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Cost-Effectiveness of Treatment Alternatives for Treatment-Refractory Pediatric Obsessive-Compulsive Disorder

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ABSTRACT

Purpose: Current guidelines for first-line treatment of childhood OCD are cognitive-behavioral therapy (CBT) utilizing exposure and response prevention (ERP), and/or antidepressant (ADM) pharmacotherapy, specifically serotonin reuptake inhibitors (SRI). Given that first-line are relatively similar in terms of clinical effectiveness, the role of costs to provide such services may help influence treatment decisions. In the case of treatment refractory pediatric OCD, this cost-effectiveness analysis (CEA) aims to further evaluate two additional, higher intensity combination therapies, namely OCD-specific Intensive Outpatient (IOP) and Partial Hospitalization Programs (PHP), to determine the additional benefits, in terms of effectiveness, that may result, and the corresponding increase in costs for these higher-intensity courses of therapy.

Results: IOP was the most cost-effective strategy in terms of change in CY-BOCS, pre/post treatment, equal to 16.42 units, followed by PHP and CBT monotherapy augmented with ADM CBT-monotherapy augmented with additional CBT and ADM-only augmented with CBT followed closely with 15.56 and 14.75 unit improvements in CY-BOCS. IOP accomplished its superior cost-effectiveness with an Incremental Cost-Effectiveness Ratio (ICER), of $48,834, lower than either of the established willingness to Pay thresholds.

Conclusions: Lack of access to high fidelity, high dose CBT paired with pharmacotherapy is an issue for OCD patients and families. Among youth who were treatment non-responsive, these results indicate the superiority of a high dosage CBT strategy, indicating the need to increase access to these treatments.

1. Introduction

Obsessive-compulsive disorder (OCD) affects 1-2% of children and adolescents (Zohar, 1999), confers significant functional (Storch, Larson et al., 2010) and familial (Lebowitz, Panza, & Bloch, 2016; Wu et al., 2016) impairment, and negatively impinges upon quality of life (Lack et al., 2009). Without treatment, children are at risk of experiencing chronic symptomology (Bloch et al., 2013; Stewart et al., 2004). Current guidelines for first-line treatment of childhood OCD are cognitive-behavioral therapy (CBT) utilizing exposure and response prevention (ERP), and/or antidepressant (ADM) pharmacotherapy, specifically serotonin reuptake inhibitors (SRI) (Geller & March, 2012; Lewin, Park et al., 2014; Lewin, Wu, McGuire, & Storch, 2014). As many as 85% of children respond to CBT monotherapy, while 50-60% respond to pharmacological monotherapy. It is unclear if combined treatment (CBT + ADM) confers additional benefit beyond CBT alone with some studies finding the affirmative (Pediatric OCD Treatment Study (POTS) Team (2004)), and others finding no advantage for children with OCD of moderate or worse severity (Storch et al., 2013a, 2013b). For those who fail to respond to first-line therapies, there is little evidence available to support clinicians, patients, and their parents/family in terms of what course of treatment to pursue next.

CBT is effective in reducing symptoms in treatment naïve children and adolescents, and may be more effective that pharmacotherapy alone (Ivarsson et al., 2015; McGuire et al., 2015; Pediatric OCD Treatment Study (POTS) Team (2004)). Pharmacotherapy consists of SRIs, approved for use in children and adolescents (Geller et al., 2003; Geller & March, 2012; Varigonda, Jakubovski, & Bloch, 2016). Comparison trials have demonstrated combined treatment and CBT monotherapy was more effective than ADM monotherapy; however, it remains unclear if there is a significant difference between combination therapy and CBT monotherapy for pediatric patients with moderate

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severity (Ivarsson et al., 2015; McGuire et al., 2015; Romanelli, Wu, Gamba, Mojtabai, & Segal, 2014). For pediatric patients with high severity (Franklin et al., 2011; Geller & March, 2012; Simpson et al., 2008), CBT combined with pharmacotherapy has been demonstrated to be effective (Franklin et al., 2011; Ivarsson et al., 2015).

The cost-effectiveness of treatments for refractory pediatric OCD has yet to be examined. For the purposes of this analysis, "refractory" is defined as individuals that have received an adequate dose of cognitive behavioral therapy (~12 weeks) and initiated ADM without significant improvement in symptomology, as measured by C-YBOCS. Patients initiated up to two ADM molecules without significant symptom improvement or discontinued due to lack of tolerability. This is definition of refractory is consistent inclusion criteria across the trials and admission criteria for the practice-based participants (Bloch & Storch, 2015). The contribution and advantage of cost-effectiveness analysis (CEA) is the ability to compare the effectiveness of treatments and their respective costs, ranking treatment alternatives by the incremental cost effectiveness ratio (ICER), a ratio of costs to effectiveness, therefore revealing the treatment strategies that yield the largest marginal effectiveness gain per unit of cost. Given that first-line therapies - combined ADM + CBT, and ADM and CBT monotherapy - are relatively similar in terms of clinical effectiveness, the role of costs to provide such services may help influence treatment decisions.

