

Cost-effectiveness analysis of radiosurgical capsulotomy versus treatment as usual for treatment-resistant obsessive-compulsive disorder

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OBJECTIVE Stereotactic radiosurgical capsulotomy (SRS-C) is an effective neurosurgical option for patients with treatment-resistant obsessive-compulsive disorder (TROCD). Unlike other procedures such as deep brain stimulation and radiofrequency ablation, the cost-effectiveness of SRS-C for TROCD has not been investigated. The authors herein report the first cost-effectiveness analysis of SRS-C for TROCD.

METHODS Using a decision analytic model, the authors compared the cost-effectiveness of SRS-C to treatment as usual (TAU) for TROCD. Treatment response and complication rates were derived from a review of relevant clinical trials. Published algorithms were used to convert Yale-Brown Obsessive Compulsive Scale scores into utility scores reflecting improvements in quality of life. Costs were approached from the healthcare sector perspective and were drawn from Medicare reimbursement rates and available healthcare economics data. A Monte Carlo simulation and probabilistic sensitivity analysis were performed to estimate the incremental cost-effectiveness ratio.

RESULTS One hundred fifty-eight TROCD patients across 9 studies who had undergone SRS-C and had at least 36 months of follow-up were included in the model. Compared to TAU, SRS-C was more cost-effective, with an estimated incremental cost-effectiveness ratio of \$28,960 per quality-adjusted life year (QALY) gained. Within the 3-year time horizon, net QALYs gained were greater in the SRS-C group than the TAU group by 0.27 (95% CI 0.2698–0.2702, $p < 0.0001$). At willingness-to-pay thresholds of \$50,000 and \$100,000 per QALY, the Monte Carlo simulation revealed that SRS-C was more cost-effective than TAU in 83% and 100% of iterations, respectively.

CONCLUSIONS Compared to TAU, SRS-C for TROCD is more cost-effective under a range of possible cost and effectiveness values.

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KEYWORDS cost-effectiveness; treatment resistant; obsessive-compulsive disorder; stereotactic radiosurgery; capsulotomy; functional neurosurgery

OBSESSIVE-COMPULSIVE disorder (OCD) is a debilitating psychiatric condition characterized by intrusive obsessions that lead to time-consuming, distressing compulsions. Its clinical severity is measured using the Yale-Brown Obsessive Compulsive Scale (Y-BOCS), with higher scores representing more severe disease (from 0 to 40).¹ In more severe cases, symptoms can greatly diminish a patient's quality of life (QOL) and impede their ability to

work and sustain meaningful relationships.² The lifetime prevalence of OCD in the United States (US) is 2%–3%,³ making it a relatively common psychiatric condition.

First-line treatments for OCD include pharmacotherapy (e.g., selective serotonin reuptake inhibitors [SSRIs], serotonin norepinephrine reuptake inhibitors⁴) and cognitive behavioral therapy with exposure and response prevention.⁵ Many patients who do not respond to first-line inter-

ABBREVIATIONS CEA = cost-effectiveness analysis; CER = cost-effectiveness ratio; CPT = Current Procedural Terminology; DBS = deep brain stimulation; ET = essential tremor; ICER = incremental cost-effectiveness ratio; MC = Monte Carlo; OCD = obsessive-compulsive disorder; QALY = quality-adjusted life year; QOL = quality of life; SRS = stereotactic radiosurgery; SRS-C = stereotactic radiosurgical capsulotomy; SSRI = selective serotonin uptake inhibitor; TAU = treatment as usual; TN = trigeminal neuralgia; TROCD = treatment-resistant OCD; US = United States; WTP = willingness to pay; Y-BOCS = Yale-Brown Obsessive Compulsive Scale.

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ventions may benefit from the addition of clomipramine or an atypical antipsychotic.^{6,7} Despite the efficacy of such treatments (i.e., “treatment as usual” [TAU]), up to 30% of individuals continue to experience severe symptoms.⁸ Fortunately, a variety of effective options exist for patients with treatment-resistant OCD (TROCD), including electroconvulsive therapy,^{9,10} transcranial magnetic stimulation,¹¹ deep brain stimulation (DBS),^{12,13} radiofrequency ablation,¹⁴ laser interstitial thermal therapy,¹⁵ and stereotactic radiosurgery (SRS).^{16,17}

In 1976, SRS was used for the first time in a patient with OCD.^{18,19} Over time, this method has been progressively used,²⁰ with one common target for TROCD emerging: the anterior limb of the internal capsule.¹⁶ Modern stereotactic radiosurgical capsulotomy (SRS-C) is an effective neurosurgical option for patients with TROCD, with response rates ($\geq 35\%$ reduction in the Y-BOCS score) of 50%–66%.^{16,17} However, unlike with procedures of comparable efficacy, such as DBS^{21,22} and radiofrequency ablation,²³ the cost and cost-effectiveness of SRS-C have not been investigated. One Dutch study found DBS for OCD to be more cost-effective than TAU in 50%–87% of cases, depending on battery rechargeability, with increasing cost-effectiveness over time.²¹ Another study showed DBS for OCD to be more cost-effective than TAU in both the United Kingdom and South Korea, again finding increasing cost-effectiveness with continued use of stimulation over time.²² Herein, we aimed to complete the first cost-effectiveness analysis (CEA) of SRS-C for TROCD by comparing the incremental cost-effectiveness ratio (ICER) to various broadly accepted willingness-to-pay (WTP) thresholds.

Methods

Using a decision analytic model,²⁴ we compared SRS-C to TAU, as defined above. Our base case for the model is an adult (age 18–65 years) with severe (Y-BOCS score 24–31) to extreme (Y-BOCS score 32–40) OCD, who has received at least 5 years of TAU without a therapeutic response (i.e., TROCD). The time horizon is 3 years following SRS-C, as that was the longest common duration of follow-up across published longitudinal studies. All model inputs were derived from a retrospective review of the relevant literature.

