Notice of correction 2/9/2018: Table 1 had reference 28 corrected to reference 38, Diefenbach and Tolin.

Treatment-Refractory Obsessive-Compulsive Disorder in Adults:
A Cost-Effectiveness Analysis of Treatment Strategies

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ABSTRACT

Objective: This study sought to assess the cost-effectiveness of 7 treatment strategies for treatment-refractory obsessive-compulsive disorder (OCD) in adults.

Methods: A model was developed to evaluate treatment alternatives for adults (18–64 years old) that consisted of 2 parts: a decision analytic model and a Markov model. The decision analytic model stratified 7 outpatient treatment strategies, and the Markov model accumulated benefits and costs across the life expectancy of a simulated cohort of individuals. The model was parameterized with probabilistic and deterministic parameters from the literature and an outcomes database to perform a Monte Carlo simulation of a hypothetical cohort of 100,000 adults with OCD to estimate net health benefits (NHBs), costs, and incremental cost-effectiveness ratio (ICER) for each treatment strategy. OCD was considered treatment refractory in adults with an OCD diagnosis who failed first-line therapies. Encounters took place from 2012 to 2015, and the analyses were performed from November 2016 to February 2017.

Results: Partial hospitalization with step-down to intensive outpatient treatment was the most cost-effective of the 7 strategies, with an estimated ICER of $7,983 and mean (SD) NHB of 10.96 (0.53) quality-adjusted life-years (QALYs) remaining. This result was 2.2 QALYs greater than that of the trial-based antidepressant and cognitive-behavioral therapy (ADM + CBT) strategy. Three additional ADM + CBT strategies were estimated not to be statistically significantly different from each other. These 4 ADM + CBT strategies outperformed both pharmacotherapy-only strategies.

Conclusions: Treatment strategies that include higher-intensity CBT, with effectiveness outcomes that approached efficacy estimates, were superior to real-world CBT strategies. However, given the limited availability of high-quality CBT, especially through use of commercial insurance networks, specialized treatment programs offer greater effectiveness than real-world therapies in achieving wellness for this severe patient population.

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Obsessive-compulsive disorder (OCD) is a debilitating mental illness affecting approximately 1.2% of adults.[1] First-line treatments include cognitive-behavioral therapy (CBT) and serotonin reuptake inhibitors (SRIs).[2] Approximately 40%–60% of adults respond to SRIs,[3] with CBT response rates ranging from 70% to 85%.[4] However, many responders continue to experience significant symptoms. Adults with treatment-refractory OCD, constituting a significant number of those seeking treatment for OCD, present a more complex clinical question regarding further treatment.[3]

Evidence regarding the efficacy of treatments for treatment-refractory OCD is difficult to interpret given inconsistent findings and leaves clinicians with little direction regarding optimal options. Augmentation of pharmacotherapy with CBT is effective, yet CBT is often not available, it may be costly when provided by outpatient practitioners, and current evidence varies in terms of dosage (number of sessions, hours per week) and duration.[4,5] In addition, although many studies report outcomes using the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS),[6,7] there is variation in the reporting[4,5] of response versus remission.[8–10]

Heterogeneity in severity among trial participants produces evidence that is difficult to apply in practice.[2,4,5,11] These trials[2,4,5,11] consist of both treatment-naive and treatment-refractory patients, across a wide-range of severity, with little evidence of effectiveness among severely ill patients and those refractory to first-line therapies. Furthermore, trial sample sizes[4,5,12–17] are small ($N < 150$), which prohibits patient subgroup analyses. The combination of severe OCD, patients with treatment-refractory illness, and the inability to stratify treatment evidence by severity presents a challenge in interpreting research evidence for clinicians treating these patients.

We sought to assess the cost-effectiveness of various treatment strategies for treatment-refractory OCD. Current evidence suggests the superiority of polytherapy,[2] consisting of combined SRI and CBT,[4,5] yet there has been no consideration of cost-effectiveness for individuals

Clinical Points

- Evidence regarding the efficacy of treatments for treatment-refractory obsessive-compulsive disorder (OCD) is difficult to interpret given inconsistent findings and leaves clinicians with little direction regarding optimal options.
- Treatment strategies that include higher-intensity cognitive-behavioral therapy (CBT) were superior to real-world CBT and pharmacotherapy augmentation. However, given the limited availability of high-quality CBT, especially through use of commercial insurance networks, specialized treatment programs offer greater effectiveness over real-world therapies in achieving wellness for individuals suffering from treatment-refractory OCD.

with treatment-refractory OCD. A recent assessment[18] of treatment strategies for adults with OCD indicated the superiority of SRIs over placebo in monotherapy, behavioral therapy (BT), and cognitive therapy (CT) over placebo therapy, and BT and CT over SRIs. CBT, in contrast to BT and CT, was not significantly different from placebo therapy or pharmacotherapy. Further, the assessment was focused on adults with OCD,[18] not those with treatment-refractory OCD—the focus of the present study, and a considerable clinical challenge. This study is intended to bridge such gaps and provide useful guidance for clinicians and payers.

