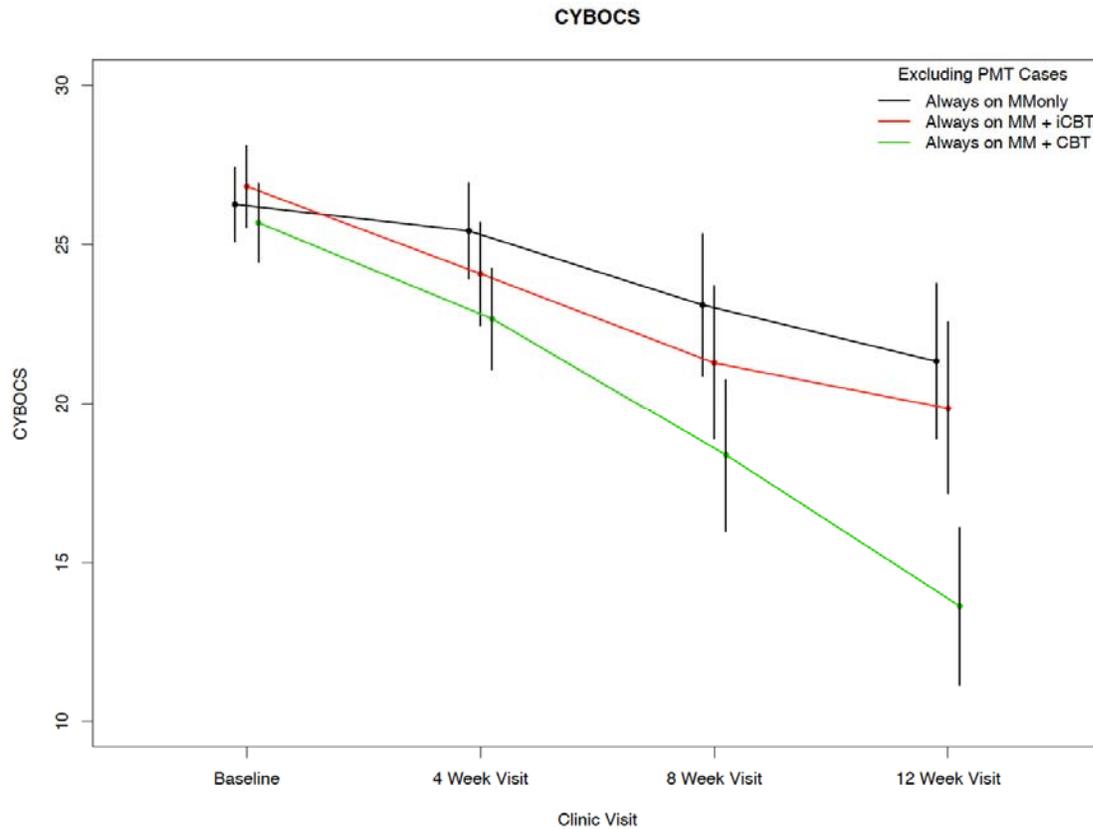
The results of the post-hoc analysis mirrored those found in the ITT analysis. In the post-hoc analysis, the percentages of participants at 12 weeks who had at least a 30% reduction in CY-BOCS baseline score were: 72.0% in MM+CBT, (95% CI, 57.4% to 86.6%), 34.9% in MM+I-CBT (95% CI, 18.6% to 51.2%), and 27.4% in MM-only (95% CI, 10.9% to 43.9%). The combined multivariate chi-square test<sup>12</sup> indicated a significant difference between groups ( $F(2, 136.57) = 6.44, p < 0.002$ ). Planned pairwise comparisons<sup>2</sup> show that MM+CBT was superior to both MM-only ( $t(73.44) = 3.77, p < 0.001$ ) and MM+I-CBT ( $t(339.35) = 3.37, p < 0.001$ ); MM+I-CBT was not statistically significant from MM-only ( $t(113.49) = 0.63, p = 0.53$ ). Planned pairwise comparisons<sup>2</sup> of CY-BOCS continuous Week 12 outcomes were comparable to the findings for RESPONSE: MM+CBT was superior to both MM-only ( $t(347.72) = 4.35, p < 0.0001$ ) and MM+I-CBT ( $t(346.22) = 3.35, p = 0.001$ ), and MM+I-CBT and MM-only were not significantly different from each other ( $t(253.95) = 0.81, p = 0.42$ ). In all secondary outcomes, MM+CBT was superior to MM+I-CBT and MM-only, which did not differ significantly from one another. Treatment effect sizes for Week 12 CY-BOCS outcomes were 0.92 (95% CI, 0.51 to 1.34) for MM+CBT v. MM-only; 0.75 (95% CI, 0.31 to 1.18) for MM+CBT v. MM+ I-CBT; and 0.18 (95% CI, -0.26 to 0.61) for MM+I-CBT vs. MM-only. The number needed to treat for MM+CBT versus MM-only to see one additional responder was 2; for MM+CBT versus MM+I-CBT was 3; and for MM+I-CBT versus MM-only was 14. The below **TABLE** provides a detailed description of point estimates, pair-wise comparisons, and the respective effect sizes on each continuous variable.

