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Surgery for epilepsy (Review)

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[Intervention Review]

Surgery for epilepsy

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ABSTRACT

Background

This is an updated version of the original Cochrane review, published in 2015.

Focal epilepsies are caused by a malfunction of nerve cells localised in one part of one cerebral hemisphere. In studies, estimates of the number of individuals with focal epilepsy who do not become seizure-free despite optimal drug therapy vary between at least 20% and up to 70%. If the epileptogenic zone can be located, surgical resection offers the chance of a cure with a corresponding increase in quality of life.

Objectives

The primary objective is to assess the overall outcome of epilepsy surgery according to evidence from randomised controlled trials.

Secondary objectives are to assess the overall outcome of epilepsy surgery according to non-randomised evidence, and to identify the factors that correlate with remission of seizures postoperatively.

Search methods

For the latest update, we searched the following databases on 11 March 2019: Cochrane Register of Studies (CRS Web), which includes the Cochrane Epilepsy Group Specialized Register and the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (Ovid, 1946 to March 08, 2019), ClinicalTrials.gov, and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP).

Selection criteria

Eligible studies were randomised controlled trials (RCTs) that included at least 30 participants in a well-defined population (age, sex, seizure type/frequency, duration of epilepsy, aetiology, magnetic resonance imaging (MRI) diagnosis, surgical findings), with an MRI performed in at least 90% of cases and an expected duration of follow-up of at least one year, and reporting an outcome related to postoperative seizure control. Cohort studies or case series were included in the previous version of this review.

Data collection and analysis

Three groups of two review authors independently screened all references for eligibility, assessed study quality and risk of bias, and extracted data. Outcomes were proportions of participants achieving a good outcome according to the presence or absence of each prognostic factor of interest. We intended to combine data with risk ratios (RRs) and 95% confidence intervals (95% CIs).

Main results

We identified 182 studies with a total of 16,855 included participants investigating outcomes of surgery for epilepsy. Nine studies were RCTs (including two that randomised participants to surgery or medical treatment (99 participants included in the two trials received medical treatment)). Risk of bias in these RCTs was unclear or high. Most of the remaining 173 non-randomised studies followed a retrospective design. We assessed study quality using the Effective Public Health Practice Project (EPHPP) tool and determined that most studies provided moderate or weak evidence. For 29 studies reporting multivariate analyses, we used the Quality in Prognostic Studies (QUIPS) tool and determined that very few studies were at low risk of bias across domains.

In terms of freedom from seizures, two RCTs found surgery (n = 97) to be superior to medical treatment (n = 99); four found no statistically significant differences between anterior temporal lobectomy (ATL) with or without corpus callosotomy (n = 60), between subtemporal or transsylvian approach to selective amygdalohippocampectomy (SAH) (n = 47); between ATL, SAH and parahippocampectomy (n = 43) or between 2.5 cm and 3.5 cm ATL resection (n = 207). One RCT found total hippocampectomy to be superior to partial hippocampectomy (n = 70) and one found ATL to be superior to stereotactic radiosurgery (n = 58); and another provided data to show that for Lennox-Gastaut syndrome, no significant differences in seizure outcomes were evident between those treated with resection of the epileptogenic zone and those treated with resection of the epileptogenic zone plus corpus callosotomy (n = 43). We judged evidence from the nine RCTs to be of moderate to very low quality due to lack of information reported about the randomised trial design and the restricted study populations.

Of the 16,756 participants included in this review who underwent a surgical procedure, 10,696 (64%) achieved a good outcome from surgery; this ranged across studies from 13.5% to 92.5%. Overall, we found the quality of data in relation to recording of adverse events to be very poor.

In total, 120 studies examined between one and eight prognostic factors in univariate analysis. We found the following prognostic factors to be associated with a better post-surgical seizure outcome: abnormal pre-operative MRI, no use of intracranial monitoring, complete surgical resection, presence of mesial temporal sclerosis, concordance of pre-operative MRI and electroencephalography, history of febrile seizures, absence of focal cortical dysplasia/malformation of cortical development, presence of tumour, right-sided resection, and presence of unilateral interictal spikes. We found no evidence that history of head injury, presence of encephalomalacia, presence of vascular malformation, and presence of postoperative discharges were prognostic factors of outcome.Twenty-nine studies reported multi-variable models of prognostic factors, and showed that the direction of association of factors with outcomes was generally the same as that found in univariate analyses.

We observed variability in many of our analyses, likely due to small study sizes with unbalanced group sizes and variation in the definition of seizure outcome, the definition of prognostic factors, and the influence of the site of surgery

Authors' conclusions

Study design issues and limited information presented in the included studies mean that our results provide limited evidence to aid patient selection for surgery and prediction of likely surgical outcomes. Future research should be of high quality, follow a prospective design, be appropriately powered, and focus on specific issues related to diagnostic tools, the site-specific surgical approach, and other issues such as extent of resection. Researchers should investigate prognostic factors related to the outcome of surgery via multi-variable statistical regression modelling, where variables are selected for modelling according to clinical relevance, and all numerical results of the prognostic models are fully reported. Journal editors should not accept papers for which study authors did not record adverse events from a medical intervention. Researchers have achieved improvements in cancer care over the past three to four decades 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.

PLAIN LANGUAGE SUMMARY

Surgery for epilepsy

Background

Focal epilepsies are caused by abnormal electrical discharges in specific (localised) parts of the brain. In up to 30% of people, these seizures are not controlled by medication. If the site of origin of these signals (the epileptogenic zone) can be located from the description of the seizures, or via findings of magnetic resonance imaging (MRI) (a medical imaging scan that uses strong magnetic fields and radio waves to produce detailed images of the inside of the body) and electroencephalography (EEG) (recording of electrical activity along the scalp), the person should be offered the chance of having the epileptogenic zone removed. We studied characteristics of people undergoing surgery and details of surgery type that might be linked to the best chance of surgical cure of epileptic seizures.

Study characteristics

We examined evidence from 182 included studies reporting the experience of 16,855 people of all ages. The evidence is current to March 2019.

Key results

In total, 10,696 people (64% of the total who had surgery in all studies) experienced a good outcome from surgery, defined as freedom from epileptic seizures.

Two randomised controlled trials (RCTs) established the superiority of surgery over use of different antiepileptic medications. Seven RCTs compared different types of surgery. Three trials found no difference in seizure outcomes; one removed 2.5cm or 3.5cm of the anterior temporal lobe (ATL - the part of the brain in which the epileptogenic zone is often located) or surgically removed the ATL with or without an additional procedure to sever the nerves that connect the two halves of the brain. The third trial found that completely removing the hippocampus (the part of the brain in which the epileptogenic zone is often located) was superior to removing only part of the hippocampus. A fourth trial showed that removing the ATL was superior to a surgical procedure using radiation therapy, Two trials showed no difference between different types of surgical procedures to remove the ATL or hippocampus and the final trial showed that for Lennox-Gastaut syndrome, results show no significant differences in seizure outcomes between those undergoing resection of the epileptogenic zone and those with resection plus corpus callosotomy.