METHODS

Conceptual model

We developed a model to evaluate treatment alternatives for adults (18–64 years old) that consisted of 2 parts: a decision analytic model and Markov model. We excluded inpatient/residential treatments given that clinicians are unlikely to recommend inpatient treatment immediately following SRI nonresponse; rather, they are most likely to explore polytherapy with varying CBT intensity. The decision analytic model stratified 7 treatment strategies, and the Markov model accumulated benefits, costs, and mortality for a simulated cohort.

Our conceptual model was parameterized with probabilistic and deterministic parameters from the literature and an outcomes database, to perform a Monte Carlo (MC) simulation of a hypothetical cohort of 100,000 adults with OCD to estimate net health benefits (NHB), costs, and incremental cost-effectiveness ratio (ICER) for each treatment strategy. Dominated strategies (eg, strategies with lower effectiveness and higher costs) were eliminated from further consideration. The remaining strategies were evaluated by ranking by the ICER and then compared to willingness-to-pay (WTP) thresholds to determine acceptability.

Our model assumed a 1-year period of disutility for disease, during which an individual received treatment. Individuals whose illness remitted were then modeled to death or 100 years of age. While death or 100 years of age following treatment is a long time horizon for evaluation, it is consistent with standard practice in cost-effectiveness evaluation (CEA)[19,20] and affords comparisons across other CEAs conducted for behavioral health diagnosis and other physical health diseases. This comparison is important to contextualize and compare these results in terms of costs and NHBs to other illnesses, especially for payers considering policy decisions for more intensive and expensive therapies for severe mental illnesses. Additional considerations for shorter time horizons were incorporated into the probabilistic sensitivity analysis.

Individuals receiving treatment strategies that included pharmacotherapy were assumed to be compliant posttreatment, and annual costs for pharmaceutical treatment were included and inflated at the health care component of the Consumer Price Index.[20] Individuals with illness that did not remit posttreatment maintained the disutility of illness and were modeled to death or 100 years. Additional treatments for individuals with nonremitting illness were not considered in this analysis, nor were other societal costs, as this analysis was performed from a commercial insurer payer perspective in the United States.

Treatment Strategies

Initial therapy for individuals presenting with OCD was the initiation of antidepressant medication (ADM) pharmacotherapy. Patients refractory to ADMs are often augmented with antipsychotic medications[4,5,11] although the latter medications have significant side effects[21–23] and mixed efficacy.[12] While CBT is a potential first-line intervention, the addition of CBT to ADM monotherapy resulted in higher response and remission than both non-CBT psychotherapy and antipsychotic medication augmentation of ADMs, although the effect varied among ADM-responsive and ADM-refractory individuals[4,12,13] and variances in efficacy versus effectiveness were found.[7] Our aim was to synthesize the evidence for treatment effectiveness and denominate in terms of NHB to assess the cost-effectiveness of all treatment strategies.

We compared 7 treatment strategies, beginning with 2 pharmacology-only strategies: ADM monotherapy[9,12] and ADM augmented with antipsychotic medication.[9] Although the patients who received ADM monotherapy had illness refractory to the treatment, this strategy was retained as a base case to which the additional 6 strategies were compared.

To evaluate ADM-CBT polytherapy, we identified 5 strategies. Trial evidence consisted of high dosage, well-controlled trials for ADM-CBT polytherapy (ADM + CBT)[9,12] and a naturalistic study[7] that we parameterized as measuring effectiveness rather than efficacy[9,12] (ie, ADM + CBT [effectiveness]) to accommodate the difference between trial efficacy and practice-based effectiveness of ADM-CBT polytherapy. The primary difference between these 2 strategies was both dosage and fidelity of CBT delivered. Dosage of CBT in the trial-based polytherapy strategies varied from 2 to 4 hours daily, 2–4 days per week.

