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TITLE PAGE

Title: Is resective surgery cost-effective for adults with epilepsy?

- **A cost-utility analysis in a publicly funded healthcare system**

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ABSTRACT

Background: Resective epilepsy surgery is an established clinical intervention, but the cost effectiveness at a national healthcare level is uncertain. This study evaluates the cost effectiveness of resective epilepsy surgery compared to medical management in adults from national healthcare and personal social services perspectives.

Methods: A de-novo decision analytic model was developed – comprising of a one-year decision tree and life-time Markov model to evaluate life-time costs and Quality Adjusted Life Years (QALYs). Data were obtained from UK epilepsy surgery centres to evaluate the costs of pre-operative assessment and the probability of undergoing resection after pre-surgical evaluation. Other clinical inputs were obtained from a systematic literature review. The main outcome of the analysis was the incremental cost-effectiveness ratio (ICER) – with a cost-effectiveness threshold set at £20,000 cost per QALY gained.

Results: Data from 762 patients informed pre-operative evaluation costs and the probability of undergoing epilepsy surgery post pre-surgical evaluation. The total lifetime cost of epilepsy treatment for people that had surgical treatment was £56,911, compared with £32,490 for medical management. Total QALYs per person for surgery were 15.91 and 13.76 for medical management. Resective epilepsy surgery was shown to be cost effective with an ICER of £11,348 per QALY gained.

Conclusions: Our data inform and strengthen recommendations to prioritise referral of those with drug refractory epilepsy to surgical centres. We provide a health economic rationale for development and support of resective epilepsy surgery programs across national healthcare systems.

KEY MESSAGES

What is already known on the topic?

Considering a nationwide healthcare system perspective, a single study has been published in a European context supporting the economic rationale of resective epilepsy surgery. That work, though, evaluates the economic rationale without including the costs of presurgical evaluation if a patient is deemed inoperable after pre-surgical evaluation.

What this study adds

Our study provides evidence of cost-effectiveness from a total healthcare perspective rather than only considering cost-effectiveness in people who have already been fully assessed as operable. Evaluating the cost-effectiveness of resective epilepsy surgery from the point of referral to epilepsy surgery programmes is reflective of treatment pathways in clinical practice. Although the costs of pre-surgical evaluation for surgery can be high, and not all people referred for epilepsy surgery will be suitable candidates for resection, funding a national epilepsy surgery program is cost effective.

How this study might affect research, practice or policy

Resective epilepsy surgery for drug resistant epilepsy is cost-effective, even when including assessment of people who are subsequently found not to be appropriate for operative intervention. The study provides increased support for referral to epilepsy surgery programs.

Glossary of terms

Cost-effective: An intervention that provides a good value for its cost, often measured by the cost per unit of health benefit. The cost-effectiveness threshold in our analysis is £20,000 per QALY gained.

Cost-utility analysis: A method that compares the cost of an intervention to its health outcomes measured using Quality Adjusted Life Years (QALYs).

Decision tree: A type of health economic model structure used to evaluate different strategies or interventions. Decision trees are typically used to evaluate short-term outcomes.

Deterministic analysis: used in models where outcomes are precisely determined by inputs.

Direct costs: Expenses directly associated with medical treatment, such as hospital stays, medications, and procedures.

Half-cycle correction: An adjustment in a Markov model to account for the fact that transitions between health states occur continuously rather than at discrete intervals.

Healthcare costs: The total expenses associated with medical care, including direct, indirect, and intangible costs.

Incremental cost-effectiveness ratio (ICER): A statistic used to summarise the cost-effectiveness of a health intervention, calculated as the difference in cost divided by the difference in effectiveness between two interventions. Effectiveness in our analysis was measured using QALYs.

Indirect costs: Costs related to lost productivity, time, and other non-medical expenses due to illness or treatment.

Markov model: A mathematical model used to represent transitions between different health states over time.

Mean costs: The average cost of an intervention or treatment across a population.

Mean QALYs: The average Quality Adjusted Life Years gained from an intervention across a population.

Monte Carlo simulation: A computational technique that uses random sampling to estimate the probability distribution of outcomes in a model.

NHS reference costs: Average unit costs of providing various healthcare services within the NHS in England.

One-way sensitivity analysis: A method to assess how the results of a model change when one parameter is varied while others are held constant.