We identified some factors associated with a better outcome from surgery, including a well-defined abnormality on the MRI scan corresponding with what was expected from the description of seizures and EEG findings, complete surgical removal of the lesion, and a history of febrile seizures (seizures associated with fever in a young child) often associated with mesial temporal sclerosis (scarring in the inner portions of the temporal lobe of the brain).

More spread out brain abnormalities that might be associated with brain injury or an abnormality of brain development were not associated with a good outcome. The presence of such abnormalities is often associated with a need to embark on more detailed pre-operative investigations including intracranial (inside the skull) EEG monitoring. We would have liked to examine the collective effect of these factors (i.e. the effect on outcome if a person has a history of febrile seizures, brain injury, and an MRI abnormality altogether); however, studies did not report enough information to allow this.

Quality of the evidence

Most studies included in this review were of poor quality and had a retrospective design (whereby individuals are recruited after the result of surgery has been recorded, which looks back for the existence of factors related to the results of surgery). Researchers used variable surgical approaches for different sites of the brain, different processes to select candidates for surgery, and different definitions of freedom from seizures after surgery, and they measured these outcomes at varying points. Fewer than half the studies gave details of complications and deaths associated with surgery.

Conclusions

We encourage researchers that future studies should have a prospective design (a design whereby individuals are recruited before surgery has taken place, which identifies factors of interest before surgery and follows up with individuals after surgery to record outcomes). Studies should use appropriate statistical methods to examine the collective effect of factors that may predict the outcome of surgery. Study authors should clearly record death during or after surgery, as well as complications and side effects from surgery.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

Surgery compared with medical treatment for epilepsy

Patient or population: adults and children with drug-resistant epilepsy suitable for surgical intervention
Settings: outpatients (following surgery in hospital)
Intervention: surgery
Comparison: medical treatment

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Medical treatment	Surgery				
Proportion free from seizures at 1 year	**71 per 1000**	**692 per 1000** (334 to 1000 per 1000)[a]	**RR 9.78** (4.73 to 20.21)	196 (2 studies)	⊕⊕◯◯ **low**[b,c]	RR > 1 indicates advantage for surgery One study measured freedom from seizures as 'all seizures impairing awareness', and another study measured freedom from seizures as ILAE Class 1
Proportion free from all seizures (including auras) at 1 year	**25 per 1000**	**375 per 1000** (52 to 1000 per 1000)[a]	**RR 15.00** (2.08 to 108.23)	80 (1 study)	⊕◯◯◯ **very low**[b,c,d]	RR > 1 indicates advantage for surgery

*The basis for the **assumed risk** is the event rate in the control group (medical treatment). The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; ILAE: International League Against Epilepsy; RR: risk ratio

GRADE Working Group grades of evidence.
High certainty (quality): further research is very unlikely to change our confidence in the estimate of effect.
Moderate certainty (quality): further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low certainty (quality): further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low certainty (quality): we are very uncertain about the estimate.

[a] Upper bounds of the corresponding risk interval revised to their maximum to align with the upper bound of the confidence interval of the relative effect.

[b] Large but imprecise effect size shown in favour of surgical treatment (downgraded due to imprecision as relatively small studies and low event rates in control groups).

[c] Downgraded due to insufficient information regarding methods of randomisation and allocation concealment provided by one of the studies.

[d] Downgraded for indirectness: results are applicable to adults (over 16 years only), with children excluded from the study.

BACKGROUND

This review is an update of a review that was previously published in the *Cochrane Database of Systematic Reviews* (Issue 7, 2015) on "Surgery for epilepsy" (West 2015).

Description of the condition

Epilepsy has been redefined very recently by the International League Against Epilepsy (ILAE) as "a disease of the brain defined by any of the following conditions: (1) at least two unprovoked (or reflex) seizures occurring > 24 h apart; (2) one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years; (3) diagnosis of an epilepsy syndrome" (Fisher 2014). Epilepsy is a common condition with a prevalence of around 1 in 200 people. Despite optimal pharmacotherapy, about 20% to 30% of individuals do not become seizure-free (Annegers 1979; Collaborative 1992; Cockerell 1995; Kwan 2000). For some of these people, surgery is a therapeutic option.

Description of the intervention

The intervention involves localisation of the epileptogenic focus and then, if the potential benefit is assessed to outweigh the risk, surgical resection. Feindel 2009 has thoroughly reviewed the history of the development of surgery for epilepsy. This work was pioneered by Victor Horsley when, in 1886, he operated on a 22-year-old man who had developed a focal epilepsy following a head injury. A highly vascular scar associated with an old depressed comminuted skull fracture was excised along with a border of cortex. The presence of a discrete cortical vascular scar and the arrest of focal motor seizures following its excision provided direct support for Hughlings Jackson's concept of the aetiology of focal epilepsy. It subsequently became evident that a variety of pathologies could give rise to the focal epilepsies. Techniques of cortical stimulation along with the advent of electroencephalography in the 1930s aided localisation. Until the 1940s, surgery was directed mainly to the convexity of the cerebral hemispheres, most often for removal of traumatic scars or tumours. The work of Frederic Gibbs and William Lennox from 1936 promoted electroencephalography (EEG) into a strategic position for diagnosis and early classification of the epilepsies. Herbert Jasper, working with Wilder Penfield, used EEG to develop new approaches for surgery for epilepsy, particularly in the temporal lobe and mesial temporal structures. A major obstacle to removal of these structures was lack of knowledge about their function (Feindel 2009). Penfield considered EEG and emerging techniques for electrocorticography (ECoG) useful if they could disclose pathological areas in the brain. If a visible lesion was not found at the place indicated by the recording of epileptic activity, Penfield usually would decline to perform a resection. A success rate of just over 50% indicated that resection limited to the anterolateral temporal cortex did not eliminate all epileptogenic tissue in many people. Researchers then provided greater focus on mesial temporal structures. Jasper noted that a cure could be effected even when no abnormality was visible in the excised material, and added, "it seems clear, therefore, that the pathophysiological state of spike foci may not always be associated with structural alterations which can be seen by present methods of microscopic examination" (Feindel 2009). This led to more detailed pathological study of excised material - an approach led by Murray Falconer with Alfred Meyer. More sophisticated EEG study, cortical stimulation, and detailed descriptions of seizure semiology revealed the importance of the human claustroamygdaloid complex in short-term memory, consciousness, and emotions. As resection of anteromesial structures became the accepted treatment for temporal lobe epilepsy, the hippocampus was elucidated as important for short-term recent memory function. This observation led to the inclusion of a neuropsychologist in most surgery selection teams. Temporary and partial suppression of one cerebral hemisphere by injection of intracarotid sodium amytal, a technique introduced by Wada, became a useful test for determining the laterality of speech function and for evaluating memory responses in people with bitemporal seizure activity. Functional magnetic resonance imaging (fMRI), along with neuropsychometry, is now superseding this initial approach.