To address this gap between practice-based and trial conditions, we added 3 additional ADM-CBT polytherapy

Table 1. Model Parameters

Category and Parameter	Value	SD	Distribution	Reference (if applicable)	Study Type
Starting value					
Y-BOCS at presentation	29.22	7.77	Normal		Outcomes database
Q-LESQ at presentation	0.45	0.17	Normal		Outcomes database
Effectiveness (change in Y-BOCS score)					
ADM	2.6	1.484	Normal	Simpson et al,[9] Simpson et al[12]	Trial
ADM + antipsychotic	3.5	1.698	Normal	Simpson et al[9]	Trial
ADM + CBT	11.2	1.147	Normal	Simpson et al,[9] Simpson et al[12]	Trial
ADM + CBT (effectiveness)	5.3	0.663	Normal	Tundo et al[7]	Trial
IOP	8.7	6.90	Normal		Outcomes database
PHP	9.6	6.70	Normal		Outcomes database
PHP/IOP	10.9	6.52	Normal		Outcomes database
Health utility (change in Q-LES-Q score)					
ADM	0.18	0.18	Normal		Outcomes database
ADM + antipsychotic	0.18	0.18	Normal		Outcomes database
ADM + CBT	0.18	0.18	Normal		Outcomes database
IOP	0.15	0.15	Normal		Outcomes database
PHP	0.12	0.20	Normal		Outcomes database
PHP/IOP	0.18	0.12	Normal		Outcomes database
Annual cost ($US, 2015)					
ADM	1,576	1,173.93	Gamma	Diefenbach and Tolin[38]	Cost
ADM + antipsychotic	5,000		Uniform		
ADM + CBT (effectiveness)	9,540	4,388.23	Gamma	Diefenbach and Tolin[38]	Cost
ADM + CBT	11,609	149.65	Gamma	Tundo et al,[7] Diefenbach and Tolin[38]	Author calculations
IOP	11,744	9,276	Gamma		Outcomes database
PHP	14,562	11,039	Gamma		Outcomes database
PHP/IOP	29,386	16,638	Gamma		Outcomes database
Transition probabilities					
Well→Dead				Allison et al[22]	US life tables
Other					
Age	30.51	12.28	Normal		Outcomes database
Sex (female referent)	0.51	0	Bernoulli		Outcomes database

Abbreviations: ADM = antidepressant medication, CBT = cognitive-behavioral therapy, IOP = intensive outpatient treatment, PHP = partial hospitalization, PHP/IOP = partial hospitalization with step-down to intensive outpatient treatment, Q-LES-Q = Quality of Life Enjoyment and Satisfaction Questionnaire, Y-BOCS = Yale-Brown Obsessive Compulsive Scale.

strategies that delivered trial-level dosage of CBT in practice-based setting. We augmented the trial evidence with data from an outcomes database maintained by a specialty center for the treatment of individuals with severe OCD. These 3 additional strategies included 2 variations in CBT intensity and dosage: intensive outpatient treatment (IOP), partial hospitalization (PHP), and a step-down strategy that included the transition from PHP to IOP (PHP/IOP). IOP consists of 12–15 hours of multimodal treatment 5 days per week. PHP consists of 30 hours of multimodal treatment 5 days per week.

Markov Model

To calculate NHBs across life expectancy of simulated individual trials, a Markov model was developed for each treatment strategy. The model included 3 health states (OCD, well, and dead) and incorporated all-cause mortality, using standard life tables,[24] based on age and sex. No evidence of long-term follow-up or rates of relapse were available; therefore, we were unable to parameterize a potential relapse OCD state in the Markov process. We assumed that OCD in simulated trials resulting in remission remained in remission for the remainder of the modeled life. Further, no evidence of adherence to pharmacotherapy among adults with treatment-refractory OCD was available, and simulated individuals were assumed to be compliant with pharmacotherapy across their modeled life spans. These 2 assumptions are limitations of our analytic method.

The period of disability related to OCD was assumed to be the duration of treatment (1 year), after which an individual either experienced remission to the well state, was nonresponsive to therapy, or died. There is little evidence of excess mortality associated with treatment-refractory OCD,[25] unlike with other severe mental illness.[26,27] Given the lack specificity for excess morbidity in treatment-refractory OCD, we incorporated estimates for excess morbidity for OCD, reported to be more applicable to individuals with severe OCD.[25] The mortality estimates used in our model did not include adjustments for specific comorbid illnesses.

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 creation 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 relapse rate and excess mortality associated with OCD. Model parameters and their underlying distributions are summarized in Table 1.