Probabilistic sensitivity analysis (PSA): A technique that evaluates the uncertainty in a model by varying multiple parameters simultaneously according to their probability distributions.

Probability distribution: A mathematical function that describes the likelihood of different outcomes in a random process.

Quality Adjusted Life Years (QALYs): A measure of the value of health outcomes, combining both the quantity and quality of life gained from an intervention.

Unit cost: The cost per single unit of service or intervention.

Utility: A measure of the preference or value that individuals place on different health outcomes ranging from 0 – 1, where 1 represents full health and 0 represents dead.

INTRODUCTION

Drug refractory epilepsy (DRE) results in increased morbidity, premature mortality,[1] and accounts for approximately 80% of healthcare costs in epilepsy care.[2] Direct costs include ongoing trials of anti-seizure medications (ASMs) - around 50% of the total cost[3,4] - and hospitalisations owing to recurrent seizures or injuries. Indirect costs of epilepsy, such as unemployment and adverse impacts from comorbidities, can be several-fold greater than the direct care costs.[5]

Epilepsy surgery has established clinical effectiveness for adults,[6–8] with up to 58% of treated individuals achieving seizure freedom.[8] Despite recommended early referral for epilepsy surgery,[9,10] there is marked under-utilisation across healthcare settings.[11–13] Over 10 million people globally are potential surgery candidates,[14] yet even in high-income countries only an estimated 1% of appropriate people are evaluated.[15]

While previous analyses have suggested that epilepsy surgery is cost effective,[16–18] these studies have relied on single centre data, [19–24] or only evaluated people who proceeded to resection.[25] Owing to their alternative models of fees and costs, economic analyses conducted from single private healthcare centres may have limited applicability for publicly funded national healthcare systems. [19–22,24] To comprehensively address the cost effectiveness of epilepsy surgery in a government-funded health care system, a model was developed over a life-time horizon, estimating quality-adjusted life years (QALYs) and health service costs for all adults referred to resective epilepsy surgical programmes.

METHODS

Our model was developed as part of the National Institute of Health and Care Excellence (NICE) Guideline on Epilepsies in children, young people and adults; NG217 published in 2022.[26] Conceptualisation and sourcing of data inputs was conducted in 2021, prior to guideline publication. The NG217 Committee consisted of UK-based experts in epilepsy, epilepsy surgeons, neuropsychologists, pharmacists, and people with lived experience of epilepsy (online supplemental 1). As part of the guideline, a detailed health economic plan was developed. A brief online version of the plan can be found on the NICE website (https://www.nice.org.uk/process/pmg36/chapter/economic-evaluation-2#measuring-and-valuing-health-effects-in-cost-utility-analyses). Model structure, inputs and results were iteratively discussed with the guideline committee for clinical validation and interpretation.[26] In instances where no data were identified, committee estimates were used to populate the model. The model was developed using Microsoft Excel and Visual Basic for Applications.

Model structure

We developed a decision analytic model comparing resective epilepsy surgery to medical management (MM) in adults from a United Kingdom National Health Service (NHS) perspective. A healthcare perspective was chosen, aligning to the NICE reference case for assessing cost-effectiveness.

A cohort of adults with epilepsy was initially followed in the model through a one-year decision tree (Figure 1). For the surgical arm, the decision tree modelled the costs and effects of pre-operative assessment and resective epilepsy surgery. The cost of pre-operative evaluation was included for those people who underwent resective epilepsy surgery and for those who underwent pre-operative evaluation but did not progress to resective epilepsy surgery (i.e., continued to receive MM). The MM arm modelled the cost and effects for one year of MM for people with drug refractory focal epilepsy – including the costs and outcomes for those who underwent pre-surgical evaluation but did not proceed to surgery. At the end of one-year, proportions of the cohort were seizure free, not seizure free, or dead.

Long-term outcomes were modelled by 49 one-year Markov cycles (covering ages 36 to 85 years; Figure 2). The states of the Markov model were 'seizure free for one year', 'seizure free for two years', 'seizure free for three or more years', 'seizure free off ASMs', 'not seizure free', and 'dead'. Within a one-year cycle, people were attributed an annual probability of remaining in their current health state, dying, or transitioning to 'seizure free' or 'not seizure free' – dependent on their original health state. Time-dependency was incorporated to track how long people were seizure free, and to capture the probability of discontinuing ASMs once seizure freedom was obtained.