Other sophisticated technological developments followed: the advent of computerised tomography in the 1970s; magnetic resonance imaging (MRI) in the 1990s; computerised analysis of ictal and inter-ictal EEG activity; fMRI with psychometric analysis and ever more sophisticated stereotaxis guiding the placement of deep electrodes for long-term EEG analysis; and surgical intervention. These techniques have been complemented by the co-registration of single-photon emission computed tomography (SPECT) and positron emission tomography (PET) findings (Feindel 2009), and, most recently, by improved co-registration and simultaneous review of both structural and functional data from PET/MRI (Shin 2015). These developments are now leading to more precise localisation of epileptogenic foci and a reduction in the risk of removing eloquent cortex. This approach has led to greater opportunity for accurate assessment for a surgical cure for any person with drug-resistant focal epilepsy. However, sophisticated technology has a place only in the setting of a good interdisciplinary team working in harmony and incorporating the skills of a neurologist, a neurophysiologist, a psychiatrist, a neuropsychologist, and a neurosurgeon with postoperative help from remedial therapists who have good scope for liaison with educational, vocational, and social services for good postoperative rehabilitation.

Success rates for resective epilepsy surgery are estimated to have increased from 43% to 85% during the period from 1986 to 1999 (Engel 1993a; Engel 2003; National 1990a). Data from multiple sources suggest that 55% to 70% of individuals un-

dergoing temporal resection and 30% to 50% of those undergoing extratemporal resection become completely seizure-free. A prospective randomised controlled trial of surgery for temporal lobe epilepsy showed that 58% of individuals randomised to surgery were seizure-free compared to 8% of those in the medical group (Wiebe 2001). Surgery is considered a valuable option for medically intractable epilepsy, even in the absence of proven drug resistance (Engel 1993b).

How the intervention might work

The rationale for the intervention is initial localisation of the epileptogenic focus followed by its surgical resection. The mainstay for investigation is MRI. Concordance between an MRI scan and EEG findings along with seizure semiology is sought. Key is accurate localisation of the epileptogenic focus to an area of the brain that might safely be removed without inducing neurological impairment. If the lesion is not well defined, further imaging via PET, SPECT, or PET/MRI may supplement accurate placement of indwelling EEG electrodes to achieve this aim (see Description of the intervention). When the epileptogenic focus can be removed safely, epilepsy may be cured with a corresponding improvement in quality of life.

Why it is important to do this review

Surgical outcomes may be greatly influenced by the presence of selected prognostic indicators (Berg 1998; Tonini 1997). However, uncertainties remain about which patients are most likely to achieve good surgical outcomes. Good surgical outcomes appear to be associated with various factors (i.e. 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 2001). However, published trial results are frequently confusing and contradictory, thus preventing inferences for clinical practice. The initial version of this Cochrane review (West 2015) was the first to investigate the association between specific prognostic factors and surgical outcomes. It complemented and updated the only systematic review to date to examine factors predictive of the outcome of epilepsy surgery (Tonini 2004). This review informs the surgical selection process and allows refinement of the risk/benefit analysis for surgical intervention.

OBJECTIVES

The primary objective is to assess the overall outcome of epilepsy surgery according to evidence from randomised controlled trials. Secondary objectives are to assess the overall outcome of epilepsy surgery according to non-randomised evidence, and to identify the factors that correlate with remission of seizures postoperatively.

METHODS

Criteria for considering studies for this review

Types of studies

In the original review (West 2015), we included studies if they satisfied the following criteria.

- Randomised controlled trial (RCT), cohort study, or case series, prospective and/or retrospective.
- A sample size of at least 30 participants undergoing surgery.
- A well-defined population (age, sex, seizure type and frequency, duration of epilepsy, aetiology, MRI diagnosis, surgical findings).
- MRI performed in at least 90% of cases.
- Expected duration of follow-up of at least one year.
- A reported outcome related to postoperative seizure control.

We excluded reports if they were provided in abstract form or in book chapters, or if they did not present sufficiently clear details about their methods; if they were written in languages other than English, Italian, French, German, or Spanish (due to the availability of translators for detailed data extraction); or if they did not meet all of the above inclusion criteria. We also excluded repeated publications from the same institution (among which we retained only the most recent for review) unless they dealt with different prognostic factors.

For this update, to provide the most clinically relevant and high-quality updated evidence, we included only new RCTs meeting the other inclusion criteria. We did not include in this updated review new studies using a non-randomised design.

Types of participants

We included children, adolescents, and adults who were considered surgical candidates and had drug-resistant focal seizures and secondarily generalised seizures of temporal or extratemporal origin (i.e. seizures that continue despite treatment with anticonvulsant medication).

Types of interventions

We included studies that provided surgical treatment for drug-resistant focal seizures and secondarily generalised seizures of temporal or extratemporal origin. For RCTs, we considered all control groups for comparison, including those given medical treatment or no treatment and those undergoing different surgical techniques.

In the original version of this review (West 2015), we considered non-randomised studies with or without control groups (i.e. case series) for inclusion.

Types of outcome measures

Primary outcomes

Seizure outcome (proportion achieving a good outcome from surgery)

The outcome of seizures after epilepsy surgery is classified according to Engel's four categories with subcategories (Engel 1987; Engel 1993b), or it is reported as such when different definitions are used (see the Table below).

Engel class	Description (subclasses)
Class 1: free of disabling seizures	1A: completely seizure-free since surgery 1B: non-disabling simple focal 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')
Class 2: almost seizure-free (rare disabling seizures)	2A: initially free of disabling seizures, but 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
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

Sources: Engel 1987; Engel 1993b.

We considered:

- 'good outcome' as seizure control or seizure-free status for at least one year, or Engel Class 1 (when individual study data quality did not allow further refinement);
- 'improved outcome' as near complete control or moderate improvement, or Engel Classes 2 and 3; and
- 'worse outcome' as slightly reduced or unchanged or worsened seizure frequency, or Engel Class 4.

We also considered, when data for these time points were available, results at 12 and 24 months. Reporting of this primary outcome using the outcome scales described above was not an eligibility requirement for inclusion in this review. However, we excluded studies that did not report an outcome related to seizure control following surgery. We considered other outcome scales that satisfied our above definitions. We divided studies into subgroups based on seizure outcomes defined by the Engel Class Scale, more than one year seizure-free, or another scale (see Subgroup analysis and investigation of heterogeneity).

For the purposes of this review, we compared a 'good outcome' (seizure remission as defined above) versus a 'poor outcome', with a poor outcome defined as improved and worse outcome categories as combined above (i.e. Engel Classes 2 to 4, or not seizure-free for at least one year). We did not consider other combinations of outcome scales. For trials that reported other combinations of outcome scales, and for studies that used a scale that did not clearly satisfy our definitions, when possible we contacted the trial authors to request further information about seizure outcome data. When further information could not be provided, we excluded studies from analysis in the review (see Data synthesis), but we retained them in the narrative section of the review.

Secondary outcomes

Seizure outcome according to prognostic factors of interest

We considered the proportion of individuals with a good outcome from surgery (see Primary outcomes) according to the following prognostic factors, which we considered to be of clinical relevance.

Pre-operative factors

- Results of pre-operative MRI: normal (i.e. no abnormality visible on MRI) or abnormal (i.e. abnormality visible on MRI).