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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 3 strategies (IOP, PHP, and PHP/IOP). Rogers Memorial Hospital (Oconomowoc, Wisconsin) oversees the outcomes database employed in this study. The database contained a total of 819 episodes between 2012 and 2015 and financial data including total charges for each individual (analyses of the data, as described later in the Methods section, took place from November 2016 to February 2017). Patient assessments were given at admission, discharge, and 12-months postdischarge. From this database, we estimated distributions for treatment effects, health utility, and costs for the 3 higher-intensity polytherapy strategies.

Treatment effects. Clinical outcomes were reported as changes in the Y-BOCS score, and remission as Y-BOCS score ≤ 14.[8] For this analysis, treatment effect was the Y-BOCS unit change posttreatment. We used the clinical trial evidence and recent reviews to create distributions for the Y-BOCS unit change for the literature-based treatment strategies. The outcomes database included assessments with the self-reported Y-BOCS, which reflect a bias toward lower Y-BOCS scores.[6] Thus, effectiveness estimates for IOP, PHP, and PHP/IOP are conservative. A small subset of the database patients (n = 67) had both self-reported and clinician-rated Y-BOCS scores. We used these clinician-rated data to parameterize starting Y-BOCS score. For each iteration, the randomly generated unit change was subtracted from the admission Y-BOCS scores obtained at simulated treatment initiation.

Net health benefits. NHBs represent the effectiveness of each strategy and are denominated in quality-adjusted life-years (QALYs).[28,29] The Short Form of the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q)[30–32] was used to assesses health utility. This instrument has demonstrated strong psychometric properties.[30,33–37] Health utilities, pretreatment and posttreatment, were reported for each of the treatment strategies in addition to the response and remission parameters. These utilities allowed for the discounting of life due to disability related to disease. Perfect health was given a score of 1 and dead a score of 0, so all health states ranged between 1 and 0. Synthesized trial evidence and the outcomes database included patient-reported assessments of health utility pretreatment and posttreatment and were used to parameterize the model. For a given individual, in each year of life, the health utility for the individual health state (well, OCD, or dead) was used to adjust the life-year to incorporate the health status. This was done for each life-year remaining posttreatment, and the mean QALYs remaining for each strategy were calculated. For each simulated individual, a pretreatment health utility was drawn from the Q-LES-Q distribution as well as posttreatment change in health utility associated with each treatment strategy. In posttreatment years, utilities for remission and OCD were drawn from the distribution and adjusted for aging. Strategies were then ranked by NHBs based on the estimate of mean QALYs remaining for a hypothetical individual receiving that therapeutic alternative.

Cost and effectiveness parameters. Two approaches were used to derive costs for treatment strategies. Costs for pharmacotherapy and CBT monotherapy strategies were estimated from the literature.[38] Total costs for the strategies including CBT were derived from a database of encounters for individuals receiving treatment and included total charge data inclusive of hospital charges, therapist and physician professional fees, pharmaceutical dispensing, and other fees for outpatient services. A 3% discount rate was applied for both costs and NHBs, consistent with recommendations and standards of practice.[19,20] WTP thresholds of $50,000[20] and $100,000[19] were employed to evaluate the competing strategies.

Monte Carlo Simulation

We parameterized each of the 7 treatment strategies with probabilistic parameters, when available, to conduct the cost-effectiveness analysis, employing MC simulation of 100,000 hypothetical individuals. Each iteration of the simulation made a random draw for each probabilistic parameter from the underlying probability distributions to reflect the uncertainty and variation in the model parameters. The simulation resulted in means and descriptive statistics for QALYs and costs for each strategy, which were then used to calculate the ICER. Resulting ICERs were then compared to our WTP thresholds for the payer perspective in the United States. The results of each simulation trial were plotted in a scatterplot of costs and effectiveness (QALY). The model was constructed and the MC simulation and sensitivity analyses performed using TreeAge Pro 2017 (TreeAge Software, Inc). Each iteration began with a random draw of 4 key parameters. Age (range, 18–64 years) and sex allowed for mortality adjustments simulating a heterogeneous adult treatment population, and starting Y-BOCS and Q-LES-Q scores introduce variation in disease and severity of illness.

