Seminar in Epileptology

Surgery for epilepsy: a systematic review of current evidence

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ABSTRACT – This seminar discusses the history and development of techniques for surgical intervention for people with refractory focal epilepsy. Published surgical success rates and prognostic factors associated with post-operative seizure freedom from individual studies have been variable and contradictory. We present here the key findings of a Cochrane systematic review of all evidence published since the introduction of magnetic resonance imaging (MRI) to pre-operative surgical assessment in 1984. Our findings show the usefulness of uncontrolled case series is now past. Future studies with a prospective controlled design should focus on specific research questions to help improve results and provide better-informed advice.

Key words: focal epilepsy, surgical resection, systematic review

Epilepsy is a common condition with a prevalence of around 1 in 200 people (Fisher *et al.*, 2014). Despite optimal pharmacotherapy, about 20% to 30% of individuals do not become seizure-free (Kwan and Brodie, 2000). For some, surgery is a therapeutic option. Focal seizures originate within networks limited to one hemisphere, which may be discretely localized or more widely distributed. They may originate in subcortical structures (Berg *et al.*, 2010). The number of individuals with focal epilepsy who do not become seizure-free despite optimal drug therapy varies according to the age of the participants and which focal epilepsies are included, but has been reported as at least 20% and in some studies up to 70%.

Where the origin of the seizures can be localised discretely, surgery is a valid option if the potential benefit is assessed to outweigh the risk (Kwan and Brodie, 2000).
Victor Horsley pioneered surgery as a treatment for epilepsy (Feindel *et al.*, 2009). In 1886, he operated on a 22-year-old man who had developed focal epilepsy following a head injury. A vascular scar was excised along with a border of cortex that resulted in cessation of the seizures. Until the 1940s, surgery was directed mainly to the convexity of the cerebral hemispheres, most often for the removal of traumatic scars and tumours. Subsequently many other causes of focal epilepsy have been discovered which are also amenable to surgery.

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Surgical techniques have been refined over the years with the development of advanced methods of pre-operative assessments, such as electroencephalography (EEG) in the 1930s, computerized tomography in the 1970s, magnetic resonance imaging (MRI) in the 1990s, as well as computerised analysis of ictal and interictal EEG activity, functional MRI with psychometric analysis, and ever more sophisticated stereotaxis guiding the placement of deep electrodes for long-term EEG analysis and surgical intervention. Most recently, these techniques have been complemented by the co-registration of single photon emission computed tomography (SPECT) and positron emission tomography (PET) findings. This approach has led to more opportunity for the accurate assessment of any person with drug-resistant focal epilepsy and thus more opportunity for a surgical cure. They have also led to more precise localization of the epileptogenic focus allowing for the removal of the minimal amount of tissue, leading to a reduction in post-operative neurological deficits.

People began paying attention to the function of the areas of the brain to be excised, becoming aware of deficits inflicted despite a cure of the epilepsy. Notably, it became clear that resection of the anteromesial structures of the temporal lobe produced short-term memory impairment. Neuro-psychological assessments have now become an important aspect of a surgical work-up.

Success rates for resective epilepsy surgery are estimated to have increased from 43% to 85% during the period 1986 to 1999 (National Institutes of Health Consensus Conference, 1990; Engel Jr *et al.*, 1993; Engel Jr *et al.*, 2003). Data from multiple sources suggest that 55% to 70% of individuals undergoing temporal resection and 30% to 50% of individuals undergoing extratemporal resection become completely seizure-free. Surgery is considered a valuable option for medically intractable epilepsy, even in the absence of proven drug resistance (Engel Jr and Shewmon, 1993).

Although it is known that surgical outcomes may be greatly influenced by the presence of selected prognostic indicators (Tonini *et al.*, 1997; Berg *et al.*, 1998), it is still uncertain which people with a focal epilepsy are most likely to achieve good surgical outcomes. Good surgical outcomes appear to be associated with a number of factors (hippocampal sclerosis, anterior temporal localisation of interictal epileptiform activity, absence of pre-operative generalised seizures, and absence of seizures in the first postoperative week) (McIntosh *et al.*, 2001). However, the published trial results are frequently confusing and contradictory, thus preventing inferences for clinical practice. We therefore performed the first Cochrane systematic review to investigate the association between specific prognostic factors and surgical outcome (West *et al.*, 2015).

