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# Dollars and Sense: Cost-Effectiveness of Epilepsy Surgery

**Cost Effectiveness of Surgery for Drug-Resistant Temporal Lobe Epilepsy in the US Neurology**

Sheikh SR, Kattan MW, Steinmetz M, Singer ME, Udeh BL, Jehi L. *Neurology*. 2020;95(1):e1404-e1416. doi:10.1212/WNL.0000000000010185

Objective: Surgery is an effective but costly treatment for many patients with drug-resistant temporal lobe epilepsy (DR-TLE). We aim to evaluate whether, in the United States, surgery is cost-effective compared to medical management for patients deemed surgical candidates and whether surgical evaluation is cost-effective for patients with DR-TLE in general. Methods: We use a semi-Markov model to assess the cost-effectiveness of surgery and surgical evaluation over a lifetime horizon. We use second-order Monte Carlo simulations to conduct probabilistic sensitivity analyses to estimate variation in model output. We adopt both health care and societal perspectives, including direct health care costs (eg, surgery, antiepileptic drugs) and indirect costs (eg, lost earnings by patients and care providers). We compare the incremental cost-effectiveness ratio to societal willingness to pay (∼US$100 000 per quality-adjusted life-year [QALY]) to determine whether surgery is cost-effective. Results: Epilepsy surgery is cost-effective compared to medical management in surgically eligible patients by virtue of being cost-saving (US$328 000 vs US$423 000) and more effective (16.6 vs 13.6 QALY) than medical management in the long run. Surgical evaluation is cost-effective in patients with DR-TLE even if the probability of being deemed a surgical candidate is only 5%. From a societal perspective, surgery becomes cost-effective within 3 years, and 89% of simulations favor surgery over the lifetime horizon. Conclusion: For surgically eligible patients with DR-TLE, surgery is cost-effective. For patients with DR-TLE in general, referral for surgical evaluation (and possible subsequent surgery) is cost-effective. Patients with DR-TLE should be referred for surgical evaluation without hesitation on cost-effectiveness grounds.

## Commentary

For the one-third of patients with drug-refractory epilepsy, surgery provides the greatest hope toward achieving the holy grail: "no seizures, no side effects." Yet complex barriers exist preventing widespread implementation, including but not limited to the steep upfront resources required for presurgical evaluation, let alone surgery itself.[1] The larger question remains—do the long-term benefits outweigh upfront costs? Even the most effective interventions are doomed if economically unsustainable.

Sheikh et al provide encouraging results.[2] They performed a cost-effectiveness analysis of resection versus continued medical management for patients with drug-resistant temporal lobe epilepsy. The workhorse of cost-effectiveness analysis is the Markov decision-analytic model in which patients are conceptualized as essentially thousands of computer-based coin flips. Each flip is based on probabilities of various outcomes informed by literature and expert opinion (ie, seizure-freedom, surgical complications, emergency room [ER] visits, etc), "utilities" attached to each outcome (ie, worth of a year of life should that outcome occur, compared with perfect health), and the totality of costs in all such outcomes. Interventions are typically deemed cost-effective if the incremental cost effectiveness ratio (ICER) is less than US$50 000 to US$150 000 per added year of "perfect health" (quality-adjusted life-year [QALY]) comparing intervention versus no intervention.

First, they asked "Is surgery cost-effective if deemed eligible for surgery?" Indeed, from the perspective of the health care system, despite the large upfront cost and rare surgical complications, it only took about 4 years to drop below US$100 000 per QALY, and they estimated lifetime US$32 000 per added QALY. Cost-effectiveness was even more robust when accounting for societal benefits of seizure reduction such as return to employment, in which resection was actually cost-saving after 10+ years. Second, they asked "Is referral for presurgical testing cost-effective," knowing that only a fraction will be deemed candidates. Once again, yes, even after considering upstream costs such as inpatient electroencephalography (EEG), positron emission tomography-computed tomography, or magnetoencephalography.