Probabilistic Sensitivity Analyses

Robustness of our results to uncertainty in model parameters and variance in clinical contexts was assessed in a probabilistic sensitivity analysis (PSA) using distributions for the probabilistic parameters and uniform distributions for the remaining deterministic parameters. This analysis inspected the results of the MC simulation and focused on the variation in costs and effectiveness for each of the strategies. It was accomplished by inspecting the scatterplot of cost and effectiveness and the confidence intervals for the means of costs, effectiveness, and ICERs from the simulation. Strategies with wider 95% confidence intervals around the means for costs and effectiveness were more sensitive to the variation in the probabilistic parameters. We lacked parameters for probability of relapse into disease or ill states and estimates of excess mortality related to disease.[26,27] To address these issues, we performed an additional sensitivity analysis to examine results across 5, 10, and 20 years.

Table 2. Cost-Effectiveness Results for Undominated Strategies

Strategy	Costs, Mean (SD), $	Incremental Costs, $	Effectiveness, Mean (SD), QALY	Incremental Effectiveness, QALY	ICER, $	Cost-Effectiveness Ratio, $
ADM	1,575 (39.37)		1.00 (0.10)			1,573
ADM + CBT	11,610 (149.65)	10,035	8.74 (0.51)	7.74	1,297	1,329
PHP/IOP	29,344 (528.76)	17,734	10.96 (0.53)	2.22	7,983	2,678

Abbreviations: ADM = antidepressant medication, CBT = cognitive-behavioral therapy, ICER = incremental cost-effectiveness ratio, PHP/IOP = partial hospitalization with step-down to intensive outpatient treatment, QALY = quality-adjusted life-year.

Table 3. Cost-Effectiveness Results (including dominated strategies)[a]

Strategy	Costs, Mean (SD), $	Incremental Costs, $	Effectiveness, Mean (SD), QALY	Incremental Effectiveness, QALY	ICER, $	Cost-Effectiveness Ratio, $
ADM	1,575 (39.37)		1.00 (0.10)			1,580
ADM + antipsychotic	4,994 (5.33)	3,420	2.65 (0.29)	1.66	2,061	1,881
ADM + CBT (effectiveness)	9,529 (137.96)	4,545	3.64 (0.34)	0.99	4,608	2,619
ADM + CBT	11,610 (149.65)	2,070	8.74 (0.51)	5.09	406	1,329
IOP	11,735 (328.46)	2,126	8.35 (0.49)	−0.39	−323	1,406
PHP	14,539 (331.13)	2,930	8.67 (0.50)	−0.06	−47,459	1,676
PHP/IOP	29,344 (528.76)	17,734	10.96 (0.53)	2.22	7,983	2,678

[a]Shading indicates dominated strategy.
Abbreviations; ADM = antidepressant medication, ADM + CBT = antidepressant medication and cognitive-behavioral therapy combination treatment, IOP = intensive outpatient treatment, PHP = partial hospitalization, PHP/IOP = partial hospitalization with step-down to intensive outpatient treatment, QALY = quality-adjusted life-year.

RESULTS

Simulated individuals in the analysis had a mean (SD) age of 30.51 (12.28) years, were equally divided among men and women, and had a mean (SD) starting Y-BOCS score of 29.22 (7.77) and Q-LES-Q score of 0.45 (0.17).

Net Health Benefits

The PHP/IOP strategy resulted in the highest NHB of the 7 strategies examined, with an estimated mean (SD) of 10.96 (0.53) QALYs remaining. This result was 2.2 QALYs greater than that of the ADM + CBT strategy. This difference represents the mean improvement in life-years remaining adjusted for the difference in quality of life resulting from the average person in PHP/IOP versus the average person in ADM + CBT. NHB, cost, and ICER results for each of the 3 undominated strategies are listed in Table 2, and results for the 7 strategies are listed in Table 3, referencing a common baseline, ADM monotherapy. Further, clinical trials ADM + CBT was not statistically significantly different ($P > .05$) in effectiveness from either IOP or PHP (Table 3). ADM + CBT, based on trial efficacy parameters, was included to make our list of strategies comprehensive but is not generally available in clinical practice and, when it is available, commercial insurance is rarely accepted. IOP and PHP are similar strategies, are increasingly available, offer similar benefits in terms of effectiveness, and are superior to ADM monotherapy, ADM augmentation with antipsychotic medication, and ADM + CBT (effectiveness).

Costs

Ordered by effectiveness in Table 2, the strategies had increasing costs that were offset by increasing effectiveness (in QALYs). The lowest-cost strategy was ADM monotherapy, at $1,575, and the highest-cost strategy was PHP/IOP, estimated at $29,344.