We included studies in which study authors referred to MRI results only as 'abnormal', as well as studies that reported specific abnormalities.

- Use of pre-operative intracranial (invasive) monitoring: yes or no.
- Mesial temporal sclerosis (MTS) on MRI or pathology: present or absent.
- Concordance of pre-operative MRI and EEG: yes or no.

Concordance relates to whether EEG discharges arise from the area of the brain identified as abnormal on MRI scan (i.e. the surgically targeted area).

- History of febrile seizures: yes or no.
- History of head injury: yes or no.
- Encephalomalacia on pathology: present or absent.
- Focal cortical dysplasia/malformation of cortical development on pathology: present or absent.
- Tumour on pathology: present or absent.

We included studies that referred to pathological results of 'tumour' and studies that reported specific tumour types.

- Vascular malformation on pathology: present or absent.

We included studies that referred to pathological results of 'vascular malformation' and studies that reported specific types of vascular malformations.

- Distribution of interictal spikes: unilateral or bilateral.

We were interested in determining whether interictal spikes (epileptiform EEG discharges noted between seizures) were related to the area to be excised at surgery, or whether they were more widespread. Terms also used in the included studies are 'lateralising versus non-lateralising spikes' (i.e. discharges on the side to be operated or on both sides of the brain) and 'focal versus non-focal spikes' or 'localising versus non-localising spikes' (i.e. discharges seen only related to the surgical site or seen to be more widespread).

Operative factors

- Extent of surgical resection: complete or incomplete.

We anticipated that the definition of a 'complete' or 'less complete' resection would be variable across studies. Most researchers based this definition on the type of surgery performed (e.g. anterior temporal lobectomy or extended resection is complete resection, selective amygdalohippocampectomy or lesionectomy is less complete resection). When study authors provided other clear descriptions, we included those studies (e.g. postoperative MRI appearance; intraoperative subdural EEG findings; intraoperative surgical description; dimensions of resected areas).

- Side of surgical resection: left-sided or right-sided resection.

Postoperative factors

- Postoperative discharges: presence or absence of EEG epileptiform discharges in the postoperative period.

We dichotomised all factors for analysis according to the definitions presented above. We included data reported according to our definitions above, as well as data reported in a way that allowed us to categorise using the above definitions (e.g. if specific MRI results were reported for all individuals, we categorised them into 'normal' and 'abnormal', or 'concordant' and 'discordant' with EEG results). We considered other definitions reported in the included studies if equivalent (or approximately equivalent) to our pre-specified definitions.

Search methods for identification of studies

Review authors carried out a MEDLINE (OVID) search for Tonini 2004, to identify relevant studies published between 1984 and 2001 (noting that 1984 coincides with the introduction of MRI). We used the results provided in that review and carried out searches to cover the time from 2001 onwards.

Electronic searches

We ran searches for the original review on 4 July 2013, and we ran subsequent searches on 14 December 2017. For the latest update, we searched the following databases on 11 March 2019.

1. Cochrane Register of Studies (CRS Web), which includes the Cochrane Epilepsy Group Specialized Register and the Cochrane Central Register of Controlled Trials (CENTRAL), using the search strategy outlined in Appendix 1
2. MEDLINE (Ovid, 1946 to March 08, 2019), using the search strategy outlined in Appendix 2
3. ClinicalTrials.gov, using the search strategy outlined in Appendix 3
4. World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP), using the search strategy outlined in Appendix 4.

We imposed language restrictions due to the availability of translators for extensive data extraction (English, Italian, French, German, or Spanish). For the latest update, we searched only for randomised controlled studies, whereas for the original review, we searched for non-randomised studies as well (West 2015). No Cochrane approved or recommended search filter is available for non-randomised studies, so for the MEDLINE search, the Information Specialist for the Cochrane Epilepsy Group chose the terms to be used for required types of non-randomised studies. We did not subject the resulting search filter to any systematic testing before use.

Searching other resources

We also examined the reference lists of included studies for further relevant studies for inclusion in this review.

Data collection and analysis

Selection of studies

Two review authors (SW and RN) independently assessed trials for inclusion. We resolved disagreements through mutual discussion and sought the opinion of a third review author (SN) when necessary.

Data extraction and management

We implemented a database search for identification and inclusion of relevant articles (i.e. those that fulfil the inclusion criteria and provide complete information about the outcome of epilepsy and prognostic factors).
SW, RN, JC, AS, and SG collected the data using a semi-structured form via a Microsoft Access database (created by SN) for each study. RR joined RN to extract data from the Spanish papers.
We considered the following variables.

- Methods of assessment of eligible studies.
- Demographic and clinical characteristics (number of patients selected for surgery, age (with special attention to patients younger and older than 12 years), sex, disease duration, history of febrile seizures or relevant central nervous system (CNS) disorder).
- MRI pre-operative diagnosis (MTS, tumours, other CNS abnormalities, normal).
- Surgical findings (age at surgery, side of resection, surgical procedure (temporal or extratemporal), extent of resection).
- Histopathological diagnosis (same categories as MRI); duration of follow-up; post-surgery findings (dropouts, adverse events).
- Prognostic indicators: different indicators are described as factors affecting the outcome of epilepsy surgery in terms of seizure remission (specifically, focal cortical dysplasia/malformation of cortical developments, febrile seizures, tumours, vascular disorders, CNS infections, MTS, abnormal MRI, EEG/MRI concordance, interictal spikes, intracranial monitoring, extent of resection, postoperative discharges, other factors studied). Mesial temporal sclerosis and tumours require pathological confirmation. We also recorded details of statistical analysis of prognostic indicators and multi-variable prognostic models (if reported).

We limited this review to prognostic factors that are clinically relevant (detailed in Secondary outcomes) and/or were reported by at least two studies.
Consensus is required for each variable reported on the data collection form; any disagreement led to a discussion of the issue by the two review authors and resolution of persisting disagreement by an independent third review author. In selected cases, an independent evaluator (SN) resolved conflicting data.

Assessment of risk of bias in included studies

Two review authors (SW and RN) assessed risk of bias, and two review authors (SN and JW) independently checked these judgements.
For RCT evidence, we assessed all domains of the current Cochrane 'Risk of bias' tool (Higgins 2011).
For the original review (West 2015), for non-randomised evidence, we employed the Effective Public Health Practice Project (EPHPP) tool, which is appropriate for case series study designs (see Appendix 5). In a post hoc review of a multi-variable prognostic model, SN assessed risk of bias according to the Quality in Prognosis Studies (QUIPS) tool (Hayden 2006).
We planned to incorporate 'Risk of bias' assessments into the analysis if deemed appropriate, using sensitivity analysis, because a secondary analysis of the data would include only studies rated as low in quality, with results presented in the Results section of the review. However, upon using the EPHPP tool, we found this tool to be inadequate to judge the relative quality of the included studies, so we concluded that incorporation of quality assessment into the analysis would be inappropriate (see Sensitivity analysis and Risk of bias in included studies for further details).