1.1. Intensive Outpatient (IOP) and Partial Hospitalization Programs (PHP)

In the case of treatment refractory pediatric OCD, this CEA aims to further evaluate two additional, higher intensity combination therapies, namely OCD-specific Intensive Outpatient (IOP) and Partial Hospitalization Programs (PHP), to determine the additional benefits, in terms of effectiveness, that may result, and the corresponding increase in costs for these higher-intensity courses of therapy. Intensive treatment approaches were selected given evidence (Storch et al., 2007, 2010b) supporting its effectiveness in pediatric OCD, as well as strong supporting data among adults with OCD (Abramowitz, Foa, & Franklin, 2003; Foa et al., 2005).

In clinical practice, two other treatment strategies are being employed to treat refractory OCD in adults (Gregory et al., 2018), have shown superior cost-effectiveness in adults, and should be evaluated for pediatric OCD. For adults with treatment-refractory OCD, a similar strategy, PHP with a step-down to IOP was determined to be the most cost-effective (Gregory et al., 2018), compared to trial-based strategies, followed by PHP and IOP individually. This study inherits shared outcomes data, and approach with a similar study for adults (Gregory et al., 2018). No evidence for the PHP to IOP step-down strategy was available for pediatric OCD patients; therefore, it was not included in this analysis. However, PHP and IOP strategies were included as comparisons to the seven trial-based strategies.

1.2. Treatment Strategies Evaluated

Specifically, this study compares a total of nine treatment strategies, in terms of net health benefits, costs and incremental cost-effectiveness. We compared nine treatment strategies, beginning with seven first line therapies identified in the trial literature. There are three primary strategies, (1) ADM-only (DeVeaugh-Geiss et al., 1992; Geller et al., 2001, 2004; Greist et al., 1990; Liebowitz et al., 2002; March et al., 1998; Riddle et al., 2001, 1992), (2) CBT-only (Barrett, Healy-Farrell, & March, 2004; Bolton & Perrin, 2008; DeVeaugh-Geiss et al., 1992; Freeman et al., 2014a, 2014b; Freeman et al., 2008; Geller et al., 2001, 2004; Greist et al., 1990; Lewin, Park et al., 2014, 2014b; Liebowitz et al., 2002; March et al., 1998; Pediatric OCD Treatment Study (POTS) Team (2004); Piacentini et al., 2011; Riddle et al., 2001, 1992; Skarphedinsson et al., 2015a, 2015b; Storch et al., 2013a, 2013b), and (3) combined ADM + CBT (Pediatric OCD Treatment Study (POTS) Team (2004); Storch et al., 2013a, 2013b). These three strategies are then augmented into four additional strategies, (4) ADM-only augmented with an additional continued course of ADM (Franklin et al., 2011), (5) CBT-only augmented with an additional continued course of CBT (Skarphedinsson et al., 2015a, 2015b), and (6) ADM-only, augmented with CBT (Franklin et al., 2011), and (7) combined ADM + CBT, augmented with an additional course of ADM + CBT. These 7 trial-based strategies are all ambulatory-based pharmacology (ADM) and behavioral therapy (CBT).

In addition to evidence from trials we included evidence for two additional higher-intensity strategies. Two additional strategies included two variations in CBT intensity/dosage (Kay, Eken, Jacobi, Riemann, & Storch, 2016; Storch et al., 2007, 2010b), (8) IOP consisting of 12-15 hours per week of multimodal treatment 4-5 days/week for 12 weeks, and (9) PHP consisting of 30 hours of multimodal treatment 5 days/week, for 12 weeks. Multimodal therapy included CBT and Exposure-response therapy (ERP) within the behavioral therapy regime, each week (Gregory et al., 2018). Both of these practice-based strategies also include substantial medication management and optimization of pharmacology during the course of therapy, and for the balance of the 12-months inclusive of the treatment episode.

Cost-effectiveness parameters for these strategies sourced from an outcomes database maintained by a specialty center that delivers these treatment modalities to individuals with severe OCD. Our aim in including these strategies was to synthesize the both trial evidence, and specialty center evidence for treatment effectiveness, and denominate in terms of effectiveness, to assess the reasonable treatment alternatives available to patients and families. This is consistent with the approach of intergrading trial evidence and outcomes from practice, in a recent assessment of CEA for adult refractory OCD (Gregory et al., 2018).

We hypothesize that these high intensity, multimodal treatment strategies, PHP and/or IOP, will be more cost-effective the trial-based treatment approaches. The results of this study can serve as a guide to support informed decision-making for providers, and patients and their parents regarding optimum treatment of refractory OCD among children and adolescents.