Cost-Effectiveness

All 3 undominated strategies, listed in Table 2, resulted in ICERs less than either of the WTP thresholds[19,20] used to evaluate the results in this analysis. PHP/IOP had an ICER of $7,983, which was greater than that of other strategies, and had greater effectiveness (10.96 QALYs) than the other strategies. Figure 1 plots the results of the cost-effectiveness analysis based on the mean values of each parameter resulting from the MC simulation. The undominated strategies make up the CEA frontier, and dominated strategies are plotted inside that frontier, depicting their inferiority to others based on either costs, effectiveness, or both.

Probabilistic Sensitivity Analysis

The PSA was performed alongside the MC simulation and tested the robustness of our results; it is plotted in Figure 2. The PSA supports the conclusions from the MC simulation, in which PHP/IOP is the most cost-effective treatment strategy. The pattern depicted in Figure 2 demonstrates stability of results in that MC trial results of each strategy cluster together and do not overlap with competing strategy. The general pattern is increasing effectiveness with increasing costs.

We examined the durability of these findings subject to various time periods (ie, 5, 10, and 20 years) versus the original MC results to age 100 or death, whichever occurred first. In all 3 time periods, the pattern of the 3 undominated strategies persisted. In a 5-year scenario, PHP/IOP failed to meet either WTP threshold, with an ICER of $133,041.

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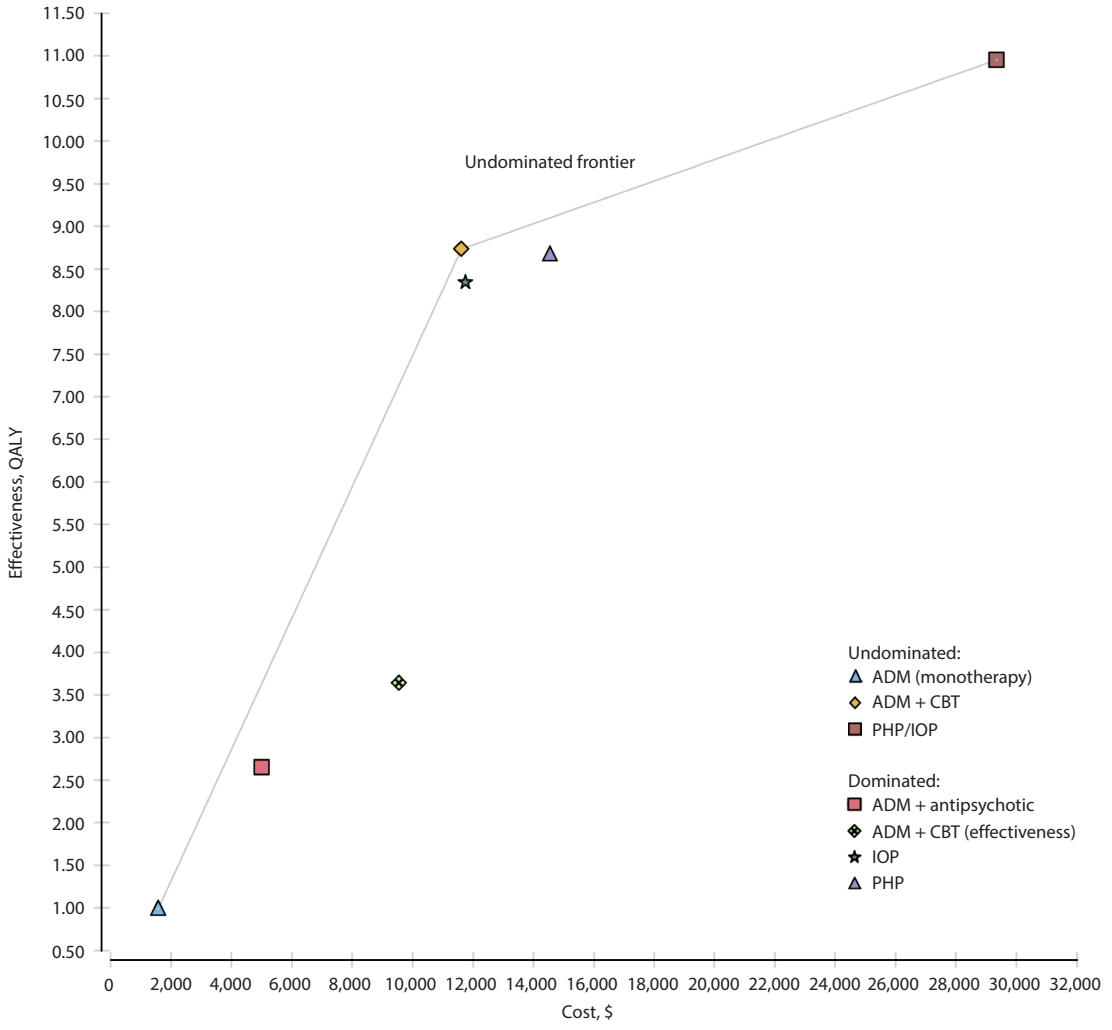
Figure 1. Cost-Effectiveness of 7 Treatment Strategies for Treatment-Refractory Obsessive-Compulsive Disorder