Measures of treatment effect

We measured the outcome of seizures after epilepsy surgery as good compared to poor overall, and according to the presence or absence of prognostic factors of interest in univariate analysis (see Types of outcome measures and Data synthesis). We analysed all outcomes as dichotomous outcomes summarised with risk ratios (RRs) and 95% confidence intervals (95% CIs). We considered multi-variable prognostic models narratively, as reported in the original study publications.

Unit of analysis issues

We did not encounter any unit of analysis issues. The unit of intervention and analysis was the individual for all included studies, and no studies were of a repeated measures (longitudinal) nature or used a cross-over design.

Dealing with missing data

We attempted to seek missing statistics from studies through contact with the study authors. In cases of missing data, we attempted to clarify the reasons for missing data to determine whether data were missing at random. We analysed all data according to the intention-to-treat principle.

Assessment of heterogeneity

We assessed the existence of clinical heterogeneity by examining differences in study characteristics and in participant demographic factors, to inform decisions regarding the combination of study data. We assessed statistical heterogeneity by visually inspecting forest plots and using a Chi² test for heterogeneity (with a P value of 0.10 for significance) and the I^2 statistic as a measure of inconsistency across studies, with an I^2 value of 50% to 75% or higher representing substantial heterogeneity (Higgins 2011). When we found considerable statistical heterogeneity according to the I^2 statistic value (> 50%), we performed meta-analysis using a random-effects rather than a fixed-effect model, in addition to subgroup and sensitivity analyses, to investigate differences in study characteristics and participant factors.

Assessment of reporting biases

To enable comparison of outcomes of interest, we would require all protocols from study authors. However, due to the large number of included studies in this review, obtaining all protocols was impractical and impossible, so we made a judgement on the existence of reporting bias. If we suspected reporting bias, we investigated further using the ORBIT classification system (Kirkham 2010).
We examined publication bias by identifying unpublished data by carrying out a comprehensive search of multiple sources and requesting unpublished data from study authors. We looked for small-study effects to establish the likelihood of publication bias, and we examined asymmetry of funnel plots.

Data synthesis

For each prognostic factor of interest individually (see point six of Data extraction and management), we performed a univariate aggregate data fixed-effect meta-analysis using the Mantel-Haenszel method to assess the presence or absence of that factor as an independent predictor of the outcome of surgery (good or poor outcome), analysed as a dichotomous outcome and presented as a pooled risk ratio with 95% confidence interval.
For post hoc analysis in the original review (West 2015), we also investigated whether effects of other prognostic factors on any individual prognostic factor had been adjusted for (e.g. in multi-variable regression models). In this case, we hoped to perform separate meta-analyses of adjusted and unadjusted estimates and to compare results. However, adjusted data presented were insufficient to allow us to perform meta-analysis of adjusted results from multivariable prognostic models; therefore we summarised all multivariable models narratively and provided narrative comparisons of multi-variable adjustments to univariate analyses.
When we found considerable statistical heterogeneity to be present (Chi² test for heterogeneity $P < 0.1$ and/or $I^2 > 50\%$), we used a random-effects meta-analysis and performed subgroup and sensitivity analyses to investigate differences in study characteristics and participant factors.

Subgroup analysis and investigation of heterogeneity

When we noted a substantial amount of heterogeneity across univariate prognostic factors, we performed further analyses such as stratification, subgroup analyses, and sensitivity analyses to examine differences in study characteristics (such as outcome and prognostic factor definition, study design, and study quality) and participant demographic factors.
Researchers measured good and poor outcomes using varying definitions across studies (e.g. a good outcome can be defined as seizure-free status for at least one year, Engel Class 1, or other equivalent definitions). We defined these scales as Engel Class Scale, more than one year seizure-free scale, and some 'other' scale (see Primary outcomes for further details). We planned to examine the effect of variation in outcome definitions by performing subgroup analysis.
Due to differences in surgical technique and/or associated pathology with location of surgery (temporal or extratemporal lobe), when applicable we also performed stratified analyses, grouping studies into the following categories: all participants in the study had temporal lobe surgery (temporal lobe); all participants in the study had extratemporal lobe surgery (extratemporal lobe); or the study included a combination of participants with temporal lobe and extratemporal lobe surgery (combination).

Sensitivity analysis

We intended to perform sensitivity or subgroup analyses to examine the effect of study quality based on 'Risk of bias' and quality assessment tools. However, due to inadequacy of the quality assessment tool used in the original review in separating studies of generally poor methodological design (majority retrospective case series) (West 2015), we decided that sensitivity or subgroup analysis according to 'quality assessment' would not be informative and would not be appropriate (see Risk of bias in included studies for more information).

Instead, as described under Subgroup analysis and investigation of heterogeneity, we considered differences in study characteristics and participant demographic factors as sources of heterogeneity in analyses. Further, in the case of a study reporting an extreme result (a particularly large effect in favour of the presence of absence of a prognostic factor), we double-checked extracted data on this factor from the study publication and investigated study-related or participant-related characteristics that could have contributed to the large effect.

'Summary of findings' and certainty of the evidence

We presented the primary outcome (seizure outcome) for studies with a randomised controlled design in 'Summary of findings' tables (Summary of findings for the main comparison; Summary of findings 2), and we judged the certainty of the evidence contributing to these outcomes according to GRADE (Grading of Recommendations Assessment, Development and Evaluation) criteria (Guyatt 2008; Hultcrantz 2017).