Literature Review: Efficacy

We conducted a PubMed search to identify clinical trials establishing the efficacy of SRS-C for TROCD by using the following terms: (“Radiosurgery”[Mesh]) AND (“Obsessive-Compulsive Disorder”[Mesh]). The search was completed in March 2021. We selected studies with original patient data and excluded any studies whose treatment response criterion varied from the broadly accepted $\geq 35\%$ reduction in the Y-BOCS score.²⁵ Single case reports were excluded. Data collected from the selected studies included sample size; patient-level preoperative Y-BOCS scores; 12-, 24-, and 36-month postoperative Y-BOCS scores; complication rates; follow-up time; study design; inclusion criteria; and response criteria.

Given the rigorous eligibility criteria for considering TROCD patients as candidates for SRS-C—namely, the requirement of 5 years of treatment nonresponse to

TAU—we hypothesized that the efficacy of TAU in our model patients would be lower than that of TAU in treatment-naïve patients. To test this hypothesis, we conducted a literature search for longitudinal studies (≥ 5 years of follow-up) focusing on the outcomes of patients with severe OCD on TAU.²⁶

Complications

Post-SRS-C complications were divided into three categories based on management strategy: inpatient (e.g., hospitalization, surgery), outpatient (e.g., prescription medication), and self-limited (e.g., over-the-counter treatment, no treatment). Only complications that significantly added to costs or detracted from effectiveness were considered for our model; therefore, only the inpatient and outpatient groups were included. No complications were considered for the TAU arm, as such would fall into the self-limited category and would not affect model outputs.

Effectiveness: The Utility Model

Utility is a quantitative measure of a patient’s subjective improvement in QOL and ranges from 1 (perfect health) to 0 (death). In CEAs, effectiveness is calculated by multiplying the net utility gained by the duration (years). The product is reported in quality-adjusted life years (QALYs), where 1 QALY equals 1 year in perfect health.²⁷ Because the Y-BOCS is not designed to measure QOL²⁸ and given the paucity of available utility data in our selected studies, we employed a utility model. Using published algorithms,¹⁴ we converted the percent change in the Y-BOCS score from baseline to last follow-up into a utility value for each patient in our sample and averaged these utilities across patients to reflect mean QOL improvement for responders to SRS-C. Separate disutility (negative utility) values from the literature were assigned to complication groups to approximate the negative impact of certain postoperative complications on QOL.¹⁴

On the basis of previous studies,^{21,29} we assumed that QOL improvement from a response to TAU would differ from the utility of SRS-C. The utility of TAU was therefore modeled using values from a previous CEA, which compared the cost-effectiveness of several nonsurgical treatments for patients with severe OCD.²⁹

Cost

We conducted our analysis from a healthcare sector perspective. This approach accounts for all monetary costs of healthcare associated with an intervention (SRS-C or TAU), regardless of who bears the cost: the third-party payer (i.e., Medicare), the hospital, or the patient (out-of-pocket expenses). It does not consider costs of transportation, patient time, productivity loss, or other nonmonetary costs, all of which would be required to adopt a societal perspective.³⁰

The aggregate cost of SRS-C was defined as the sum of the cost of one preoperative assessment, three follow-up visits, pre- and postoperative MRI, one bilateral SRS-C, and any hospital (facility) fees or additional out-of-pocket expenses. Costs associated with TAU included the costs of pharmacotherapy as well as exposure and response pre-

vention with a wide range and standard error to account for variability in individual treatment plans. Under the assumption that most responders to either SRS-C or TAU would remain on some form of pharmacological therapy while discontinuing additional therapies, we defined a separate variable for a lower-cost version of TAU and designated it as an incremental cost each year after treatment response. All cost data, including costs associated with complications, were collected from the 2021 Centers for Medicare & Medicaid Services Physician Fee Schedule (based on Healthcare Common Procedure Coding System [HCPCS]/Current Procedural Terminology [CPT] codes)³¹ and from the published literature.^{29,32,33}

Decision Analytic Model

We created our model using TreeAge Pro Healthcare 2021 (TreeAge Software LLC). The model placed patients within one of two treatment arms: SRS-C or TAU alone. Patients undergoing SRS-C could become responders at 1, 2, and 3 years. However, SRS-C and TAU were not mutually exclusive since SRS-C patients who did not respond continued to receive TAU. When an SRS-C patient responded, their subsequent incremental cost per year after surgery transitioned from the full costs of TAU to a lower-cost version of TAU. We chose this approach on the basis of data from DBS studies, which have shown that patients with TROCD who did respond tended to discontinue one or more of their long-standing psychotropic medications.^{34–36} On the other hand, patients on TAU alone were given 1 year to respond. This decision was made on the basis of a 5-year longitudinal study showing that approximately 82% of patients with severe OCD who responded to TAU did so within the first 2 years of initiating treatment. Approximately 8% did so during year 3. Less than 6% responded in year 4 and less than 3% in year 5.²⁶

For SRS-C patients, all complications throughout the 3-year treatment period were assigned to year 1 in the model for simplicity. By extension, costs and disutilities associated with complications were factored into the final calculations once and did not accumulate over time. For both treatment arms, there was no incremental utility or disutility for continuing as a nonresponder. Finally, mortality rate was not considered in our model given the short time horizon and the negligible added mortality risk in either treatment arm.

Statistical Analysis

We analyzed our model using TreeAge Pro Healthcare 2021. To account for uncertainty and variability, we parametrized model inputs using pooled means and standard deviations and performed a Monte Carlo (MC) simulation. We examined the primary model output (ICER) using a WTP threshold approach. The ICER (\$/QALY) was calculated by dividing incremental cost (difference in cost [\$] between treatment arms) by incremental effectiveness (difference in QALYs gained between treatment arms). According to current accepted definitions of cost-effectiveness, definite cost-effectiveness is achieved at less than \$50,000/QALY, intermediate cost-effectiveness at anywhere between \$50,000 and \$100,000/QALY, and cost-