Abbreviations: ADM = antidepressant medication, CBT = cognitive-behavioral therapy, IOP = intensive outpatient treatment, PHP = partial hospitalization, PHP/IOP = partial hospitalization with step-down to intensive outpatient treatment, QALY = quality-adjusted life-year.

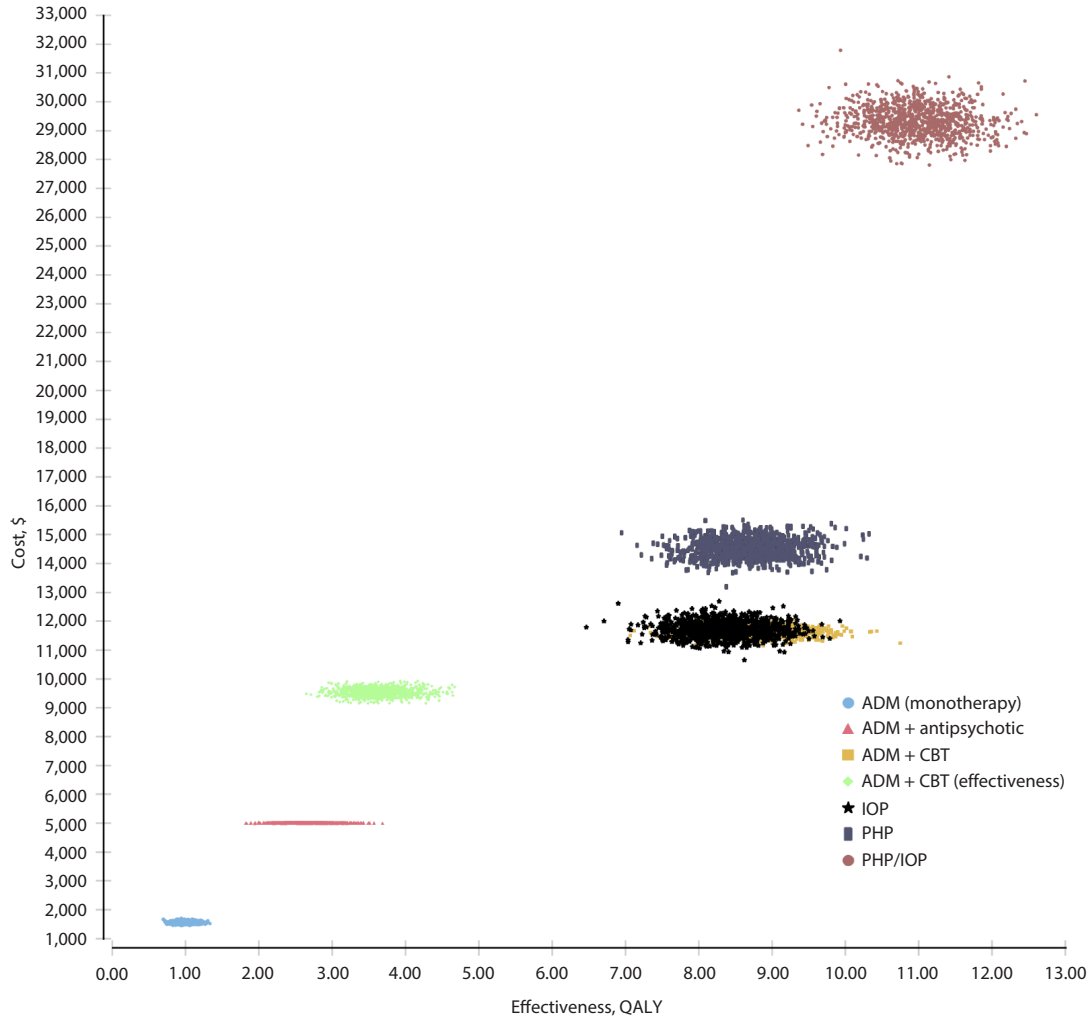
Across a 10-year period, the PHP/IOP strategy has an ICER of $52,967, slightly higher than a $50,000 WTP threshold used in Europe but less than the $100,000 WTP threshold employed in the United States.[20] Extending to a 20-year scenario, the PHP/IOP strategy is less than both WTP thresholds, with an ICER of $23,875 per QALY. These differences in ICERs over time are due to the differences in accumulated QALYs posttreatment.