RESULTS

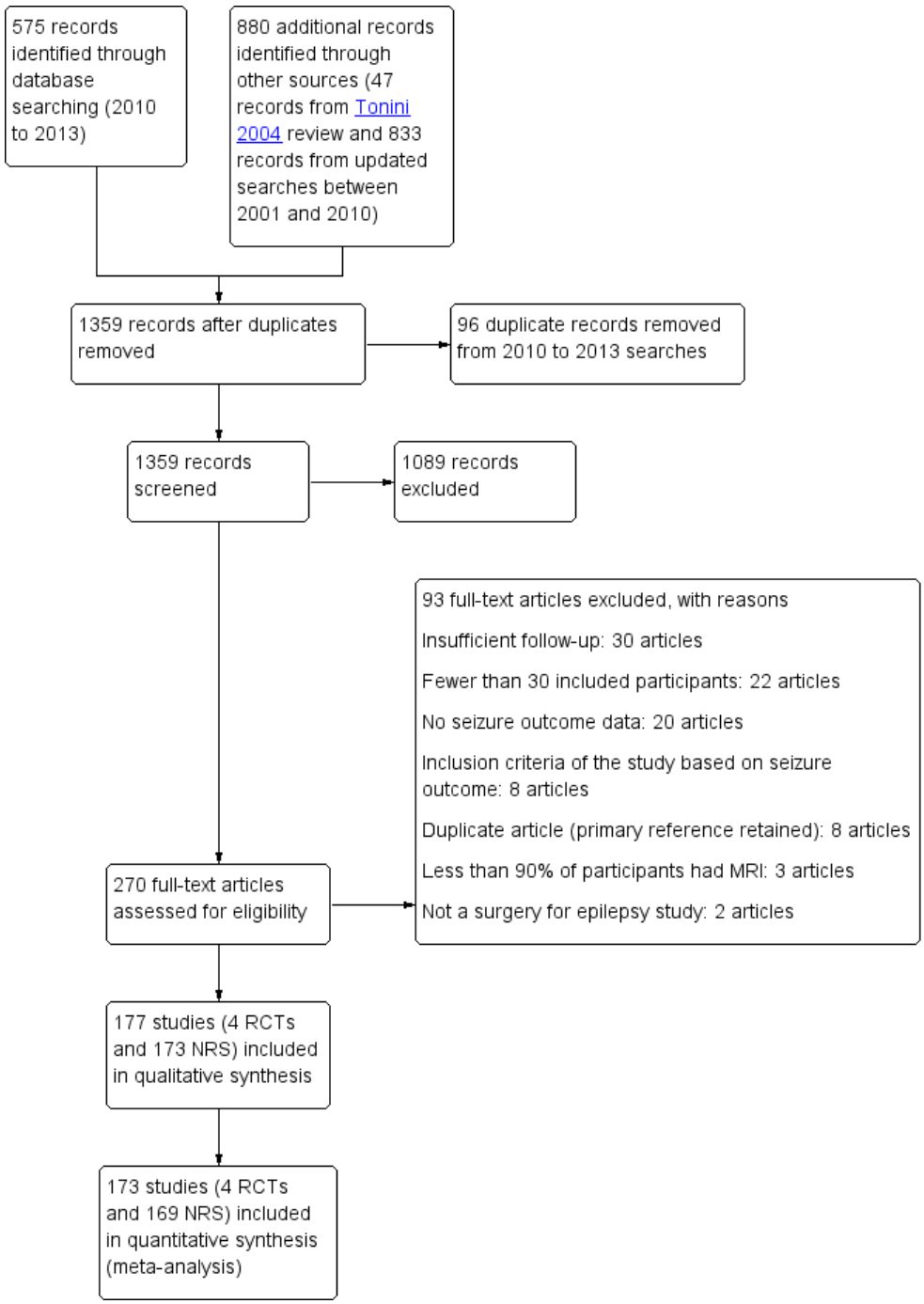
Description of studies

Results of the search

A MEDLINE search conducted over the years from 1984 to 2001 identified 1051 records, 619 of which we excluded as 'prognosis of seizures after surgery was not measured' (in other words, no seizure outcome data were recorded); 383 met other exclusion criteria of the review (see Tonini 2004 for further details). The Tonini 2004 review included 47 studies; we screened these studies for inclusion in our review as 'records found from other sources'.

From searches conducted by the Cochrane Epilepsy Group between 2001 and 2010, we identified 833 records. From searches conducted after the initiation of this review in 2010, we identified 575 records. We used the search strategies outlined in Electronic searches to conduct database searches from 2001. We removed 96 duplicate records from those identified between 2010 and 2013 and screened 1395 records (title and abstract) for inclusion in the review. We excluded 1089 records based on title and abstract and assessed 270 full-text articles for inclusion in the review. We excluded 93 studies from the review (see Excluded studies below) and included 177 studies from the original review (West 2015). See Figure 1 for the PRISMA study flow diagram for the original version of this review, including RCTs and non-randomised studies.

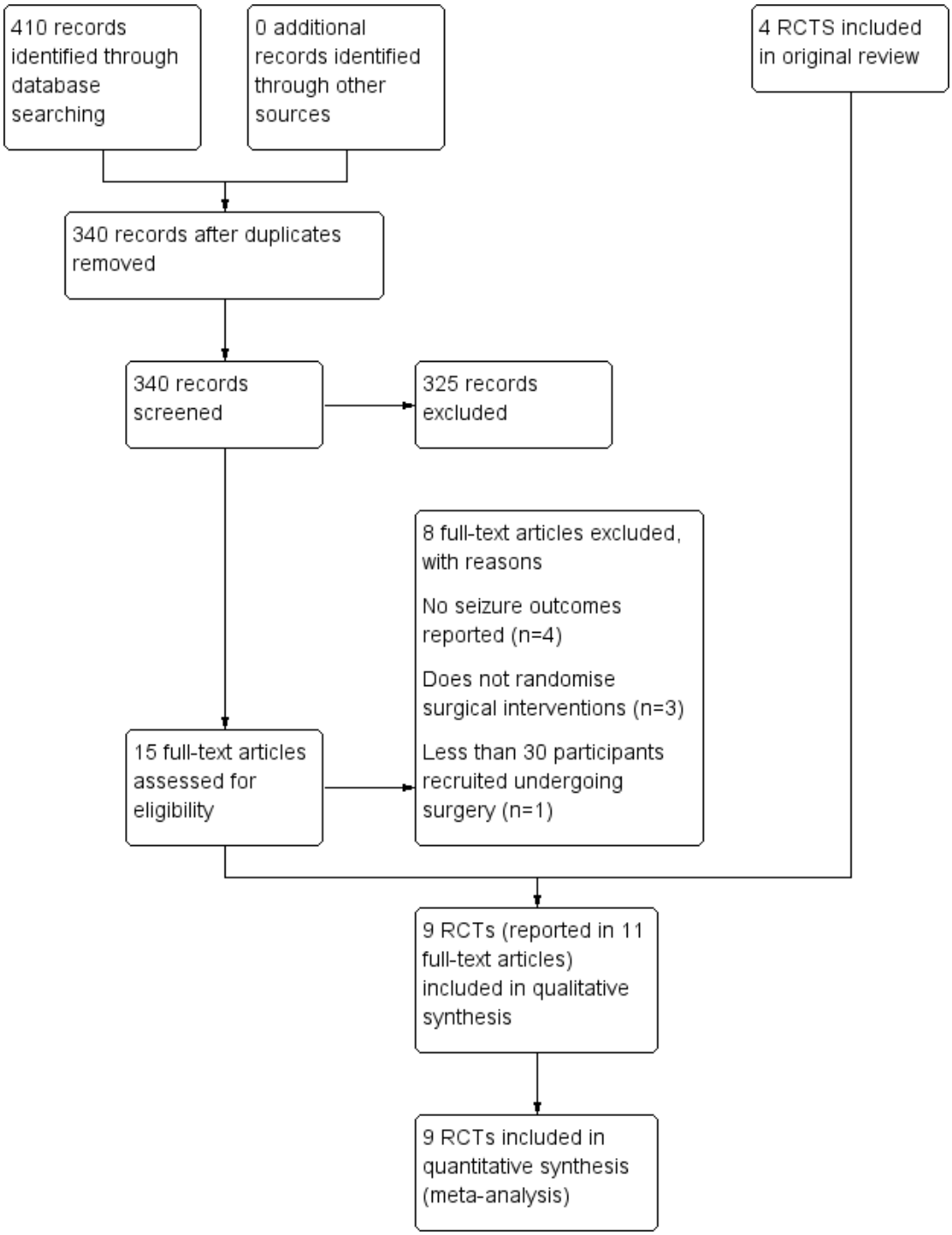
Figure 1. Study flow diagram (original review: randomised controlled trials (RCTs) and non-randomised studies (NRSs) included).