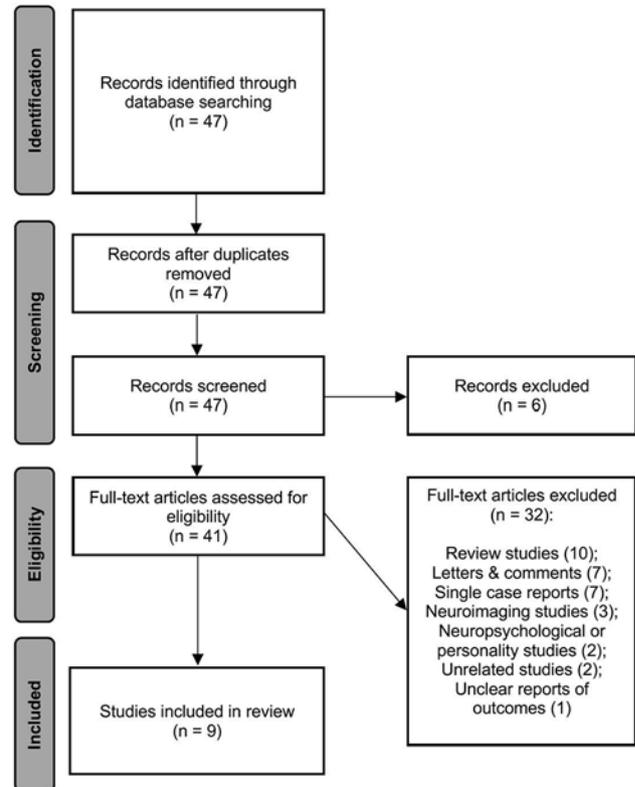


FIG. 1. PRISMA flow diagram. Data added to the PRISMA template (from Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 2009;6[7]:e1000097) under the terms of the Creative Commons Attribution License.

ineffectiveness at greater than \$100,000/QALY gained.³⁷ We also examined the cost-effectiveness ratio (CER) of SRS-C. The CER is a noncomparative calculation found by dividing the cumulative cost of SRS-C by the cumulative QALYs gained from SRS-C in the 3-year model. While the ICER is useful for comparing the cost-effectiveness of SRS-C with that of TAU, the CER represents the absolute cost per QALY of a single treatment arm. The results of the MC simulation were further analyzed using both probabilistic and deterministic sensitivity analyses. A *p* value < 0.01 was considered statistically significant.

Results

Literature Review

Our PubMed search yielded 47 initial results (see Fig. 1 for our PRISMA flowchart).³⁸ From the 9 studies selected for data collection (published 2008–2020), we identified a total of 158 unique patients who had undergone SRS-C for TROCD between 1988 and 2018.^{39–47} One additional study, a comprehensive systematic review from 2018, was used to cross-reference data and eliminate duplicates.¹⁷

Across all patients, the mean baseline (preoperative), 12-month, 24-month, and 36-month Y-BOCS scores were 34 ± 3.9 , 22 ± 9.6 , 19 ± 9.1 , and 16 ± 9.6 , respectively. The mean follow-up was 43 ± 29.6 months. The mean overall

reduction in the Y-BOCS score was 18 ± 11 , with an average reduction of 24 ± 7.6 for responders ($n = 100$) and 9 ± 8.9 for nonresponders ($n = 58$). On the basis of the response criterion of $\geq 35\%$ reduction in Y-BOCS score from baseline to last follow-up, 63% of patients were categorized as responders. Comprehensive outcomes and complications data from our systematic review are listed in Table 1.

A comparative analysis of the SRS-C ($n = 158$) and TAU ($n = 113$) samples showed several significant differences: higher average baseline Y-BOCS scores in the SRS-C versus TAU group (33.8 vs 27.5, $p < 0.0001$), different gender distributions (% female: 43% vs 54%, respectively, $p < 0.0001$), and a higher rate of comorbid depression (60% vs 30%, respectively, $p < 0.0001$). Age at the time of intervention did not differ significantly between groups (37.0 vs 38.5 years, respectively, $p = 0.1122$).

Decision Analytic Model

For an overview of our completed model, see Fig. 2. All base case model inputs and distributions are included in Table 2. The mean base cost of SRS-C, which included four office visits (\$238), the procedure itself (\$1728), two MRI studies (\$329), estimated hospital fees (\$2988), and estimated out-of-pocket expenses (\$5200), was $\$10,483 \pm \3535.53 .^{32,33} The large standard deviation of \$3535.53 is representative of the significant variability in hospital fees and out-of-pocket expenses associated with SRS-C (other values in this calculation are fixed and based on Medicare reimbursement amounts). The mean yearly cost of TAU was $\$5372 \pm \3995 , whereas the annual reduced-cost version of TAU after treatment response was $\$1576 \pm \1173.93 .²⁹ Using a published algorithm as our utility model, we converted the mean percentage change in the Y-BOCS score (50.66%) into a utility value of 0.214 ± 0.047 .¹⁴

MC Simulation

Based on the results of our MC simulation ($n = 100,000$), SRS-C was more cost-effective than TAU with an estimated ICER of $\$28,960/\text{QALY}$ gained. Furthermore, when examined under a WTP threshold of $\$50,000/\text{QALY}$ gained, SRS-C attained definite cost-effectiveness relative to TAU for TROCD. The mean CER (i.e., total cost to gain 1 QALY) for SRS-C was $\$73,659/\text{QALY}$. The mean CER for TAU was $\$663,450/\text{QALY}$, which may be explained by the low net effectiveness of TAU (0.02) over a 3-year time horizon. See Table 3 for a summary of cost-effectiveness rankings.

Net cost for SRS-C over 3 years was $\$21,023$ compared to $\$13,269$ for TAU. Estimated costs from complications were $\$74,877$ (inpatient management) and $\$109$ (outpatient management). Net effectiveness of SRS-C over 3 years was 0.29 QALYs compared to 0.02 QALYs for TAU. Incremental effectiveness was 0.27 QALYs (95% CI 0.2698–0.2702, $p < 0.0001$). Effectiveness was influenced by year of response, with SRS-C responders (without complications) in years 1, 2, and 3 gaining 0.60, 0.40, and 0.19 QALYs over the 3-year time horizon, respectively.