2. Materials and Methods

Our approach was adapted from previous CEA analyses for treatment-refractory OCD among adults (Gregory et al., 2018), and adhered to CHEERS good practice guidelines for cost-effectiveness analyses (Husereau et al., 2013a, 2013b), standards for decision analytic models (Hunink, 2014), and generally accepted cost-effectiveness techniques (Drummond, 2005; Gold, 1996). Departures from these standards, primarily due to paucity of parameters and evidence, are noted, as well as potential impacts of these departures are discussed relative to results and in the limitations. The adult model (Gregory et al., 2018) compared three first-line therapies with two higher intensity strategies, combining evidence from clinical trials, for first-line therapies, and results from an outcomes database for the two high intensity strategies. We followed previous work (Gregory et al., 2018), save for the elimination of a pharmacology strategy, augmenting ADM with antipsychotic medication, due to the lack of indication for this course of therapy in children. Inpatient/residential treatments strategies were eliminated from consideration, given that clinicians are unlikely to pursue inpatient treatment following initial refractory response, in favor of combination therapies with higher CBT intensity. The key difference between the model for adults, and this model and subsequent analysis for pediatric refractory OCD, is the assessment of the cost-effectiveness over a single year. We were unable to incorporate a Markov Model into our decision analytic model, to accumulate the benefits of treatment beyond the initial treatment year, due to the paucity of evidence regarding long-term (> 1 year) data regarding relapse and changes in subclinical symptomology, and the reemergence of disease in youth, and eventually adulthood for pediatric patients suffering from OCD and

receiving any of the nine strategies.

The decision analytic model (Hunink, 2014) was used to perform a Monte Carlo (MC) simulation of a hypothetical cohort of 100,000 children and adolescents with OCD to estimate costs, and incremental cost-effectiveness ratio (ICER) for each treatment strategy. First, we calculate cost-effectiveness estimates for each of the nine strategies, and sort them descending by cost, then effectiveness, in this case unit change in CY-BOCS. This differs from other CEAs, where effectiveness is denominated in quality adjust life years (QALY) (Neumann & Cohen, 2018; Weinstein, Torrance, & McGuire, 2009; Whitehead & Ali, 2010; Wouters, Naci, & Samani, 2015). The calculation of QALYs requires health utility measures for a given disease or condition, in this case OCD among youth.

Due to a lack of evidence regarding health utilities for pediatric OCD, we denominated effectiveness in terms of change in CY-BOCS, pre/post treatment. While these limits the comparison of cost-effectiveness to other diseases or conditions, it allows the comparison of treatment strategies within a specific disease, OCD in this case. The results demonstrate the cost per unit change in CY-BOCS, allow comparison and ranking of treatment alternatives, and the identification of the treatment strategy offering the largest improvement in CY-BOCS per unit of cost (2017 U.S. dollars).

Once all cost-effectiveness results are calculated, dominated strategies (e.g., strategies with lower effectiveness and higher costs) were then eliminated from further consideration. The remaining strategies were evaluated by ranking by ICER. The model included both probabilistic and deterministic parameters from the literature and an outcomes database, maintained by a specialty center providing high intensity therapy for pediatric OCD.

The model assumed a one-year period of disutility for disease, during which an individual received treatment for OCD. These results are therefore limited to reporting cost-effectiveness for one-year following treatment. Analyses were conducted from the payer perspective in the United States, evaluated using Willingness to Pay (WTP) thresholds of $50,000 and $100,000 (Drummond, 2005; Gold, 1996), and conducted commensurate with published analytical and reporting standards, deviations from which are noted above (Husereau et al., 2013a, 2013b).

2.1. Model Parameters

Model parameters were sourced from both the literature and an outcomes database. We identified effectiveness and costs estimates and the distributional characteristics, which allowed for the specifications of distributions for each model parameter. If no distributional information was available, we used a deterministic parameter from the literature. Several desired parameters were not available, including health utilities, relapse rate and excess mortality associated with OCD, as previously noted, and limiting the results to the 12 months including, and following treatment. Model parameters and their underlying distributions are summarized in Table 1.

2.1.1. Outcomes Database

A specialty center providing OCD treatment developed an outcomes database containing assessments of treatment effectiveness, quality of life assessments and costs for treatment episodes for two high intensity combined strategies (Kay et al., 2016; Storch et al., 2007, 2010b), IOP, PHP. Rogers Memorial Hospital oversees the outcomes database employed in this study. The database contained a total of 264 care episodes between 2012-2015, and financial data including net reimbursement charges for each individual. Patient assessments were given at admission, discharge, and 12-months post-discharge. From this database, we estimated distributions for treatment effects, effectiveness, and net reimbursement costs for the two higher intensity combination strategies and included them alongside the seven trial-based strategies.