What were the objectives of the Cochrane Review (West *et al.*, 2015)?

The primary objective of the review was to assess the proportion of individuals achieving a good outcome from surgery and the prevalence of unwanted effects.

The secondary objective was to identify prognostic factors which were correlated with the outcome of surgery. The prognostic factors of interest in this review were:

– Pre-operative Factors
  • Presence of normal pre-operative MRI results
  • Use of pre-operative invasive monitoring
  • Concordance of pre-operative MRI and EEG
  • History of febrile seizures
  • History of head injury
  • Distribution of interictal spikes (unilateral or bilateral)
– Operative and post-operative factors
  • Complete surgical resection
  • Side of surgical resection (left or right)
  • Presence of post-operative epileptiform discharges
– The following pathologies:
  • Mesial temporal sclerosis (MTS)
  • Encephalomalacia on pathology
  • Focal cortical dysplasia or malformation of cortical development
  • Tumour
  • Vascular malformation

Relevant studies were identified by searching MEDLINE (Ovid), the Cochrane Central Register of Controlled Trials, Cochrane Central Register of Controlled Trials, ClinicalTrials.gov, and World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) from 1984 to July 2013.

We included studies of a randomised, cohort, case control or case series design with an expected duration of follow-up of at least one year, recruiting a sample of surgical candidates of any age with a drug-resistant epilepsy. For inclusion, at least 90% of patients had to have had pre-operative MRI (some studies were completed in the era of computerised tomography) and studies had to report on a group of at least 30. Studies must also have reported an outcome relating to remission of seizures after surgery for inclusion; see *table 1* for accepted classifications of good and poor outcomes for the review.

Table 1. Definitions of seizure outcome following epilepsy surgery.

Outcome[1]	Definition	Cochrane Review outcome definition[1]
Engel Class Scale	**Class 1: Free of disabling seizures** 1A: Completely seizure-free since surgery 1B: Non-disabling simple partial seizures only since surgery 1C: Some disabling seizures after surgery, but free of disabling seizures for at least 2 years 1D: Generalised convulsion with antiepileptic drug withdrawal only Class 2 (rare disabling seizures 'almost seizure-free')	Good outcome
	Class 2: Almost seizure-free (rare disabling seizures) 2A: Initially free of disabling seizures but has rare seizures now 2B: Rare disabling seizures since surgery 2C: More than rare disabling seizures after surgery, but rare seizures for at least 2 years 2D: Nocturnal seizures only	Poor outcome
	Class 3: Worthwhile improvement 3A: Worthwhile seizure reduction 3B: Prolonged seizure-free intervals amounting to greater than half the follow up period, but not less than 2 years	
	Class 4: No worthwhile improvement 4A: No significant seizure reduction 4B: No appreciable change 4C: Seizures worse	
Seizure Freedom[3]	**Seizure freedom for one year or more** Equivalent to Engel Class 1 for one year or more	Good outcome
	No seizure freedom or seizure freedom for less than one year Equivalent to Engel Class 2-4 or Engel Class 1 for less than one year	Poor outcome
International League Against Epilepsy (ILAE) Classification[3]	**Class 1:** Completely seizure-free; no auras	Good outcome
	Class 2: Only auras; no seizures	
	Class 3: One to three seizures per year; with or without auras	Poor outcome
	Class 4: Four seizure days per year to 50% reduction of baseline seizure days; with or without auras	
	Class 5: Less than 50% reduction of baseline seizure days to 100% increase of baseline seizure days; with or without auras	
	Class 6: More than 100% increase of baseline seizure days; with or without auras	

[1]Studies reporting other outcome scales or other combinations of the scales above were not included in analysis of the review.
[2]All individuals must be classified as achieving a good or poor outcome of surgery for comparison in the review.
[3]Classed as "Other" scale. Seizure freedom at two, three, four and five years also included as "Other" outcome scales.

Patient demographics, study design, and outcome data were extracted from published articles of all studies. For individual factors of interest, studies were combined in fixed-effects meta-analysis to assess the presence or absence of that factor as an independent predictor of the outcome of surgery. Heterogeneity (variability) between studies was assessed by comparing study characteristics, visually inspecting forest plots, and using the I^2 statistic as a measure of inconsistency across studies. Random-effects meta-analysis

was also performed as a sensitivity analysis if considerable heterogeneity was present in statistical analysis (I^2 greater than 50%) (Higgins and Green, 2011).