Model inputs

The probability of obtaining seizure freedom in year one was derived from two randomised controlled trials (RCTs)[7,8] identified in the clinical review conducted as part of the guideline update.[26] The starting age of the model cohort was 35 years – aligned with the average age of people included in the larger RCT.[8] The proportion of males in the model was 46.7%. This proportion was obtained from the long-term outcome study for resective epilepsy surgery,[27] as this study reported on a significantly larger cohort size in comparison to the rest of our outcome data and was based on UK outcomes. The probability of surgical mortality was also obtained from this dataset.[27] Probability of a permanent complication resulting from resective epilepsy surgery was set at 4.0%.[28–31] Data inputs for the one-year decision tree are presented in Table 1.

Table 1: Economic model data inputs
Model inputs: clinical outcomes. MM=medical management. ASM=anti-seizure medication. SMR=standardised mortality ratios. LnRR=log response ratio, SE=standard error, NA=not applicable.

Data input	**Base case value**	**Probability distribution**
One year decision tree outcomes		
Probability of 'not being seizure free' in the MM arm	96.7% [7,8]	Beta (Alpha: 59, Beta: 2)
Risk ratio	0.42 [7,8]	Lognormal (LnRR: -0.87, SE: 0.16)
Probability of mortality in the surgery arm	0.77% [27]	Beta (Alpha: 5, Beta: 644)
Probability of long-term complication from resective epilepsy surgery	4.0% [28–31]	NA
Long-term Markov model outcomes		
Annual probability of remission surgery	Various annual probabilities (see online supplemental 2) [27]	Beta
Annual probability of relapse surgery	Various annual probabilities (see online supplemental 2) [27]	Beta
Annual probability of remission MM	5.6% [32]	Beta (Alpha: 62, Beta: 184)
Annual probability of relapse MM	22.0% [32]	Beta (Alpha: 42, Beta: 17)
Annual probability of discontinuing ASMs each year $\geq$ 3 years of seizure freedom	15.7% [33]	NA
Probability of reoperation	4.0% (Committee assumption)	NA
SMR 'seizure free' surgery	2.42 (see online supplemental 3)	Made probabilistic based on the probability distributions applied for the SMR of seizure free MM and the SMR of not seizure free.
SMR 'seizure free' MM	1.78 [34]	Lognormal LnRR = 0.575, SE = 0.678
SMR 'not seizure free'	5.40 [28–31]	Lognormal LnRR = 1.686, SE = 0.158
Utility value – 'Seizure free' surgery'	0.858 [27,35]	See online supplemental 4
Utility value – 'Seizure free' medical management	0.869 [35]	See online supplemental 4
Utility value – 'Not seizure free'	0.689 [35,36]	See online supplemental 4
Utility decrement – annual decrement for long-term complications of surgery	**0.2 [28–31]**	**NA**
Utility value - Dead	**0**	**NA**

Owing to an absence of long-term RCT data relating to epilepsy surgery, outcomes for surgery and MM were obtained from two long-term observational studies (Table 1).[27,32] Transition probabilities were calculated for the risk of relapse (transitioning from 'seizure free' to 'not seizure free') and remission (transitioning from 'not seizure free' to 'seizure free'). Annual probabilities for relapse and remission in the MM arm were calculated from the cumulative probabilities previously reported,[32] assuming a constant rate of remission and relapse over the five-year period. Transition probabilities in the surgical arm were calculated differently to those in the MM arm because annual data were available for the number of people entering remission and relapsing (up to year 15). These data were used to calculate individual annual probabilities up to year 15 and were subsequently extrapolated beyond this for the remainder of a person's lifetime (online supplemental 2). The committee assumed a lifetime 4% probability of re-operation.

Standardised Mortality Ratios (SMRs) for 'seizure free' and 'not seizure free' individuals were applied to the general population mortality rates.[37] The SMR for 'not seizure free' and 'seizure free' MM were obtained from published estimates.[28–31,34] The SMR for 'seizure free' following epilepsy surgery was adjusted to account for the differing definitions of seizure freedom in our two long-term outcome studies (online supplemental 3).[27,32]

Health state utilities (Table 1) were based on reported values for people who were 'seizure free'; 'people experiencing a ≥50% reduction in seizures'; and 'people experiencing a <50% reduction in seizures'.[35] The utility for 'seizure free' in the surgical arm was adjusted to account for different definitions of seizure freedom (online supplemental 4). To obtain a utility value for 'not seizure free', data on the proportion of people experiencing a ≥50%

reduction in seizures, and people experiencing a <50% reduction in seizures,[36] were multiplied by published utility values.[35] A yearly utility decrement of 0.2 was applied for those who experienced long term complications from surgery.