For this latest update, only RCTs were eligible for inclusion (see Types of studies). We identified 410 records from the databases and search strategies outlined in Electronic searches. We removed 70 duplicate records and screened 340 records (title and abstract) for inclusion in the review. We excluded 325 records that were clearly irrelevant and screened the full-text articles of 15 records. We included five studies (reported in seven full-text articles) and excluded eight full-text articles that did not report a seizure outcome, recruited less than 30 surgical participants or did not randomise surgical interventions.

See Figure 2 for the PRISMA study flow diagram for inclusion of RCTs from the original version and this updated version of the review.

Figure 2. Study flow diagram (2019 update: randomised controlled trials (RCTs) only included).



Therefore in total, we included 182 studies within this updated review: 173 non-randomised studies from the original version of the review (West 2015), and nine RCTs (four RCTs from the original review and five new RCTs in this update).

Included studies

We included 182 studies in this review (Aaberg 2012; Adam 1996; Adelson 1992; Alfstad 2011;Alonso-Vanegas 2018; Althausen 2013; Arruda 1996; Awad 1991; Babini 2013; Barbaro 2018; Battaglia 2006; Baumann 2007; Bautista 2003; Bell 2009; Benifla 2006; Berkovic 1995; Blount 2004; Blume 2004; Boesebeck 2007; Boshuisen 2010; Brainer-Lima 1996; Britton 1994; Caraballo 2011; Cascino 1995; Chabardes 2005; Chang 2009; Chee 1993; Chkhenkeli 2007; Choi 2004a; Chung 2005; Cossu 2005; Cossu 2008; Costello 2009; Cukiert 2002; Dagar 2011; Dalmagro 2005; Delbeke 1996; Dellabadia 2002; de Tisi 2011; Devlin 2003; Ding 2016; Donadio 2011; Dorward 2011; Duchowny 1998; Dunkley 2011; Dunlea 2010; Dwivedi 2017; Elsharkawy 2008a; Elsharkawy 2009a; Elsharkawy 2011a; Engman 2004; Erba 1992; Erickson 2005; Fauser 2004; Fujiwara 2012; Garcia 1991; Garcia 1994; Gelinas 2011; Georgakoulias 2008; Gilliam 1997a; Gilliam 1997b; Goldstein 1996; Greiner 2011; Grivas 2006; Gyimesi 2007; Hader 2004; Hajek 2009; Hallbook 2010; Hamiwka 2005; Hartley 2002; Hartzfield 2008; Hemb 2010; Holmes 1997; Holmes 2000; Jack 1992; Janszky 2003a; Janszky 2003b; Jaramillo-Betancur 2009; Jayakar 2008; Jayalakshmi 2011; Jeha 2006; Jehi 2012; Jennum 1993; Jeong 1999; Kan 2008; Kang 2009; Kanner 2009; Kilpatrick 1997; Kim 2009; Kim 2010a; Kim 2010b; Kloss 2002; Knowlton 2008; Kral 2007; Krsek 2013; Kuzniecky 1993; Kwan 2010; Lackmayer 2013; Lee 2006; Lee 2008; Lee 2010a; Lee 2011; Lei 2008; Li 1997; Li 1999; Liang 2010; Liang 2012; Liava 2012; Lopez-Gonzalez 2012; Lorenzo 1995; Madhavan 2007; Mani 2006; Mathern 1999; McIntosh 2012; Mihara 2004; Miserocchi 2013; Morino 2009; Morris 1998; O'Brien 1996; O'Brien 2000; Oertel 2005; Paglioli 2006; Paolicchi 2000; Park 2002; Park 2006; Perego 2009; Perry 2010; Phi 2009; Phi 2010; Pinheiro-Martins 2012; Prevedello 2000; Raabe 2012; Radhakrishnan 1998; Rausch 2003; Remi 2011; Roberti 2007; Rossi 1994; Russo 2003; Sagher 2012; Sakamoto 2009; Salanova 1994; Sarkis 2012; Schramm 2011; Seymour 2012; Sinclair 2003; Sindou 2006; Sola 2005; Spencer 2005; Sperling 1992; Stavrou 2008; Suppiah 2009; Swartz 1992; Tanriverdi 2010; Tatum 2008; Terra-Bustamante 2005a; Terra-Bustamante 2005b; Tezer 2008; Theodore 2012; Tigaran 2003; Tripathi 2008; Trottier 2008; Urbach 2007; Ure 2009; Velasco 2011; Vogt 2018; Walz 2003; Weinand 1992; Wellmer 2012; Widdess-Walsh 2007; Wiebe 2001; Wieshmann 2008; Wray 2012; Wyler 1995; Wyllie 1998; Yang 2011; Yeon 2009; Yu 2009; Yu 2012a; Yu 2012b; Zangaladze 2008; Zentner 1995; Zentner 1996).

We included nine studies of a randomised controlled design. Six studies randomised the type of surgical intervention: anterior temporal lobectomy (ATL) compared to selective amygdalohipppocampectomy (SAH) compared to parahippocampectomy (PHC) (Alonso-Vanegas 2018); stereotactic radiosurgery (SRS) or ATL (Barbaro 2018), resective surgery or combined resection and corpus callosotomy (CCT) (Ding 2016), ATL with or without anterior CCT (Liang 2010), subtemporal of transsylvian SAH (Vogt 2018); partial versus total hippocampectomy (Wyler 1995) and one study randomised length of surgical resection; 2.5-cm or 3.5-cm tailored temporal lobe resection (Schramm 2011). Two studies (n = 196) randomised adults over the age of 16 and children and adolescents under the age of 18, respectively, to immediate surgery in Wiebe 2001 or to medical treatment (antiepileptic drugs) with placement on a waiting list for surgery in Dwivedi 2017.

All other 173 studies were of a non-randomised design and did not include a control group in the study design.

See Characteristics of included studies and Table 1 for detailed study characteristics and participant demographics in all 182 included studies. Below we provide a summary.

A total of 16,756 participants in the 182 studies underwent a surgical procedure for intractable epileptic seizures, and 99 participants from two RCTs received medical treatment. Therefore in total 16,855 participants were included in the review.

In terms of the participants undergoing a surgical procedure, study authors reported gender for 13,608 participants from 154 studies (7714 male (57%) and 5894 female (43%)), and data were missing for 3148 participants from 28 studies (19% of total participants). A measure of the age of participants at surgery (see Table 1) was available for 157 studies (86% of total studies), ranging from 0 years to 86 years at surgery. Age at surgery was not available for 2707 participants from 25 studies (14% of total studies). Given that adults are classified as over the age of 18 years, 31 studies included adults only (17% of total studies; 2433 participants), 23 studies included children only (13% of total studies; 1247 participants), and 103 studies included both adults and children (56% of total studies; 10,374 participants). A measure of the duration of epilepsy among participants (see Table 1) was available for 113 studies (62% of total studies; 10,553 participants), ranging from 0 years to 86 years. Duration of epilepsy was not available for 6203 participants from 69 studies (38% of total studies).