What were the findings of the Cochrane review (West *et al.,* 2015)?

Study design and quality

In total, 177 studies with 16,508 patients undergoing surgery were identified as eligible for the Cochrane review (see West *et al.* [2015] for the list of included studies). Four studies of a prospective randomised design were included; three randomising the type or length of surgical resection and one randomising patients to surgery or antiepileptic drug treatment. Surgery was found to be superior to antiepileptic drug treatment (risk ratio [RR]: 7.67; 95% confidence interval [CI]: 2.50 to 23.51; 80 patients; Wiebe *et al.* [2001]); 23 out of 40 receiving surgery achieved freedom from seizures that impaired awareness after one year, compared to three out of 40 medically treated patients. Total hippocampectomy was found to be superior to partial hippocampectomy (RR: 1.82; 95% CI: 1.12 to 2.93; 70 patients; Wyler *et al.* [1995]) in terms of seizure freedom at one year. No differences were found between 2.5-cm and 3.5-cm resections (RR: 1.02; 95% CI: 0.86 to 1.20; 207 patients; Schramm *et al.* [2011]) or between anterior temporal lobectomy with and without corpus callosotomy (RR: 1.22; 95% CI: 0.85 to 1.76; 60 patients; Liang *et al.* [2010]) in terms of seizure freedom at one or two years, respectively.

The remaining studies were non-randomised; 17 were prospective and the remaining 156 were retrospective or of unclear design. None of these studies included a control group for the surgical intervention group. See *table 2* for details of all study characteristics.

Quality was assessed for all included studies using the Cochrane Risk of Bias tool (Higgins and Green, 2011) for randomised studies and the Effective Public Health Practice Project (EPHPP) tool (Thomas *et al.*, 2004) for non-randomised studies. Criteria considered were study design, presence of blinding, selection bias, confounding data collection, incomplete outcome data, intervention integrity and analysis. The majority of studies were judged to be of moderate or weak quality due to non-randomised design. This poor quality must be taken into account when interpreting the results of the Cochrane Review.

Surgical outcome and relation to prognostic factors

In total, 10,518 patients (65%) out of 16,253 contributing to the analysis achieved a good outcome of surgery (*table 2*). Outcome of surgery, according to the presence of the prognostic factors of interest, is summarised in *table 3*. Presence of mesial temporal sclerosis or tumour on pathology, concordant pre-operative MRI and EEG, history of febrile seizures, unilateral interictal spikes, and complete surgical resection were shown to be independent predictors of a good outcome of surgery, while normal pre-operative MRI, the need to use pre-operative invasive monitoring, presence of focal cortical dysplasia, or malformation of cortical development on pathology and left-sided resection were shown to be independent predictors of poor outcome of surgery. History of head injury, presence of encephalomalacia, or vascular malformation on pathology and post-operative epileptiform discharges were not shown to be independent predictors of seizure outcome.

Safety of surgical resection

The reporting of adverse events was inadequate, with only 74 out of the 177 included studies (42%) reporting on mortality and morbidity following epilepsy surgery. Adverse events were recorded for 1,308 (14%) of the 9,512 participants involved in these 74 studies. The number of adverse events occurring per person was not specified. Events were defined as follows (with percentage of 1,308 total events):
Undefined: 98 (7.5%); infection/fever: 251 (19.2%); motor impairment (mono-, hemi-, facial pareses along with cranial nerve involvement): 220 (16.8%); visual field defect: 173 (13.2%); haemorrhage: 56 (4.3%); language impairment: 42 (3.2%); CSF leak or collection: 36 (2.8%); cognitive impairment to include memory loss: 34 (2.6); hydrocephalus: 24 (1.8%); and miscellaneous (including deep venous thrombosis, status epilepticus, cerebral oedema and urinary incontinence): 10 (0.8%). Detail of reporting including timing and duration of event, relation to surgery, and severity of event (transient effect, permanent deficit, or death) was very poor and few studies made any reference to postoperative cognition, quality of life, or mental state.