Critics will be suspicious of the staggering number of assumptions behind probability distributions which may or may not apply to the patient at hand, or costs which may differ widely between settings. The most interesting question here actually becomes: "Under what assumptions would surgery NOT be cost-effective?" They found surgery remained cost-effective if initial postoperative seizure freedom was at least 21% (it is actually more like 70%), patient's age is less than 97 to allow sufficient life expectancy to accrue future cost savings, cost of surgery was no more than 5 times what they used in their modeling, and at least 5% of all persons referred for presurgical testing would actually be considered candidates. These are just about as robust sensitivity analyses as one can possibly imagine, and extend prior work.[3]

So, are we done? Can we use these data to conclude that all drug-refractory potentially eligible candidates should strive toward surgery? The short answer is probably yes if it fits with their individual goals, or at least these data strongly support cost-effectiveness. But, as you may expect, it's complicated. While the investigators made outstanding efforts to explore relevant variables, no study can tackle every dimension. Their analysis did not factor in invasive intracranial EEG monitoring, which is becoming standard of care for most cases other than unifocal temporal epilepsy with concordant noninvasive testing. While adding the burden and cost of invasive monitoring could render these conclusions overly optimistic, at least other research allays this concern by supporting the cost-effectiveness of intracranial EEG itself.[4] Also unstudied were children, extratemporal epilepsy (where cost-effectiveness might be worse due to lower effectiveness), a comparison of surgery to responsive neuromodulation or deep brain stimulation. Data also relied on ER/hospitalization rates/costs within Cleveland Clinic which might not generalize to other less resource-rich centers.

At a higher level, the very notions of ICERs and QALYs have skeptics. The ICER assumes a valid dollar amount exists for what a year of good health is worth, which is inherently arbitrary. In contrast to European nations, the Affordable Care Act actually forbids Medicare from using ICERs for coverage decisions because QALYs may disadvantage disabled or older patients who start off with lower "utilities" which is quite relevant to epilepsy patients. Furthermore, cost-effectiveness is surely not motivation in and of itself to pursue invasive surgery. This study more so illustrates that we do not have to choose between society's bottom line and the interests of the individual patient—they agree. Sheikh et al calculated possible long-term cost-savings to society, and prior Markov simulations add that anterior temporal lobectomy adds on average about 7.5 QALYs per person,[5] which would make surgery the "dominant" strategy in cost-effectiveness lingo (ie, both lower ultimate cost and more effective than the alternative). More importantly, to be valid, these analyses assume that we can accurately measure costs (which are notoriously nontransparent in health care), what a year of imperfect health is worth, and that the value of a year in a particular health state is static over a lifetime which is questionable. For example, the present study borrowed QALY estimates from a small single-center study[5] where patients completed "standard gamble" questions to calculate the value of a year of life in different health states (ie, seizures, side effects, surgical complications): one minus the chance of immediate death that a person would accept to avoid living the rest of their life with a particular health problem. This value propagates throughout the model by assuming that 1 year at "100% health" is equivalent to 5 years at "20% health." And such calculations do not account for the very real psychological fear of undergoing brain surgery which for some patients is an insurmountable barrier regardless of societal cost-saving. In short, whereas the total "cost" numerator is complicated enough, the nuts and bolts of the "effectiveness" denominator (QALY) are even more fiercely challenging to meaningfully capture.

While cost-effectiveness analysis requires a dizzying array of assumptions pertaining to the enormous number of inputs related to cost, chance, and valuation of life itself, this study nicely demonstrates the big-picture cost-effectiveness of surgery, supporting its widespread use and sustainability. Sheikh et al are to be praised for their valiant effort from expert investigators rigorously synthesizing an enormous amount of data, as this adds useful fodder for already entrenched enthusiasm behind temporal lobectomy for drug-refractory patients. While concern about the intense upfront resources required to determine surgical candidacy or undergo surgery is real and without an easy fix, and future work could round out the above variables and populations not considered here, this work provides evidence that the investment will likely pay off in the end, barring the most extreme of assumptions.

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