To address the potential differences between trial evidence, which tends to assess efficacy of treatment due to experimental design, high fidelity of intervention, and random assignment to treatment, controlling for heterogeneity in patient populations, and effectiveness evidence from the outcomes database, we assessed the reported patient characteristics from trials and compared with the characteristics of the patient population receiving treatment from the specialty center, and found no statistically significant differences in key parameters ($p > 0.05$) including disease severity and demographics. Further, they key difference between the trial evidence and outcomes database is the lack of randomization and experimental design in the outcomes database, essentially no control group. The outcomes database reports treatment and cost outcomes for a similar patient population but lacks a control group. While reporting effectiveness versus efficacy, we believe the incorporation of the additional two strategies from the outcomes database is merited given the similarity in the patient populations, fidelity controls on the intervention. These two additional strategies are essentially augmentations of combined ADM + CBT, with significantly higher doses of CBT, longer duration of treatment, and additional structured activities than the trial-based strategies which are exclusively ambulatory, with no additional day services to support patients and families.

2.1.2. Treatment Effectiveness

Clinical outcomes were reported as changes in the CY-BOCS, and remission as ≤ 14 (Lewin et al., 2011). We used a CY-BOCS threshold of 14, for two primary reasons, (1) a higher threshold is more conservative given the high severity of disease among treatment-refractory populations, and (2) to maintain consistency and comparability with previously published work on CEA among treatment-refractory adults (Gregory et al., 2018). For this analysis, treatment effect defined as the change in CY-BOCS units, post-treatment. We used the clinical trial evidence and recent reviews to create distributions for the CY-BOCS unit change for the literature-based treatment strategies, as noted in Table 1. The outcomes databased included self-reported CY-BOCS, which reflect a bias towards lower CY-BOCS assessment (Steketee, Frost, & Bogart, 1996). Thus, effectiveness estimates for IOP, and PHP are conservative. A small subset of the database ($n = 67$) patients had both self-reported and clinician-rated CY-BOCS. We used these clinician-rated data to parameterize starting CY-BOCS. For each iteration, the randomly generated unit change was subtracted from the admission CY-BOCS drawn at simulated treatment initiation.

2.1.3. Costs and Cost-Effectiveness

Costs estimates used in this study consist of the total direct or reimbursement costs for the 12-months inclusive of the intervention, including costs for continuance of pharmacology beyond the initial course of therapy ($\sim$12 weeks) on all nine strategies, medical management related to pharmacology, and any follow-up behavioral therapy. Direct reimbursement costs are equivalent to costs faced by payers, whether government, commercial insurance coverages or private pay in the United States, adjusting for the payer mix reported in the Truven Marketscan database, which reports post-adjudicated claims data – an estimate of direct costs faced by payers. Two approaches were used to derive costs for treatment strategies. Costs for the seven trial-based strategies were estimated from the literature, as indicated in Table 1, and derived from the Truven Marketscan database (Truven). Using Truven, we analyzed treatment episodes for pediatric OCD and estimated costs for both CBT and pharmaceutical costs, over a three-year period from 2015 – 2017. For IOP and PHP strategies, we analyzed encounter data from the specified outcomes database. Total costs for the IOP and PHP strategies, including CBT, were derived from the outcomes database of encounters for individuals receiving treatment, and included net reimbursement data, essentially claims or reimbursements, analogous to the definition of costs derived from analysis of Truven Marketscan data. These data are inclusive of outpatient

Table 1
Model Parameters.

Measure	Parameter	Mean	SD*	Distribution	Source
Baseline CY-BOCS	CY-BOCS at Initiation of Treatment	24.39	4.77	Normal	(Barrett et al., 2004; Bolton & Perrin, 2008; "Cognitive-behavior therapy, sertraline, and their combination for children and adolescents with obsessive-compulsive disorder: the Pediatric OCD Treatment Study (POTS) randomized controlled trial," 2004; DeVeaugh-Geiss et al., 1992; Freeman et al., 2014a, 2014b; Freeman et al., 2008; Geller et al., 2001, 2004; Greist et al., 1990; Lewin, Park et al., 2014, 2014b; Liebowitz et al., 2002; March et al., 1998; Piacentini et al., 2011; Riddle et al., 2001, 1992; Storch et al., 2013a, 2013b; Torp et al., 2015)
Benefit (Δ in CY-BOCS)	CBT only	12.58*	6.11	Normal	(Barrett et al., 2004; Bolton & Perrin, 2008; "Cognitive-behavior therapy, sertraline, and their combination for children and adolescents with obsessive-compulsive disorder: the Pediatric OCD Treatment Study (POTS) randomized controlled trial," 2004; DeVeaugh-Geiss et al., 1992; Freeman et al., 2014a, 2014b; Freeman et al., 2008; Geller et al., 2001, 2004; Greist et al., 1990; Lewin, Park et al., 2014, 2014b; Liebowitz et al., 2002; March et al., 1998; Piacentini et al., 2011; Riddle et al., 2001, 1992; Storch et al., 2013a, 2013b; Torp et al., 2015)
	Non-remit, then more CBT	7.66*	5.85	Normal	(Skarphedinsson et al., 2015a)
	Non-remit, then add ADM	9.45*	6.90	Normal	(Skarphedinsson et al., 2015a, 2015b)
	ADM Only	7.65*	6.51	Normal	("Cognitive-behavior therapy, sertraline, and their combination for children and adolescents with obsessive-compulsive disorder: the Pediatric OCD Treatment Study (POTS) randomized controlled trial," 2004; DeVeaugh-Geiss et al., 1992; Geller et al., 2001, 2004; Greist et al., 1990; Liebowitz et al., 2002; March et al., 1998; Riddle et al., 2001, 1992)
	Non-remit, then more ADM	4.73*	6.78	Normal	(Franklin et al., 2011)
	Non-remit, then add CBT	11.22*	6.68	Normal	(Franklin et al., 2011)
	ADM + CBT	11.14*	6.83	Normal	("Cognitive-behavior therapy, sertraline, and their combination for children and adolescents with obsessive-compulsive disorder: the Pediatric OCD Treatment Study (POTS) randomized controlled trial," 2004; Storch et al., 2013a, 2013b)
	Intensive Outpatient (IOP)	16.42	8.94	Normal	Outcomes Database
	Partial Hospitalization (PHP)	16.26	8.94	Normal	Outcomes Database
Costs (2017$)	CBT	$2372	$116	Gamma	Author Calculations
	ADM‡	$1315‡	$503	Gamma	Author Calculations
	ADM + CBT‡	$3687‡	$416	Gamma	Author Calculations
	Intensive Outpatient (IOP)	$10,722	$7,690	Gamma	Outcomes Database
	Partial Hospitalization (PHP)	$19,464	$12,214	Gamma	Outcomes Database