Discussion of the findings of the Cochrane review (West *et al.,* 2015)

The 177 included studies were of variable size and design, were conducted in a range of countries, and recruited a wide range of participants of different ages and with different durations of epilepsy. A wide range of surgical techniques were carried out across these studies and different scales were used to measure the outcome of surgery.
The recent consensus from the International League Against Epilepsy, Kwan *et al.* (2010), proposes that a

Table 2. Summary of study characteristics, patient characteristics and overall seizure outcome.

Characteristic or demographic	Number of studies and patient information available for [n (%)]	Summary of characteristic or demographic[1]
Gender	149 studies (84%) 13,360 patients (81%)	7,591 male patients (57%)
Age at surgery	152 studies (86%) 13,801 patients (84%)	Range: 0 to 86 years
Age group recruited into study	152 studies (86%) 13,801 patients (84%)	Adults only: 28 studies (18%); 2,285 patients (17%) Children only: 21 studies (14%); 1,147 patients (8%) Both: 103 studies (68%); 10,374 patients (75%)
Duration of epilepsy	110 studies (62%) 10,391 patients (63%)	Range: 0 to 86 years
Type(s) of surgical resection performed	168 studies (95%) 15,661 patients (95%)	Temporal lobe only: 76 studies (45%); 7,942 patients (51%) Extratemporal lobe only: 15 studies (9%); 1,058 patients (6%) Both types: 77 studies (46%); 6,661 patients (43%)
Study design	168 studies (95%) 15,771 patients (96%)	Prospective (randomised): 4 studies (2%); 373 patients (2%) Prospective (non-randomised): 17 studies (11%); 1,499 patients (10%) Retrospective (non-randomised): 144 studies (86%); 13,557 patients (86%) Prospective and retrospective (non-randomised): 3 studies (1%); 342 patients (2%)
Outcome scale used[2]	177 studies (100%) 16,508 patients (100%)	Engel Class Scale: 117 studies (65%); 10,619 patients (64%) More than one year seizure-free: 42 studies (24%); 3,981 patients (24%) Other scale: 18 studies (11%); 1,908 patients (12%)
Follow-up of studies	177 studies (100%) 16,508 patients (100%)	Range: 0 to 366 months
Seizure outcome[2]	173 studies (98%) 16,253 patients (98%)	Proportion achieving a good outcome: 10,518 patients (65%) Range across studies: 13.5%-92.5% achieving a good outcome.
Total	177 studies, 16,508 patients[3]	

[1]Summary statistics including percentages are based on the information available.
[2]See *Table 1* for definition of outcome scales.
[3]See West *et al.* (2015) for reference list of included studies.

treatment's success should be defined by sustained freedom from seizures, as that is the only efficacy outcome consistently associated with improved quality of life (and in the UK, the only efficacy outcome that allows a patient to drive legally). This justifies our focus on at least 12 months' seizure freedom in this review.

We found the reporting of related adverse events to be sparse and very poor; complications and/or surgery-related deaths were reported in less than half of included studies, often lacking specific detail of the nature and consequence of the event (transient or permanent) and the timing of events. Few studies contained any reference to postoperative cognition or mental state.

From the data available, the message for the clinician when consulted by a person with intractable epilepsy, is clear. If selection criteria are met, there is a 1 in 11 chance of improvement with the next antiepileptic drug and a 2 in 3 chance of improvement with surgery. Furthermore, we have observed that, overall, the surgical procedures have a low complication rate. This

Table 3. Prognostic factors for a good outcome of surgery in all included studies.