Sensitivity Analyses

Using probabilistic sensitivity analysis, MC simula-

tion outputs were plotted on a cost-effectiveness acceptability curve (Fig. 3). At WTP thresholds of $\$50,000$ and $\$100,000$ per QALY, we found that SRS-C was more cost-effective than TAU in 83% and 100% of iterations, respectively. In Fig. 4, a subset of 5000 samples was drawn at random from the hypothetical cohort of 100,000 to generate an incremental cost-effectiveness scatterplot, graphically displaying the impact of incremental cost and incremental effectiveness on the probability of cost-effectiveness given WTP thresholds of $\$50,000/\text{QALY}$ (Fig. 4 left) and $\$100,000/\text{QALY}$ (Fig. 4 right).

Finally, deterministic sensitivity analysis was used to create a tornado diagram (Fig. 5) that illustrates the effects of varying each parametrized input in our decision analytic model on the overall ICER. All costs, probabilities, and utilities were varied within a sensitivity range 20% above and below the mean values. In order of descending effect, four parameters (with sensitivity ranges) contributed $> 80\%$ of overall ICER variance: cost of SRS-C ($\$8386$ to $\$12,580$), 1-year probability of response to SRS-C (0.30 to 0.46), cost of TAU ($\$4312$ to $\$6468$), and utility of SRS-C (0.17 to 0.26). With a higher cost of SRS-C or lower 1-year probability of response to SRS-C, cost of TAU, or utility of SRS-C, the ICER increased significantly, and vice versa. The cost of complications requiring inpatient management ($\$59,901$ to $\$89,853$) had little to no impact on overall ICER, despite carrying such a large cost. Overall, based on sensitivity analysis, SRS-C remained cost-effective compared to TAU under a broad range of cost and effectiveness values.

Discussion

This study, which is the first economic evaluation comparing SRS-C to TAU for TROCD, shows that SRS-C is more cost-effective despite having higher costs. Under the broadly accepted WTP threshold of $\$50,000/\text{QALY}$, SRS-C has an 83% probability of being cost-effective, reaching 100% cost-effectiveness at a WTP threshold of $\$100,000/\text{QALY}$. Since this is the first cost-effectiveness study of SRS-C for TROCD, no comparable analyses exist.

The cost-effectiveness of nonpsychiatric indications for SRS has been explored in several studies. Caruso et al. conducted a cost-comparative study of SRS versus open resection for brain metastases, arteriovenous malformations, and acoustic neuromas and found that the average 12-month cost of SRS was $\$32,869$, $\$29,698$, and $\$32,039$, respectively.³² Despite the fact that these represent the net costs from a single year, they exceed our cumulative 3-year SRS-C cost of $\$21,023$. This difference could be indication specific. SRS-C consists of two lesions (bilateral anterior limb of the internal capsule) created in a single session; however, brain metastases may require multiple lesions (> 2), and complex arteriovenous malformations may require multiple SRS sessions, both of which contribute to higher costs.⁴⁸

Gandhoke et al. compared the cost-effectiveness of microvascular decompression versus SRS for patients with trigeminal neuralgia (TN) and found that the net cost of SRS over 10 years was $\$8073$; however, costs were examined from a hospital perspective (i.e., costs included only

TABLE 1. Literature review of patients with TROCD who underwent SRS-C

Authors & Year	No. of Pts*	Y-BOCS Score				Mean Response Rate at Last FU (no.)	Complications	
		Mean at Baseline (SD)	Mean at 12 Mos (SD)	Mean at 24 Mos (SD)	Mean at Last FU (SD)		Requiring Outpatient Management	Requiring Inpatient Management
Rück et al., 2008 ³⁹	8	32.8 (3.99)	14.4 (12.77)	NA	139.5 (35.09)	62.5% (5/8)	Unilat radiation necrosis w/ subsequent apathy, memory problems, & executive dysfunction (n = 1); sexual disinhibition resulting in job loss & severely impaired social functioning (n = 1)	Brain edema (peak size at 1 yr post-SRS-C), hospitalization w/ Sx of apathy, incontinence, & seizures; at last FU Sx (except seizures) persisted (n = 1)
Lopes et al., 2009 ⁴⁰	5	32.2 (1.48)	20.2 (10.35)	19.4 (10.40)	48 (0)	60% (3/5)	Persistent HA for 2 wks requiring oral corticosteroids (n = 1)	NA
Kondziolka et al., 2011 ⁴¹	3	37.3 (2.88)	23.6 (13.57)	17.3 (13.01)	41.7 (13.50)	66.7% (2/3)	NA	NA
Sheehan et al., 2013 ⁴²	5	32.2 (1.30)	12.5 (0.70)	18.7 (10.69)	22.2 (11.73)	80% (4/5)	NA	NA
Lopes et al., 2014 ⁴³	12	33.5 (3.20)	21.8 (12.64)	NA	55.1 (23.33)	66.7% (8/12)	ME (duration <1 wk) requiring mood stabilizers w/in 12 mos of SRS-C (n = 2, both w/ history of ME)	NA
Rasmusen et al., 2018 ⁴⁴	15 40	33.0 (4.63) 34.1 (3.05)	30.6 (7.53) 20.2 (7.32)	24.0 (8.85) 17.8 (7.60)	33.6 (4.96) 30.3 (8.58)	46.7% (7/15)† 75% (30/40)‡	Significant edema w/ HA w/o additional sequelae w/in 12 mos of SRS-C, requiring DXP (1–2 mg/day) for 1 mo (n = 5); ME requiring mood stabilizers w/in 12 mos of SRS-C (n = 3; all w/ history of ME); abulia after repeat single-shot SRS-C leading to unemployment, Sx improved after oral DXP (n = 1)	Symptomatic bilat edema w/ radionecrosis & cyst formation; failed treatment w/ bevacizumab followed by shunt placement, open resection of necrotic material, suffered fall during neuro-rehabilitation w/ a large SDH leading to PCA occlusion; at last FU, remained in minimally conscious state (n = 1)
Spatola et al., 2018 ⁴⁵	10	32.7 (4.76)	18.3 (9.66)	17.0 (6.21)	41.0 (38.36)	80% (8/10)	NA	NA
Gupta et al., 2019 ⁴⁶ ¶	40	33.5 (4.39)	23.7 (9.62)	NA	43.4 (21.45)	45% (18/40)	Post-SRS-C edema on MRI became symptomatic & required short-course steroid treatment, cyst was formed at site of lesion; Sx resolved (n = 1)	NA
Peker et al., 2020 ⁴⁷	20	36.0 (4.32)	22.0 (8.14)	17.0 (11.34)	36 (0)	75% (15/20)	Persistent HA (n = 2), symptomatic brain cyst (n = 1), both pts treated w/ 2-wk course of oral corticosteroids, Sx resolved	NA

DXP = dexamethasone; FU = follow-up; HA = headache; ME = manic episode; NA = not applicable; pt = patient; PCA = posterior cerebral artery; SDH = subdural hematoma; Sx = symptoms.