SD = standard deviation
CY-BOCS = Children's Yale-Brown Obsessive-Compulsive Scale
CBT = cognitive behavior therapy; consisted of 14 sessions of 1 -h duration
ADM = antidepressant medication
* Calculated using Cohen's (Cohen, 1988) formulas for pooled mean and pooled SD
‡ 12-month course of ADMs and includes 10 medication management visits over 12 months. Medication costs calculated using Truven MarketScan Database.

hospital charges, behavioral therapist and physician professional fees for pharmaceutical and any related medical management, pharmaceutical dispensing and other fees for outpatient services. Both cost estimation procedures aligned to the perspective of the analysis – that of a payor in the United States.

3. Theory and Calculations

3.1. Monte Carlo Simulation

Using the Probabilistic parameters derived from the literature and outcomes database (Table 1), a Monte Carlo (MC) simulation was conducted to estimate the cost-effectiveness of each of the treatments independently, then compare them to determine the most cost-effective alternative. The simulation was based on 100,000 hypothetical children, with a diagnosis of OCD, and a treatment-refractory severity and treatment profile. Each iteration randomly selected a value of each probabilistic parameter, necessary to calculate the cost-effectiveness for each trail, and each treatment within each trial, representing cost-effectiveness estimates for each hypothetical child on each of the nine treatment strategies. The simulation returned the means and descriptive statistics for costs and effectiveness for each strategy. The ICER was calculated based on the MC simulation results and used to compare results among strategies. The model was constructed, and the MC simulation and sensitivity analyses performed using Tree Age Pro 2018. To aid in interpretation, results are plotted in scatterplot of cost in dollars ($) versus effectiveness (change in CY-BOCS).

3.2. Probabilistic Sensitivity Analysis

Robustness of our results to uncertainty in model parameters and variance in clinical contexts was assessed with Probabilistic Sensitivity Analyses (PSA), using distributions for the probabilistic parameters and uniform distributions for the remaining deterministic parameters. The results were evaluated using a PSA derived from the distributions associated with each parameter. The scatterplot of costs versus effectiveness, and the confidence intervals for means of costs, effectiveness, and ICERs were evaluated to determine which parameters exhibited the most sensitivity to variation, or uncertainty in model parameters. The PSA repeated the simulation of the hypothetical cohort of 100,000 children, 1,000 times, This allowed for the inspection of results from repeated iterations of the MC simulation By inspecting the scatterplot we examined the homogeneity within each treatment strategy and the homogeneity between strategies to assess the robustness of our findings. Strategies with wider 95% confidence intervals around the means for costs and effectiveness were more sensitive to the variation in the probabilistic parameters.

4. Results

4.1. Effectiveness

Ranking each strategy by effectiveness, unit changes in CY_BOCS, IOP was the most effective strategy, demonstrating a reduction in CY-BOCS, equal to 16.42 units. IOP was followed by PHP, and CBT-monotherapy augmented with ADM. CBT-monotherapy augmented with additional CBT and ADM-only augmented with CBT followed closely with 15.56 and 14.75 unit improvements in CY-BOCS, respectively. Complete results for effectiveness, costs, and cost-effectiveness are detailed below in Table 2.