Prognostic factor of interest	Number of studies (patients) reporting prognostic factor		Proportion with a good outcome				Risk Ratio (95% CI)[1]
			Factor present		Factor absent		
Normal MRI	42	(3,956)	687/1,252	(55%)	1,816/2,704	(67%)	0.78 (0.73, 0.82)
Use of intracranial monitoring	21	(1,547)	448/762	(59%)	564/785	(72%)	0.85 (0.78, 0.93)
Mesial temporal sclerosis on pathology	46	(4,430)	1,340/1,796	(75%)	1,663/2,634	(63%)	1.17 (1.12, 1.23)
Concordant preoperative MRI and EEG	23	(1,778)	824/1,200	(69%)	313/578	(54%)	1.25 (1.15, 1.37)
History of febrile seizures	15	(1,368)	343/440	(78%)	615/928	(66%)	1.09 (1.01, 1.17)
History of head injury	7	(551)	100/159	(63%)	242/392	(62%)	0.99 (0.86, 1.13)
Encephalomalacia on pathology	4	(274)	9/35	(26%)	90/239	(38%)	0.67 (0.37, 1.21)
Focal cortical dysplasia or malformation of cortical development on pathology	45	(3,529)	672/1,183	(57%)	1,584/2,346	(68%)	0.90 (0.85, 0.95)
Tumour on pathology	41	(3,357)	595/806	(74%)	1,512/2,551	(59%)	1.23 (1.14, 1.32)
Vascular malformation on pathology	19	(1,488)	89/139	(64%)	785/1,349	(58%)	1.07 (0.94, 1.21)
Unilateral interictal spikes	18	(1,414)	504/732	(69%)	406/682	(60%)	1.14 (1.05, 1.24)
Complete surgical resection	40	(3,013)	1,277/1,716	(74%)	725/1,297	(56%)	1.41 (1.32, 1.50)
Left-side surgical resection	36	(2,933)	988/1,479	(67%)	1,041/1,454	(72%)	0.94 (0.90, 0.98)
Post-operative epileptiform discharges	6	(542)	132/200	(66%)	262/342	(77%)	0.91 (0.68, 1.22)

[1]Risk ratios in italics are statistically significant. Risk ratio greater than 1 indicates the presence of the factor is associated with a good outcome of surgery and risk ratio less than 1 indicates the presence of the factor is associated with a poor outcome of surgery (*i.e.* absence of the factor is associated with a good outcome of surgery).

is in line with other reports showing that less than 5% of patients have permanent post-operative neurological deficits secondary to accidental damage of central nervous system (CNS) tissue (Engel Jr, 1996; Engel Jr *et al.*, 2003). The percentage adverse event prevalence of 7.3% is highly likely to be an overestimate of the prevalence of permanent neurological deficit, as many studies did not record which events were only transient and more than one event could be recorded in the same person. We should emphasise that very few studies addressed the important issue of formally reassessing any postoperative impairment of cognition, speech and language, social function-

ing, or altered mental state (all linked to quality of life). This aspect should be written into future research protocols.

The extent of resection was the strongest determinant of outcome in our review, particularly with extratemporal surgery. The dilemma for the surgeon is that larger areas of resection are likely to be associated with a higher complication risk. The extent of resection is affected by the underlying pathology, the site of surgery, and the development of investigational and surgical procedures.

The good outcome associated with the presence of abnormal MRI is expected and probably largely reflects

a variety of CNS conditions, which we know are associated with a good prognosis, such as tumours, mesial temporal sclerosis (MTS), and many congenital malformations. These are discrete structural lesions that lend themselves to complete resection. For example, tumours carried a higher chance of seizure remission at 12 months than other CNS disorders (RR of presence versus absence for 12-month remission: 1.23; 95% CI: 1.14 to 1.32). Non-specific or ill-defined non-tumoural lesions, *e.g.* white matter abnormalities, are less easy to delineate. Thus, they are less easy to resect completely without causing significant damage. This results in a poor surgical outcome.

A reasonable prospect of seizure freedom is not ruled out with normal MRI. Jayakar *et al.* (2008) report on a cohort (predominantly of children) with non-lesional intractable focal epilepsy undergoing resective surgery. After two years of follow-up, 44 of 101 participants were seizure-free. Factors that correlated with good outcome were the presence of convergent scalp EEG, focal interictal spikes ($p<0.005$), and completeness of resection ($p<0.0005$). Dorward *et al.* (2011) studied children with extratemporal, non-lesional epilepsy. Outcome was classified as Engel class 1 or 2 in 54.5% of the children who underwent resection of the lesion or multiple sub-pial resections. The results were obtained through the use of invasive monitoring with grid/strip electrodes.

There is a strong association between MTS and a history of febrile seizures. The term "mesial temporal sclerosis" as an alternative to "hippocampal sclerosis" was introduced in recognition of the frequent involvement of mesial limbic structures adjacent to the hippocampus. Neocortical neuronal loss and gliosis (temporal lobe sclerosis [TLS]) was studied by Thom *et al.* (2009), who identified TLS in 30 of 272 surgically treated cases of hippocampal sclerosis. There was a history of a febrile seizure as an initial event in 73% of patients with TLS compared with 36% without TLS. Febrile status was seen in 27% of the febrile seizures. The changes of TLS may be due to an enhanced vulnerability of superficial cortical neurons in maturing neocortex, from an early cerebral event in a small group of children. The good outcome associated with a history of febrile seizures can be interpreted in the light of its association with a mesial temporal sclerosis being a more readily selectable lesion.