Pre-operative assessment resource use for individuals undergoing pre-surgical evaluation were collected from adult surgical centres in England and Wales using a standardised data capture form (online supplemental 5). Each centre recorded data for a minimum of 50 consecutive patients who had completed surgical work-up between the start of 2018 and the end of 2019. It was thought inappropriate to sample data in 2020 or 2021 as epilepsy care was severely affected by the COVID-19 pandemic. Data were anonymised and aggregately analysed to obtain the mean number of pre-surgical evaluation tests per patient. The cost of pre-surgical evaluation was calculated by multiplying the mean number of tests by the unit cost and summing these (online supplemental 6).

Unit costs used in the model were obtained from NHS-specific published sources.[38,39] Costs for amytal testing, magnetoencephalography and electrocorticography were obtained from the participating centres that provided these tests. A number of costs used in the model are updated here and so differ slightly from those published in the NICE guideline (online supplemental 7).[36]

Potential adverse consequences of epilepsy surgery include immediate complications such as infection or haemorrhage, which can usually be treated promptly and often have no long-term sequalae. Also, there are small risks of stroke and mortality. The average long-term cost of surgical complications, this encompassing all potential surgical complications, was taken to be £5,000 per year over a lifetime horizon. This figure was thought likely an over-estimate by the NICE Committee, but retained to avoid positive bias in the model.

The cost of outpatient contacts included the cost of an initial neurology appointment, subsequent neurology appointments and primary care consultations (online supplemental 6). In-patient and emergency admission costs were also included in the analysis (online supplemental 6). Probability of service use for the costs of outpatient contacts and admissions was obtained from previous literature,[40] and informed by expert committee opinion. The NICE committee estimated the proportion of people who would receive each ASM and assumed people with drug resistant epilepsy would receive an average of 2.5 ASMs. The total annual cost of ASMs per person was calculated to be £1,082 (online supplemental 6). The cost of the resective operation itself was £10,185.[38]

Analysis

To calculate overall cost effectiveness, costs and QALYs for each cycle were calculated by multiplying the proportion of the cohort in each state by the corresponding cost or utility, with a half-cycle correction applied. Costs and QALYs were discounted at 3.5% to reflect time preference –in line with the NICE reference case. Costs and QALYs were summed across the lifetime horizon (50 years). The incremental cost-effectiveness ratio (ICER) was calculated by dividing the difference in total costs for surgery and MM by the difference in QALYs.

The model was run probabilistically using Monte Carlo simulation (10,000 times) to account for the uncertainty around input parameters. A probability distribution was defined for most model inputs. For each simulation, a value for each input was randomly selected simultaneously from its respective probability distribution; mean costs and mean QALYs were re-calculated using these values. Main results of the model are presented probabilistically. One-way sensitivity analyses are presented deterministically.

For the probabilistic analysis a beta distribution was applied to the following data inputs: probability of not being seizure free for MM, probability of mortality in the surgery arm, probability of relapse and remission for surgery and MM, and the probability of being a surgery candidate. A gamma or beta distribution was applied to the average number of pre-surgical evaluation tests. The distribution applied was dependent on the usage of each specific test. When the average resource use per person was above one, a beta distribution was applied – a gamma distribution was applied to remaining tests (online supplemental 6). A gamma distribution was applied to the cost of surgery and the utility values used in our model (online supplemental 4). A log-normal distribution was applied to the risk ratio for seizures at one year (surgery versus waiting list) and the SMRs (Table 1).

A total of 18 deterministic one-way sensitivity analyses were conducted (online supplemental 7). These included using utilities from different sources; altering the costs for surgery and pre-surgical evaluation; employing a 15-year time horizon; assuming people did not discontinue their ASMs once they obtained seizure freedom; and assuming a higher cost for pre-surgical investigations.

The model was systematically checked by the health economist undertaking the analysis (AB); this included inputting null and extreme values to check that results were plausible. The calculations were systematically checked by a second experienced health economist (DW). The model was made available to registered stakeholders of the guideline during public consultation.