4.2. Costs

While IOP was the most effective strategy, it accomplished the estimated reduction in CY-BOCS with the second highest costs ($10,726), more than three times the cost of the second most effective strategy, CBT-monotherapy augmented with ADM ($2,883). The seven trial strategies ranged in cost from $1,135 to $3,687. The substantial differences in costs between the trial and specialty-center strategies are primarily due to the differences in the intensity and duration of CBT dosage during treatment, while costs for pharmacotherapy were relatively consistent across strategies (when employed). PHP was the costliest strategy, at $19,466, but was dominated by IOP. Notably, PHP provided the same effectiveness as CBT Mono, augmented with ADM, at one-sixth the costs.

4.3. Cost-Effectiveness

Combining both effectiveness and costs, we conclude that IOP is the most cost-effective strategy for treatment of refractory OCD in children, delivering the highest change in CY-BOCS (+16.42) per unit of cost. This equates to an ICER of $48,834, less than both established WTP thresholds of $50,000 and $100,000 (Drummond, 2005; Gold, 1996). Beginning with the lowest cost strategy, ADM monotherapy, Table 2 arranges strategies based on increasing costs, and improving effectiveness. Strategies with increased costs, but decreases in effectiveness, are dominated, and depicted with negative ICER values, and are excluded from consideration. The remaining strategies represent the cost-effectiveness frontier, where adding incremental costs results in incremental effectiveness. CEA suggests that strategies with the higher effectiveness and costs are merited, subject to the WTP threshold(s).

ADM monotherapy was the least costly, and least effective of the treatment strategies evaluated, and serves as the baseline strategy. Fig. 1 below plots all nine strategies and the cost-effectiveness frontier from ADM-mono to IOP. Strategies lying within (to the right) of the frontier represent dominated strategies. Three strategies, CBT-monotherapy augmented with CBT, CBT + ADM, and PHP, are absolutely dominated (Drummond, 2005; Gold, 1996), meaning they provide lower effectiveness than comparable strategies, and thus would not be chosen using strict cost-effectiveness decision calculus. The remaining strategies are extended dominated, indicating they are inferior to IOP, but are reasonable alternatives in terms of cost-effectiveness, as they provide proportionally less effectiveness and costs. These alternatives are reasonable choices, when superior treatment strategies are available. Faced with limited choices (e.g., no IOP available), CBT-monotherapy, augmented with additional CBT or ADM would be feasible second choice strategies.

4.4. Probabilistic Sensitivity Analysis (PSA)

Results from the PSA, depicted in Fig. 2 below, demonstrated two important dimensions of reliability in our results. First, there was relative homogeneity in the results for each of the strategies, depicted by the tight clustering of cost and effectiveness results from the MC simulation. Second, all strategies were heterogeneous versus other strategies, showing little overlap of their centroids with those of other strategies. Comparing Figs. 1 and 2, the mean estimates in Fig. 1 are approximately the centroids of the scatterplot of each strategy in Fig. 2. We conclude that the analysis is less sensitive to a single parameter, and benefits from the incorporation of probabilistic parameters to account for the uncertainty in the underlying parameters.

5. Discussion

These results are consistent with recent findings for treatment-refractory adults (Gregory et al., 2018) wherein high intensity multimodal therapy is the most cost-effective treatment strategy for treatment-refractory pediatric OCD. In addition to the superiority demonstrated by the IOP strategy in reducing OCD severity, as indicated by pre/post changes in CY-BOCS, these data suggest that initial treatment with CBT-monotherapy, augmented as needed with additional CBT, and/or the addition of ADM is a viable treatment option

Table 2
Cost-Effectiveness Results

Strategy	Costs (2017$)	Incremental Costs	Effectiveness (Change in YBOCS)	Incremental Effectiveness	ICER
ADM Mono	1,315		7.65		
ADM Mono, Add ADM	2,147	832	10.65	3.00	277.63
CBT Mono	2,372	225	12.58	1.93	116.34
ADM Mono, Add CBT	2,816	444	14.75	2.17	204.73
CBT Mono, Add ADM	2,883	67	16.26	1.51	44.54
CBT Mono, Add CBT*	3,295	411	15.56	(0.70)	(590.47)
ADM + CBT*	3,687	804	11.14	(5.12)	(156.97)
IOP	10,726	7,842	16.42	0.16	48,834
PHP*	19,466	8,740	16.26	(0.16)	(56,039)

* Dominated strategies (e.g. decreasing effectiveness relative to cost).

when high-intensity IOP is unavailable due to access, be it due to actual availability of services or financially infeasibility.

Interestingly, these findings differed slightly from Gregory et al. (Gregory et al., 2018) in that IOP was superior to PHP to IOP transition. This may reflect that IOP has a similar dose of ERP relative to PHP which is longer but has additional non-ERP components, that are associated with partial hospitalization, which are absent from intensive outpatient programs. It also may be a dose effect ceiling exists such that additional treatment time does not confer further benefits.