EEG/MRI concordance is correlated with a better surgical outcome, although it is clear that results will depend very much on the mix of pathologies underlying the epilepsy. Studies containing a large number with discrete lesions, such as tumours, are likely to show more concordance and a better outcome than studies with a predominance of less discrete lesions, as can be the case with many neurodevelopmental abnormalities.

The need for intracranial monitoring itself implies that there is uncertainty in the location and extent of an epileptogenic zone, often accompanied by indeterminate neuroimaging. The association between the need for intracranial monitoring and a poor outcome is therefore not surprising. In these cases, fewer than 50% may become seizure-free, postoperatively. Poor localisation is also reflected in the fact that participants with unilateral interictal spikes are significantly more likely to achieve a good outcome of surgery than participants with bilateral interictal spikes. The persistence of postoperative discharges is likely to reflect these very same issues. There are units that will re-operate very quickly when postoperative discharges are identified. The heterogeneity of our results does not allow us to support this approach. It is but one example of how properly conducted research should, in the future, help determine the appropriate care pathway (see below).

There are limitations to this review. These include the fact that studies report different criteria for seizure outcome and a variable length of follow-up, and have retrospective designs that increase the risk of bias in data collection. In addition, variables that could affect outcome were examined mostly in univariate analyses without considering the effects of other prognostic features or confounders. Despite these limitations, our results provide some clinical guidance for the selection of the best surgical candidates. The criteria adopted to identify the indications and the applications of epilepsy surgery are constantly evolving. Continuing attempts need to be made to define patient and procedure-related prognostic indicators.

We do feel that further studies with a prospective design are needed to help improve results and hence provide better-informed advice. It seems that the usefulness of yet another uncontrolled case series is now past. For the future, the primary outcome measure for intervention studies ought to be seizure freedom at set time points with a minimum of one year of follow-up. Assessment should be blinded and linked to quality of life measurement. The design should be a randomised controlled trial, appropriately powered with a focus on specific research questions that remain as unanswered today by this large body of literature as they did when Victor Horsley helped the young Scot in 1886.

There are many questions to answer but they should address the issues of extent of resection for temporal and extratemporal lesions, the definition of care pathways for the most cost-efficient and effective preoperative selection, intervention for non-lesional focal epilepsy, bilateral and postoperative spikes, and when to tail antiepileptic drugs, among many others. Clear data on risks (adverse events, their nature, and timing), as well as benefits, should always be recorded.

Protocols should include pre- and postoperative measures of speech and language, cognition and social functioning, along with a mental state assessment. There will be methodological difficulties and adequate powering will require multi-centre approaches. Improvements in the development of cancer care over the past three to four decades have been achieved by answering well-defined questions through the conduct of focused RCTs in a step-wise fashion. The same approach to surgery for epilepsy is required. □

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TEST YOURSELF

(1) Which of the following are associated with improved surgical outcome?
A. Presence of mesial temporal sclerosis or tumour
B. Concordant pre-operative MRI and EEG
C. History of febrile seizures
D. Unilateral interictal spikes
E. Complete surgical resection

(2) There has been one published trial (Wiebe *et al.,* 2001) randomising participants to surgery or antiepileptic drug treatment. Based on the results of this trial, how many individuals per 1,000 would be expected to achieve freedom from seizures which impair awareness after one year:
A. When receiving medical treatment?
B. When receiving surgery?

(3) Which of the following should be included in the methodology of future studies on establishing the benefit, or otherwise, of surgical intervention for people with an intractable epilepsy.
A. Primary outcome measure of seizure freedom at set time points
B. Minimum of one year of follow-up
C. Assessment should be blinded
D. Quality of life measurement included
E. Randomised controlled trial design
F. Powered appropriately
G. Pre- and postoperative measures of speech and language, cognition, and social functioning
H. Pre- and postoperative measures of mental state assessment

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com, under the section "The EpiCentre".