* Number of TROCD pts specifically undergoing SRS-C, regardless of other treatments tested in study.

† Single shot.

‡ Double shot.

¶ Two pts with suicidal ideation (1 with comorbid severe bipolar I disorder; 1 with comorbid severe major depressive disorder), resolved with adjustment of patient's own medications (likely unrelated to SRS-C).

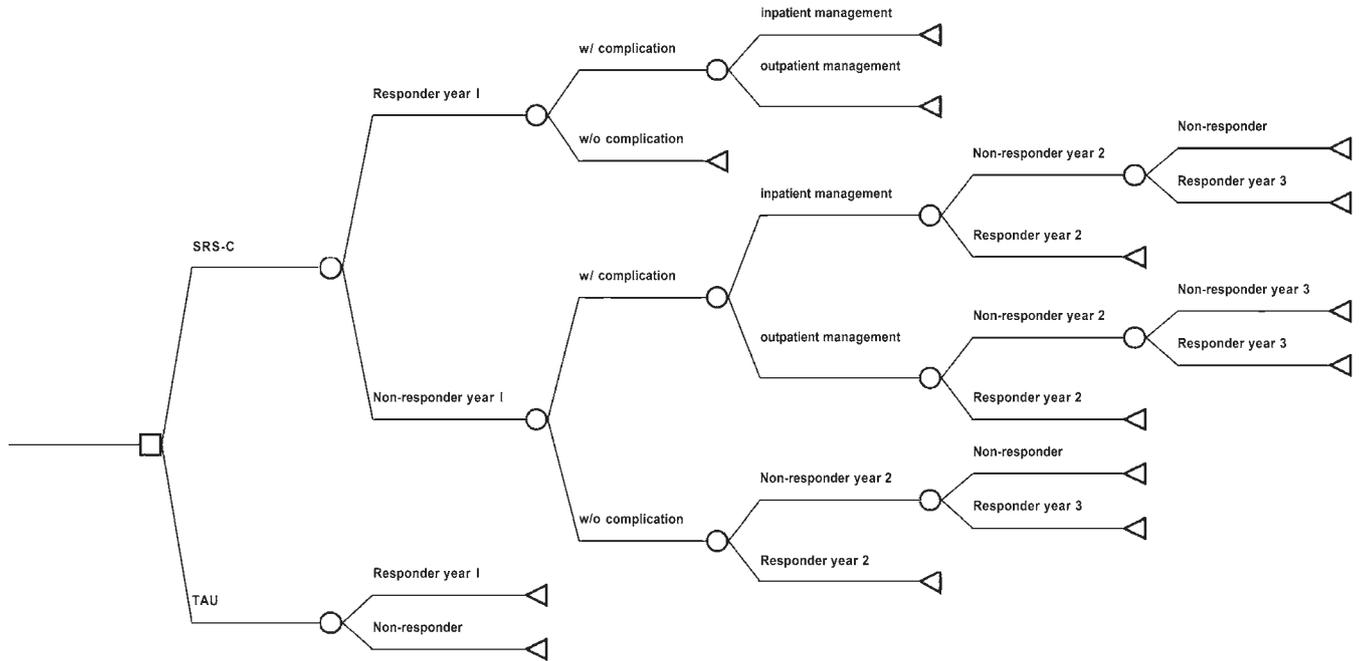


FIG. 2. Decision analytic model compares cost-effectiveness of SRS-C versus TAU for TROCD within a 3-year time horizon. Individual payoff formulas at terminal branches were omitted for simplicity.

TABLE 2. Model inputs

Input	Mean	SD	Distribution	Authors & Year
Probabilities				
Response to SRS-C				
In yr 1	0.38	0.137	Beta	
In yr 2	0.10	0.078	Beta	
In yr 3	0.16	0.078	Beta	
Response to TAU	0.03	0.03	Beta	Garnaat et al., 2015 ²⁶
Complications after SRS-C				
IPT	0.01		Uniform	Pomeraniec et al., 2018 ⁵⁵
OPT	0.99		Uniform	
Utilities (QALY)				
SRS-C	0.21	0.05	Normal	Kumar et al., 2019 ¹⁴
TAU	0.18	0.18	Normal	Gregory et al., 2018 ²⁹
IPT	-0.35	0.02	Normal	Kumar et al., 2019 ¹⁴
OPT	-0.02	0.01	Normal	Kumar et al., 2019 ¹⁴
Costs (\$)				
SRS-C*	10,483	3,535.53	Gamma	
TAU	5,372	3,995	Gamma	Gregory et al., 2018 ²⁹
Pharmacotherapy alone	1,576	1,173.93	Gamma	Gregory et al., 2018 ²⁹
IPT†	75,000	25,000	Gamma	
OPT	109.44		Uniform	CMS ³¹

CMS = Centers for Medicare & Medicaid Services; IPT = inpatient; OPT = outpatient.
 * Includes CPT codes 61798, 61799, 70557 (x2), 99204, and 99214 (x3), as well as an estimate of hospital fees based on Gandhoke et al., 2019,³³ and assumptions based on Caruso et al., 2015.³²
 † Mean cost for IPT based on an assumption; large standard deviation included to account for extreme variance.