5.1. Limitations

The lack of health utility data for pediatric OCD, and many other mental illnesses prohibits our ability to estimate the Quality-Adjusted Life Years (QALYs) (Weinstein et al., 2009; Wouters et al., 2015) gained for each of the nine strategies, as is convention in cost-effectiveness analyses (Drummond, 2005; Gold, 1996). This limitation restricts our results to costs per unit change in CY-BOCS during the initial treatment year, and doesn't allow for the accumulation of costs and benefits over the lifetime of a hypothetical individual with OCD and receiving treatment. This underestimates both the benefits of treatments in terms of quality of life gained, and costs, especially given the necessity for maintenance pharmacotherapy beyond the initial treatment year. That said, these data provide guidance to providers, parents and patients, as to the most cost-effective treatment alternative for the ensuing treatment year. We believe, based on recent findings for adults (Gregory et al., 2018), that the inclusion of health utilities and QALYs would enhance the cost-effectiveness of IOP, as large changes in CY-BOCS

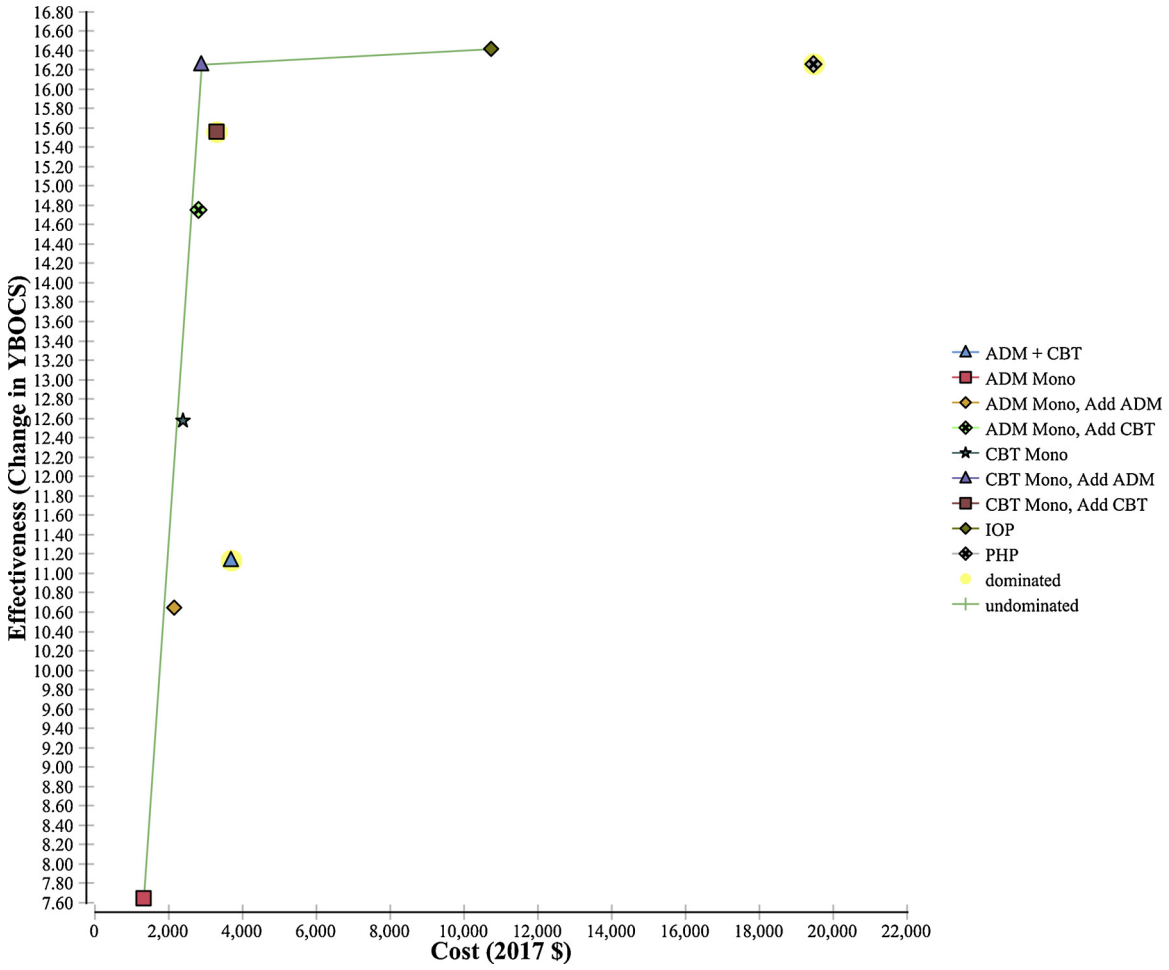

Fig. 1. XXX.