RESULTS

Fourteen epilepsy surgical centres were contacted and ten provided data for a total of 762 adult individuals (online supplemental 8). The mean number of preoperative evaluation tests per person and corresponding unit costs for each test are presented in online supplemental 6. The average cost of preoperative assessment was £8,182 per person.

The proportion of people undergoing resective epilepsy surgery, having completed preoperative evaluation, was 41.3% (315/762). This included people who were eligible for resective epilepsy surgery and for whom surgery went ahead or was due to take place. People who were eligible for surgery but did not consent to surgery are not captured in this group.

For the probabilistic base case results, the total cost per person for surgery was estimated to be £56,911, and the total cost for MM was £32,490 (Table 2). Total QALYs per person for surgery was 15.91 and MM 13.76. Overall, resective epilepsy surgery was found to be cost effective with an ICER of £11,348 per QALY gained (Table 2). Deterministic results are listed in online supplemental 9.

Table 2: Cost effectiveness results per person (probabilistic results).

QALY=Quality-adjusted life-years.

.	**Surgery**	**Medical management**	**Surgery minus medical management**
Assessment for resective surgery cost	£20,823	£0	£20,823
Resective surgery cost	£10,201	£0	£10,201
Outpatient appointment cost	£3,631	£5,517	-£1,887
Anti-seizure medication cost	£14,522	£20,022	-£5,500
Admission cost	£3,254	£6,951	-£3,697
Reoperation costs	£678	£0	£678
Complications cost	£3,804	£0	£3,804
All costs	£56,911	£32,490	£24,442
QALYs	15.91	13.76	2.15
Incremental cost per QALY gained			£11,348

The results of the probabilistic analysis are illustrated in Figure 3, where each of the 10,000 iterations is plotted. Resective epilepsy surgery had a 97.0% probability of being cost effective at NICE's threshold of £20,000 per QALY gained (indicated by the proportion of iterations to the right of the dotted line). There was a 99.5% probability of surgery being cost effective at NICE's upper threshold of £30,000 per QALY gained (not shown in graph).

In all deterministic sensitivity analyses, resective surgery was cost effective at NICE's £20,000 threshold per QALY, apart from when the time horizon was reduced to 15 years (ICER: £28,093) and when the overall worst-case scenario was employed (online supplemental 9). The overall worst-case scenario comprised of all the scenarios tested in the one-way sensitivity analyses that favour MM to surgery (online supplemental 7). This sensitivity analysis was conducted to test these assumptions, but the NICE committee noted that the overall worst-case scenario was highly unlikely to be representative of clinical practice.

A one-way sensitivity analysis was undertaken assuming the highest cost of pre-surgical evaluation across all ten surgical centres (£13,178 compared to £8,182) – illustrating that surgery remained cost-effective with an ICER of £16,679 per QALY gained. Another sensitivity analysis incorporated a higher cost for stereo-EEG (sEEG). This analysis assumed that 60% of people undergoing sEEG received standard sEEG (the NHS reference cost used in the base case analysis [£14,638]) and 40% of people received a more complex sEEG (£39,577; costs obtained from two participating surgical centres). This resulted in a mean cost for sEEG of £24,613. The results of this analysis indicated that epilepsy surgery was still cost-effective at £12,889 per QALY gained. Results of all 18 deterministic one-way sensitivity analyses are provided in online supplemental 9.

An analysis was also conducted altering the probability of receiving surgery post pre-surgical evaluation. When the probability of receiving surgery is higher (60%), the ICER was £8,042 per QALY gained and when the probability of receiving surgery is lower (26%), the ICER was £16,389 per QALY gained.

DISCUSSION

The clinical effectiveness of epilepsy surgery is established in appropriately selected cases. Despite this, resective surgery for people with drug resistant epilepsy is under-utilised.[6–8,11–13] Scarce budgets drive the need for cost-effectiveness analyses to support and expand epilepsy surgery programs.[41] Analysis of whether referral for epilepsy surgery is cost-effective, irrespective of whether a given individual proceeds to resection, is essential.