TABLE 3. Cost-effectiveness rankings over a 3-year time horizon

Strategy	Cost	Incremental Cost	Effectiveness (QALY)	Incremental Effectiveness (QALY)	ICER (\$/QALY)
TAU	\$13,269	—	0.02	—	—
SRS-C	\$21,023	\$7,754	0.29	0.27	\$28,960

direct expenditures to the hospital).³³ Although we expect the cost of SRS for TN to approximate that of SRS-C for TROCD, this difference in cost perspective, as well as the fact that SRS for TN is always unilateral (single lesion), significantly limits any direct comparison.

Using Medicare reimbursement as a proxy for direct costs calculated from a societal perspective, Ravikumar et al. examined the cost-effectiveness of three neurosurgical treatments for essential tremor (ET): MRI-guided focused ultrasound, DBS, and SRS.⁴⁹ One-year costs of SRS for ET (including the cost of preoperative imaging/planning and complication costs) were \$20,013 ± \$1036. To facilitate comparison, we ran our decision analytic model through the 1st year alone and found that the estimated 1-year cost of SRS-C for TROCD (including the costs of imaging, planning, office visits, medications, and complications) was \$16,341 ± \$1256. Of the indications discussed, the costs of SRS for ET seem to approximate most closely those of SRS-C for TROCD, yet the difference between the two is statistically significant, with SRS-C for TROCD costing \$3824 ± \$118.54 less than SRS for ET (95% CI \$3513.60–\$4134.40, $p < 0.0001$). As in our discussion of Gandhoke and colleagues' SRS for TN study, we could attribute this finding to differences in cost perspective. Because our study includes costs limited to a healthcare sector perspective, as opposed to the more comprehensive societal perspective, it is possible that the cost inputs in our model are underestimates; however, our rigorous deter-

ministic sensitivity analysis demonstrated that even a 20% variation above or below our model inputs, including the cost of SRS-C, would not significantly affect overall cost-effectiveness. In fact, 1-way sensitivity analysis revealed that with a 20% increase in the cost of SRS-C, the ICER was \$30,725.78 per QALY, which is well under the broadly accepted WTP threshold of \$50,000/QALY.

Given the lack of consistency in reported costs across multiple indications for SRS, our study highlights the need for greater public access to healthcare economics data. This applies not only to Medicare, Medicaid, and public insurance systems but also to the private sector. Though we acknowledge that in a price-competitive market with a complex healthcare system, exact cost values may not always be readily accessible, accurate cost data and increased transparency are imperative for future CEAs to take a truly societal perspective. In particular, there is a paucity of large, multicenter, prospective cost-effectiveness trials. Ideally, these would collect cost and utility data as well as safety and efficacy data in a real sample with a structured follow-up at multiple institutions to account for cost differences and would generate reproducible (i.e., generalizable) conclusions. The results of these studies can not only influence medical decision-making at the physician level but also reach hospital administrators, insurance companies, and government healthcare programs such as Medicare and Medicaid.⁵⁰ Indeed, in the growing field of psychiatric stereotactic and functional neurosurgery, there

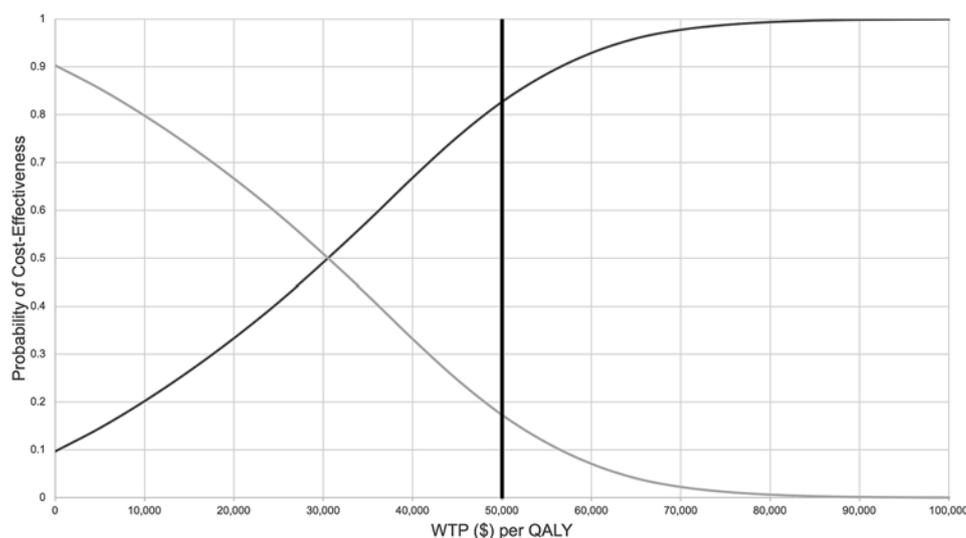


FIG. 3. Cost-effectiveness acceptability curve shows results from the MC simulation ($n = 100,000$) and probabilistic sensitivity analysis. The SRS-C (*black*) curve dominates the TAU (*gray*) curve. Thus, SRS-C is shown to be more cost-effective than TAU in 83% and 100% of iterations at \$50,000/QALY and \$100,000/QALY, respectively. The *black vertical line* marks the broadly accepted WTP threshold of \$50,000 per QALY.