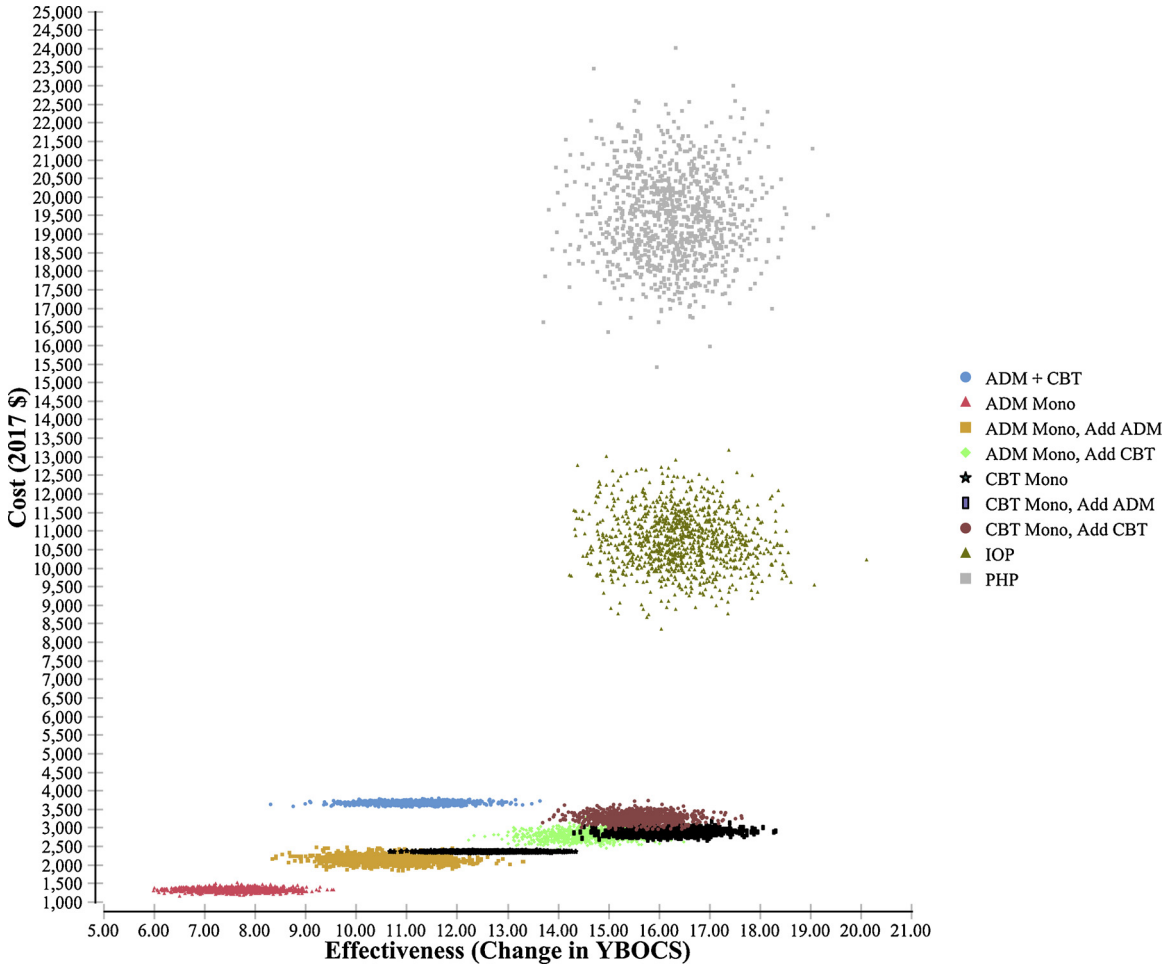

Fig. 2. XXX.

would correspond with significant gains in quality of life and thus health utility resulting from treatment.

In addition to the lack of quality of life evidence to calculate QALYs, the incorporation of evidence for two practice-based strategies, along with trial evidence presents a limitation to the interpretation of these results. Trial evidence estimates efficacy wherein practice-based outcomes estimate effectiveness, tangential to efficacy, but interpreted as less/lower, or inside the efficacy frontier. Essentially, our effectiveness estimates are conservative assessments of the performance of IOP and PHP strategies. The fact that these strategies outperform trial strategies (efficacy estimates of performance) lend more credibility to the results herein, given that there estimates of performance were conservative, effectiveness-based parameters,

6. Conclusions

The lack of access to high fidelity, high dose CBT paired with appropriate pharmacotherapy is an issue for OCD patients and their families. Among youth who were treatment non-responsive, these results indicate the superiority of IOP, a high dosage CBT strategy, as well as CBT-based trial strategies, indicating the need to increase access to these treatments. A significant challenge is the lack of trained therapist available to deliver CBT, and the lack of integrated approaches joining CBT-therapists and corresponding ADM medication management from physicians. These results provide a basis to refocus the treatment of severe, refractory OCD on expanding training for therapists to deliver high fidelity high dose CBT, in conjunction with requisite pharmacotherapy.

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