Our nationwide multicentre pre-surgical evaluation survey included costs of *all* adults referred for pre-surgical evaluation, thereby reflecting real-world costs of an epilepsy surgery program. We demonstrate epilepsy surgery for drug resistant epilepsy is cost effective, in 97.0% of simulations, at NICE's threshold of £20,000 per QALY gained. As such, this study provides a more definitive economic rationale for referral to epilepsy surgery programs. These data are broadly applicable to other government-funded healthcare settings. The economic rationale for resective epilepsy surgery in low income to middle income healthcare countries requires specific consideration (online supplemental 10). It could be argued that the impetus for epilepsy surgery may be even greater in resource underprivileged settings, given the increased risk from seizures and the poor availability of ASMs.

Pre-surgical evaluation itself is a significant proportion of the total cost of epilepsy surgery. 58.7% of people in our cohort who underwent pre-surgical evaluation did not proceed to resection. Prior studies have omitted this group when assessing the cost-effectiveness of epilepsy surgery (online supplemental 11).[22,25] Pre-surgical evaluation does, though, provide valuable insights to optimise patient care in those who do not proceed to surgery including uptake of alternative therapies, such as neuromodulation, and identification of psychogenic non-epileptic/functional dissociative seizures. Capturing these potential benefits was not within the scope of our analysis. Similarly, indirect benefits from resection – for example the ability to return to the workforce, resume greater duties in the home and other factors improving socioeconomic productivity were not captured here as these are not part of NICE Methodology. Benefit from epilepsy surgery would reduce indirect costs and thereby likely render epilepsy surgery even more cost effective.

The cost of sEEG is variable depending on the complexities of a person's epilepsy. The cost of sEEG used in the base case analysis was obtained from NHS reference costs,[38] although the NICE committee acknowledged this cost may be an underestimate for more complex cases. Since model development, the frequency with which sEEG is used in pre-surgical evaluation has increased in addition to an increase in costs. The sensitivity analysis conducted assuming a higher cost for sEEG likely covers the increase in costs but does not account for the increased frequency with which sEEG is deployed (please see online supplemental 7). In our model, 20% of candidates received sEEG as part of their pre-surgical evaluation. A separate sensitivity analysis was conducted where it was assumed that the cost of pre-surgical evaluation was higher, using the highest total cost of pre-surgical evaluation across all participating centres (£13,178) – resulting in an ICER of £16,679 per QALY gained. In the sensitivity analysis where the cost of sEEG was increased, the cost of pre-surgical evaluation was £10,607 with an ICER of £12,889. Comparison of these analyses demonstrates that the total cost of pre-surgical evaluation / sEEG has scope to increase and still be cost-effective at NICE's £20,000 threshold. Further research is, though required to determine the ICER of surgery using frequencies of sEEG over and above 20% as well as more complex (higher cost) sEEG implantations.

Utility values in our model were obtained from a non-drug refractory population owing to a lack of data in a drug-refractory cohort. Although, the utility values used in the model derive from a relatively large UK study, several sensitivity analyses were conducted using different utility values to assess this uncertainty. The results of these analyses indicated the model was potentially sensitive to the utility values used, but, even under the most conservative assumption, the ICER was less than £20,000 per QALY (online supplemental 9). The guideline committee discussed that drug-refractory specific utility values would likely increase the cost-effectiveness of epilepsy surgery owing to a greater utility difference between 'seizure free' and 'not seizure free'. Those who have previously had drug resistant epilepsy may place a higher utility on seizure freedom compared to those in the non-drug refractory population. Also, those who are 'not seizure free' in a drug refractory cohort may be experiencing more severe or frequent seizures compared to those experiencing seizures in the non-drug refractory population. Seizure frequency and severity were not measurable outcomes in our analysis. These potential additional benefits from resective surgery could result in cost savings and a greater utility difference between surgery and MM, which would render surgery even more cost-effective.

Paediatric cases were not included in our analysis. The logistical organisation for epilepsy surgery is different for children in the United Kingdom where resective epilepsy surgery is carried out at four designated Children's Epilepsy Surgery Service (CESS) Centres. There may be certain additional costs in children, for example the potential need for imaging to be performed under general anaesthesia. It is, though, inferred that epilepsy surgery is likely to be more cost effective in children, both in terms of direct and, perhaps especially, indirect costs as earlier control of seizures offers the prospect of earlier drug reduction better access to education and employment, greater social mobility and decreased risk of mortality.[42]

Similarly, it could be argued that for people younger than 35 years at the time of surgical resection (35 years being the entry-point for our model) cost effectiveness may be increased.