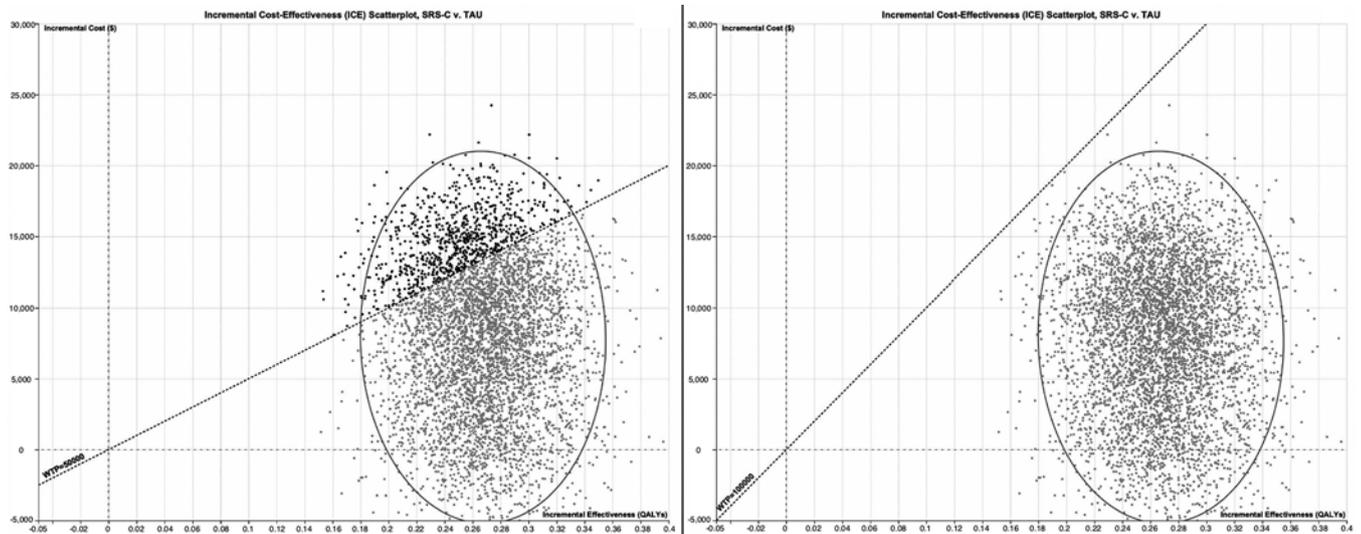


FIG. 4. Incremental cost-effectiveness scatterplots of SRS-C versus TAU at a \$50,000 WTP threshold (**left**) and \$100,000 WTP threshold (**right**). Five thousand representative samples were drawn at random from the hypothetical cohort of 100,000 in our MC simulation, and incremental cost versus incremental effectiveness was plotted. *Gray points* (left) represent iterations of our model resulting in ICERs that meet the criteria for “definite” cost-effectiveness (i.e., they fall under the \$50,000/QALY WTP threshold, *black dotted line*), whereas *black points* represent iterations with ICERs that meet “intermediate” cost-effectiveness criteria (i.e., they lie above the \$50,000/QALY WTP threshold but below the \$100,000/QALY WTP threshold, *black dotted line*). This is evident in the right panel, in which *gray points* encompass iterations meeting criteria for both definite and intermediate cost-effectiveness and there are no *black points*. The *gray ellipses* represent the 95% confidence interval.

is a great need for high-quality CEAs, as insurance coverage (and, consequently, healthcare resource allocation) for the surgical treatment of psychiatric illness is disproportionately lower than that for nonpsychiatric indications.^{51,52}

Furthermore, in light of the fact that the incidence of treatment resistance in OCD is quite high and considering that the probability of a response to TAU after 3 years is quite low, perhaps criteria for the surgical treatment of TROCD are too stringent with regard to the duration of disease.^{26,53} At most centers, the current accepted number is ≥ 5 years;^{39–47} however, there is some evidence that it would be reasonable to enroll patients after 3 or 4 years, as long as they have fulfilled all other requirements for symptom severity and treatment refractoriness such as multiple failed first-line pharmacotherapeutics (including SSRIs and clomipramine), adjunctive medication trials, cognitive behavioral therapy, and the more recently approved transcranial magnetic stimulation.^{26,54} One meta-analytic study of DBS for TROCD found that a younger age at OCD onset (2-year difference; $p < 0.03$) was present in nonresponders than in responders (there was no statistically significant difference in age at the time of surgery between the two groups).¹² Therefore, given the findings suggesting that earlier treatment may be more effective and that continued TAU after 3 years may unnecessarily prolong severe disease or delay symptom relief, it is reasonable to consider early intervention, especially in view of the results presented here.

Study Limitations

Several important limitations apply to this study. First, we assumed that responders in either treatment arm would remain responders for the duration of the model. Nevertheless, it is possible that some patients would relapse despite

a strong initial response.^{45,46} Second, our 3-year time horizon restricts complications to those occurring up to 36 months after surgery. In our aggregate sample, this captured approximately 99% of all complications; however, certain rare but significant complications may arise between years 4 and 5, such as a symptomatic radionecrotic cyst requiring surgery.⁵⁵ We found that available data were insufficient to carry the model past 3 years without adding significant uncertainty. This limitation is mitigated by the fact that we would not expect the effectiveness of SRS-C to decrease with a longer time horizon given the durability of treatment;³⁹ thus, it is likely that the cost-effectiveness of SRS-C would not change with a longer time horizon. It is worth noting that although an included study from 2008³⁹ reported severe cognitive dysfunction in several patients following SRS-C, we chose not to include those complications in our utility model; however, this is not necessarily a limitation. Cognitive outcomes from the past decade worth of trials have shown stable to improved cognition in many cases;⁵⁶ therefore, excluding the effects of postoperative cognitive change on QOL in our utility model may underestimate SRS-C–related improvement in QOL. Additionally, though many SRS-C and TAU group characteristics differed, most (except gender distribution) likely led to an underestimation of SRS-C’s cost-effectiveness given the higher baseline clinical severity and higher prevalence of comorbid depression in the SRS-C group than in the TAU group. Third, our utility model is based on a meta-analytic study comparing the efficacy of neuroablation versus DBS for TROCD.¹⁴ Thus, utilities associated with SRS-C and disutilities associated with complications are indirect derivations and should be interpreted as approximations of true utility. Clinical trials for TROCD should move to