DISCUSSION

These CEA findings reinforce current knowledge regarding ADM and CBT combination therapies for treatment of refractory OCD. Existing evidence suggests the superiority of ADM-CBT combination therapy over ADM monotherapy and antipsychotic medication augmentation of ADM. CBT provided in an IOP, PHP, or clinical trial (ADM + CBT) was superior to real-world CBT (ADM + CBT [effectiveness]). However, given the limited availability of high-quality CBT in general, especially through use of commercial insurance, specialized treatment programs that accept commercial insurance most likely offer greater effectiveness than real-world therapies in achieving wellness among this extreme patient population. Our cost estimates for clinical trial outpatient CBT are very likely significantly underestimated given the scarcity of this treatment modality using commercial insurance. Further, our results demonstrate the superiority of PHP/IOP therapy over all treatment strategies, which may reflect high-intensity treatment with a clear step-down transition necessary to support the wellness of this complex patient population.

There are several important considerations when interpreting these results. Current evidence, particularly trial evidence, represents results from relatively heterogeneous

Figure 2. Probabilistic Sensitivity Analysis Scatterplot



Abbreviations: ADM = antidepressant medication, CBT = cognitive-behavioral therapy, IOP = intensive outpatient treatment, PHP = partial hospitalization, PHP/IOP = partial hospitalization with step-down to intensive outpatient treatment, QALY = quality-adjusted life-year.

populations in terms of severity and degree of treatment naïveté. We chose to parameterize this analysis for treatment-refractory adults with higher disease severity, as evidenced by our starting Y-BOCS score. However, it is likely that those within the treatment database represent a more impaired sample relative to those enrolled in clinical trials due to more severe functional impairment, comorbidity, and complex/substantial treatment history. What constitutes response versus remission of OCD symptoms remains controversial.[9] We chose to parameterize both remission and response; we found no evidence for the proportion of responsive versus remitted patients that face OCD relapse over the life course and thus were unable to incorporate this into our analyses.

Weight gain[22,23] and other metabolic issues[21] are associated with antipsychotic medications. These morbidities require an additional adjustment to health status for individuals receiving antipsychotics in any of the treatment strategies in order to incorporate the disutility associated with these side effects. We were unable to incorporate excess morbidity associated with either comorbid psychiatric conditions or the sequelae associated with treatment or pharmacotherapy. Given the baseline severity of individuals receiving pharmacotherapy and the chronic nature of OCD, we assumed these individuals will remain on pharmacotherapy for the duration of their simulated life, following the treatment period, and did not incorporate any variation in compliance or persistence with pharmacotherapy. Deterministic parameters, specifically for the literature-based strategies, were employed due to a lack of distributional evidence or samples for these strategies.

The outcomes database, while representing a substantial sample, employed self-reported Y-BOCS scores rather than clinician-rated Y-BOCS scores. In addition, diagnoses of OCD in the database were a result of clinician consensus rather than a structured interview. Our results show PHP/IOP step-down as the most cost-effective strategy and that

PHP, IOP, and clinical trials CBT were superior to other interventions.

These results represent an important synthesis of knowledge to inform treatment decisions for individuals suffering from OCD, specifically to clinicians and patients facing treatment decisions. These data suggest that stronger and higher-intensity doses of CBT, augmented with indicated pharmacotherapy, are the most effective and cost-effective treatments for adults with severe treatment-refractory OCD. Indeed, more intensive treatment programs dominated real-world therapies in terms of cost-effectiveness, suggesting the need to further promulgate such intervention programs that are accessible for severely ill patients using commercial insurance.

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Potential conflicts of interest: **Dr Storch** had and **Dr Riemann** and **Mr Kay** have clinical and operational leadership roles with Rogers Memorial Hospital. **Drs Gregory**, **Quast**, and **De Nadai**, **Ms Hall**, and **Mr Smith** have no conflicts to report.

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Additional information: The outcomes database is owned and maintained by Rogers Memorial Hospital. Inquiries regarding the database and potential access to these data and further results should be forwarded to Mr. Brian Kay (Brian.Kay@rogershospital.org).

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