We also did not specifically explore stratification by learning ability. People with learning disabilities may require additional appointments, more time within appointments and specialist provision to undergo relevant testing (for example imaging and video-telemetry). This was difficult to capture here, although prospective evaluation for cost effectiveness of resective epilepsy surgery in people with learning disability may be worthwhile. The NICE Committee emphasised in their discussions that people with learning disability must not be excluded from epilepsy surgery programmes.

LIMITATIONS

There are several limitations to our study. Treatment effects in our analysis are based on two small RCTs, and therefore long-term outcomes were calculated using observational studies.[27,32] RCT evidence assessing the effectiveness of epilepsy surgery will likely always be short-term owing to ethical concerns associated with conducting longer-term RCTs – delaying epilepsy surgery when this is of proven benefit would not reflect clinical equipoise. One-year seizure freedom rates reported in the observational studies correlated well with the RCT data.

Owing to data availability at the time of model development, our long-term effectiveness data was based on two studies[27,32] – one for ascertaining the long-term effectiveness of surgery,[27] and the other for MM.[32] As the definition of seizure freedom differed in these studies, amendments were made to the surgery data to account for seizure freedom being inclusive of focal aware seizures (FAS; online supplemental 2). The MM study employed a stricter definition of drug refractory epilepsy,[32,43] and therefore the model cohort may have had more severe drug refectory epilepsy. The committee however noted that reported relapse and remission values seemed compatible with current clinical practice. The long-term data for both studies was extrapolated differently (online supplemental 2). In summary, data were extrapolated based on best fit. These values and the methodology were discussed with the guideline committee who concluded that the probability values correlated with UK clinical practice.

Utility values were obtained from a non-drug refractory population due to an absence of data for drug-refractory populations. Several sensitivity analyses were therefore conducted using different utility values. Analyses indicated the model was sensitive to utility values – but all ICERs were still less than £20,000 per QALY gained. Drug-refractory specific values would likely favour surgery due to a greater utility difference between health states.

Certain resource allocation assumptions were based on committee expertise (for example: cost of complications; probability of reoperation) or from centres who offered specific investigations. Owing to a lack of published data on the cost of fMRI, the committee assumed fMRI to be of the same cost as an MRI. The committee noted that this would likely result in an underestimation of the true fMRI cost but agreed that this assumption would not alter the results of the cost-effectiveness analysis as this test was infrequently utilised (online supplemental 6). Costs of preoperative assessment were also tested in two sensitivity analyses (assuming a higher and lower cost) and results were found to be robust (online supplemental 7 and 9).

A post-operative complication rate of 4% was employed although recent data suggest this may be lower.[44,45] A lower complication rate would deem surgery more cost effective. Given the emergence of novel data since the publication of NICE Guidance in 2022 and changes in clinical practice (for example increased utilisation of sEEG), further research should refine and iteratively analyse cost-effectiveness of resective surgery. We would advocate always analysing the whole epilepsy surgical pathway across multiple centres in this future work.

CONCLUSION

Resective epilepsy surgery is cost effective from a national health service perspective when considering all people referred for surgical assessment, not just those who proceed to resection. Prompt referral to epilepsy surgery centres for evaluation of pharmacoresistant epilepsy would, therefore, seem essential. Confirming cost-effectiveness of referral for epilepsy surgery should offer increased support to development and delivery of epilepsy surgery programmes.

Figure Legends

Figure 1: One-year decision tree model. Binary outcomes in the epilepsy surgery pathway that reflect clinical decision making and possible outcomes are illustrated. In this one-year decision tree model evaluating resective epilepsy surgery and medical management, after one year people can either be alive or dead dependent on their seizure status.

Figure 2: Long-term Markov model demonstrating possible health states in the epilepsy treatment pathway. A schematic of the long-term Markov model where people can be either, seizure for a given period of time (prescribed or not prescribed anti-seizure medications), not seizure free or dead.

Figure 3: Cost-effectiveness plane. The cost effectiveness plane illustrates the results of the probabilistic sensitivity analysis, plotting each of the 10,000 iterations. Overall resective surgery had a 97% probability of being cost effective at the standard NICE threshold of £20,000 per Quality Adjusted Life Year gained.

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Ethics approval disclosure statement:

The study collected anonymised data from tertiary epilepsy centres as detailed in the framework of the NICE 217 Guideline and thereby did not require formal Ethics Approval.

Competing interests

The authors declare no direct conflicts of interest

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