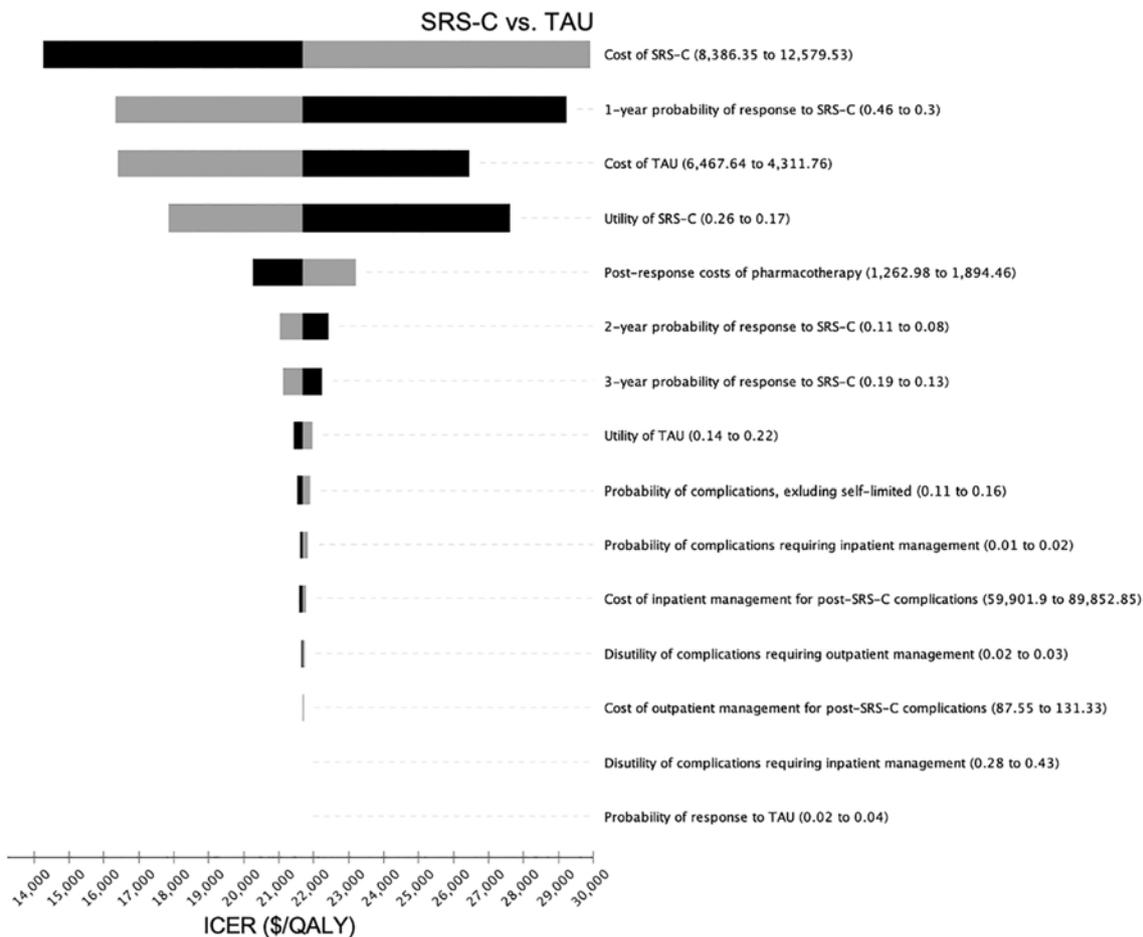


FIG. 5. A tornado diagram displays the effect of varying each parametrized input on the ICER. All costs, probabilities, and utilities were varied within a sensitivity range 20% above and below the mean values. *Black bars* show the impact of an increase, and *gray bars* show the impact of a decrease in the variable value on overall ICER.

include QOL measures (e.g., EQ-5D, SF-36) in addition to the standard efficacy measures (e.g., Y-BOCS) to ensure that future health economics studies have sufficient data to back more generalizable claims of cost-effectiveness.

The findings of this study are also limited by our healthcare sector cost perspective. Though we initially sought to employ a societal perspective, this proved difficult given the lack of available or reliable cost data for less tangible items such as productivity, education, and transportation. In particular, we did not include costs or disutilities associated with healthcare utilization outside the scope of each treatment arm. This means that the costs of healthcare services (e.g., emergency room or urgent care visits) for non-OCD and nontreatment-related reasons are not included. Furthermore, much of our cost data came from Medicare reimbursements, meaning that our exact findings may not be easily reproducible outside the US.

Additionally, though our cost data were drawn from US public insurance data, according to the 2020 US Census, approximately 66.5% of Americans are privately insured, with approximately 35% insured by Medicare/Medicaid.⁵⁷ Though including private insurance reimbursement values for SRS-C in our model could have led to greater general-

izability, we were unable to acquire nationally representative private insurance data for this study because of a lack of transparency and access to such data. However, of those privately insured, approximately 55% receive healthcare coverage through their employer.⁵⁷ With that in mind, we noted that approximately 60% of our SRS-C sample was unemployed at the time of the procedure. Thus, within our study population, the exclusive use of public insurance data may have led to more representative and generalizable results than for a study population with less functional impairment. Future healthcare economic analyses should strive to include these data, and private insurers should work to increase reimbursement transparency.

Finally, though there is a well-documented increased risk of suicidality in patients with OCD, especially those with comorbid depression or mood disorders, we were unable to include this in our model. For one, attempts to estimate the monetary cost or specific disutility associated with either suicidal ideation or suicide attempt (e.g., psychiatric hospitalization, medication changes, inpatient therapy, etc.) were limited by a lack of available data. Second, theoretically, responding to treatment reduces this risk, but attempts to quantify the reduction were also lim-

ited by a lack of data. In our SRS-C sample of 158 patients, 1% (n = 2) experienced suicidal ideation (with no suicide attempts or hospitalizations) after radiosurgery. Both patients were from the same study⁴⁶ and had comorbidities (bipolar I disorder; major depressive disorder) that further increased this risk. However, considering that these additional costs would have been attributed to the TAU group, this would have further supported our conclusion that SRS-C for TROCD is cost-effective.

Conclusions

Despite certain limitations, as compared to TAU, SRS-C for TROCD is more cost-effective under a range of possible cost and effectiveness values. While prior studies have demonstrated the safety and efficacy of SRS-C, our study adds it to the growing list of cost-effective alternatives for patients with TROCD.

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Disclosures

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Supplemental Information

Previous Presentations

This work was presented as a digital poster at the Congress of Neurological Surgeons 2021 Annual Meeting held in Austin, TX, on October 19, 2021.

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