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<sup>1</sup> When conducting analyses based on imputed data sets, Chi-square results are combined and reported commonly as an F-statistic. In our case, we used the SAS macro COMBCHI (Allison, PD. SAS Macros. <http://www.pauldallison.com/Download3.html>. Updated June 14<sup>th</sup>, 2011. Accessed June 14<sup>th</sup>, 2011.)

<sup>2</sup> Adjusted degrees of freedom are presented as suggested by Barnard and Rubin (1999) and implemented using the EDF option in SAS (Barnard, J., and Rubin, D.B. (1999). "Small-sample degrees of freedom with multiple imputation." *Biometrika* 86(4), 948-955.)

**Figure.** Estimated mean CY-BOCS scores at each time point for subjects who remained in their assigned study arm without ancillary treatment



Points are group-specific estimated mean CY-BOCS scores at each time point for subjects who remained in their assigned study arm without ancillary treatment. Point-estimates were derived from the fitted linear mixed models, averaged over site, gender, age (<12 versus  $\geq 12$ ), and baseline severity (CGI-S < 5 versus  $\geq 5$ ). Error bars are point-wise 95% CIs.

**Table.** In-Protocol Treatment Analysis

Effect Sizes	Responder Status	CY-BOCS	NIMH-GOCS
MM+CBT v. MM-Only	0.45 (0.21, 0.68)	0.92 (0.51, 1.34)	0.98 (0.54, 1.43)
MM+CBT v. MM+I-CBT	0.37 (0.15, 0.59)	0.75 (0.31, 1.18)	0.75 (0.32, 1.17)
MM+I-CBT v. MM-Only	0.07 (-0.16, 0.31)	0.18 (-0.26, 0.61)	0.24 (-0.19, 0.66)

Abbreviations: CY-BOCS, Children's Yale-Brown Obsessive Compulsive Scale; NIMH: National Institute of Mental Health Global Obsessive Compulsive Scale; MM = Medication Management; I-CBT: Instruction in Cognitive Behavioral Therapy Procedures by Psychiatrist; CBT: Cognitive Behavioral Therapy by Psychologist.

<sup>a</sup> Responder Status scores range from 0.0 to 1.00 reflecting the percentage of responders.

<sup>b</sup> CY-BOCS scores range from 0 to 40 with larger scores reflecting more OCD symptoms.

<sup>c</sup> NIMH-GOCS scores range from 1 to 15 with larger scores reflecting more OCD symptoms.

<sup>d</sup> For Responder Status: estimated rate of response (30% reduction of CY-BOCS from baseline) at Week 12 (95% CI). For CY-BOCS, NIMH, and CGI-S estimated mean score at Week 12 (95% CI) from the fitted linear mixed models, averaged over site, gender, age (<12 versus ≥12), and baseline severity (CGI-S<5 versus ≥5).

<sup>e</sup> For Responder Status: between-groups difference in estimated response rate at Week 12 (95% CI). For CY-BOCS, NIMH, and CGI-S: between-groups difference in estimated mean score at Week 12 divided by the pooled standard deviation of the outcome at Week 12, otherwise known as Cohen's *d* (95% CI). Cohen's *d* between 0.50-0.79 is considered a medium effect; Cohen's *d* ≥ 0.80 is considered a large effect.<sup>3</sup> All effect size estimates are reported such that positive scores indicate that the first treatment group was superior to the comparison group in functioning.

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<sup>3</sup> Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2nd ed.). New Jersey: Lawrence Erlbaum.