The type of surgical resection performed was available for 173 studies (95% of total studies). Researchers in 94 studies reported a single-lobe surgery; 8090 participants from 79 studies (43% of total studies) underwent temporal lobe resection only; 1058 from 15 studies (8% of total studies) underwent extratemporal lobe resection only; and 79 studies (44% of total studies) including 6761 participants reported both temporal and extratemporal lobe

resection.

A total of 144 studies identified 13,557 participants via a retrospective design (79% of 177 studies); 26 studies identified 2120 participants via a prospective design (14% of studies); three studies identified 342 participants via a combination of prospective and retrospective designs (2% of studies); and nine studies did not state the method of identification of the 670 participants and it could not be deduced (5% of studies).

Follow-up in the 182 studies ranged from 0 to 366 months. We specified in our inclusion criteria (see Criteria for considering studies for this review) that studies must have an 'Expected duration of follow-up of at least one year' for inclusion; therefore we excluded studies that did not specify the duration of follow-up at all, studies that reported the duration of follow-up as definitely less than one year, and studies that provided unclear information on how many participants were followed up for at least one year. A number of studies included participants with less than 12 months' follow-up but did not include these participants in postoperative seizure outcomes or made it possible for us to separate data for participants followed up for less than or longer than 12 months. We considered these studies to have an expected follow-up longer than one year. Similarly, we considered studies that reported a mean or median follow-up time greater than 12 months but no expected minimum follow-up of at least 12 months. At least two review authors closely examined follow-up information from all studies before deciding whether to include or exclude the study.

We defined three types of outcome scales appropriate for the primary seizure outcome (see Primary outcomes). Forty-two studies reported seizure outcome according to a 'more than one year seizure-free scale' (23% of total studies; 3981 participants), 119 studies reported seizure outcome according to the 'Engel Class Scale' (65% of total studies; 10,705 participants), and 21 studies reported seizure outcome according to some 'other scale' (12% of total studies; 2070 participants). Other scales we deemed to meet our definition of a 'good outcome' were as follows.

- Seven studies reported more than two years of seizure freedom (Engman 2004; Goldstein 1996; Gyimesi 2007; Holmes 2000; Jeong 1999; Lee 2006; Mathern 1999), one reported more than three years of seizure freedom (Rossi 1994), and one reported more than five years of seizure freedom (McIntosh 2012).
- Seven studies reported seizure outcome according to the classification proposed by the International League Against Epilepsy (ILAE 2001) as follows.
    - Class 1, completely seizure-free; Class 2, aura alone with no seizure; Class 3, one to three seizure days/year; Class 4, 50% reduction in baseline number of seizure days; Class 5, less than 50% reduction in baseline number of seizure days; and Class 6, more than 100% increase in baseline number of seizure days.
        - We considered ILAE Class 1 to correspond to Engel Class 1A, and ILAE Classes 1 and 2 together to correspond to Engel Class 1 (see Primary outcomes); therefore if a study reported a 'good outcome' to be ILAE Class 1 (poor outcome classes 2 to 6) or ILAE Classes 1 and 2 (poor outcome classes 3 to 6), we accepted this as a satisfactory 'other' scale. Five studies defined ILAE Class 1 as a good outcome (de Tisi 2011; Dwivedi 2017; Kral 2007; Lackmayer 2013; Vogt 2018), and two defined ILAE Classes 1 and 2 as a good outcome (Sakamoto 2009; Yang 2011). We did not accept any other combinations of ILAE classes as an outcome that measured seizure freedom.
- Four studies reported seizure freedom by the Engel Class Scale but not as our definition above, where a good outcome corresponds to Engel Class 1 and a poor outcome corresponds to Engel Classes 2 to 4 (see Primary outcomes); two studies defined a good outcome as Engel Class 1A and a poor outcome as Engel Classes 1B to 4 (Boshuisen 2010; Phi 2010), one study defined a good outcome as Engel Class 1A to B and a poor outcome as Engel Classes 1C to 4 (Boesebeck 2007) and one study defined a good outcome (seizure remission) as at least Engel Class IB between 25 and 36 months of follow-up (Barbaro 2018). As the definitions in these studies did not match our definition of the Engel Class Scale, but these definitions do measure seizure freedom, we deemed these three studies to report a satisfactory 'other' scale.

Four of the 182 included studies (255 participants) did not report an outcome scale that we deemed satisfactory for measuring seizure freedom; three studies defined a good outcome as Engel Classes 1 and 2 and a poor outcome as Engel Classes 3 and 4 (Krsek 2013; Kwan 2010; Ure 2009), and one study defined a good 'other' outcome as 'seizure free or rare seizures' and a poor outcome as 'less than 80% reduction in seizures' (Kuzniecky 1993). We did not include these four studies in the meta-analysis (see Effects of interventions).

Excluded studies

We excluded a total of 101 studies from the review. We excluded 30 studies with insufficient follow-up (in other words, follow-up was not defined, follow-up was less than a year, or an unknown proportion of participants were followed up for less than a year) (Acar 2008; Alpherts 2008; Binder 2009; Busch 2011; Chang 2007; Choi 2004b; Cohen-Gadol 2003; Colonnelli 2012; Coutin-Churchman 2012; D'Angelo 2006; da Costa-Neves 2012; Dulay 2006; Dulay 2009; Ferrari-Marinho 2012; Ferroli 2006; Freitag 2005; Ghacibeh 2009; Harvey 2008; Hellwig 2012; Helmstaedter 2004; Hu 2012; Junna 2013; Limbrick 2009; Ogiwara 2010; Roth 2011; Smyth 2007; Stefan 2004; Vachrajani 2012; Vadera 2012; Zupanc 2010). We excluded 23 studies with fewer than 30 participants (Bauer 2007; Bindu 2018; Bourgeois 2007; Caicoya 2007; Cukiert 2009; Danielsson 2009; Datta 2009; Engel Jr 2012; Haegelen 2013; Lee 2010; Lodenkemper 2007; Mikati 2004; Moien-Afshari 2009; Negishi 2011; Nikase 2007; Placantonakis 2010; Rocamora 2009; Sakuta 2005; Soeder 2009; Teutonico

2008; Upchurch 2010; Wetjen 2009; Yasuda 2010b). We excluded 24 studies that did not report any seizure outcome data (Alemany-Rosales 2011; Andersson-Roswall 2010; Baxendale 2005; Bell 2010; Carne 2004; D'Argenzio 2011; Elsharkawy 2009b; Fauser 2008; Griffin 2007; Hervas-Navidad 2002; Hildebrandt 2005; Lutz 2004; McClelland 2007; McClelland 2011; Oertel 2004; Park 2010; Schatlo 2015; Stavem 2005; Stavem 2008; Tong 2015; Vogt 2016; Wang 2016; Wetjen 2006; Yasuda 2010a). We excluded eight studies in which the inclusion criteria were based on seizure outcome (i.e. only participants with postoperative seizures or who were seizure-free were included) (Boshuisen 2012; Buckingham 2010; Elsharkawy 2011b; Jehi 2010; Lach 2010; Schwartz 2006; Stefan 2008; Vadlamudi 2004). We excluded eight duplicate studies and retained the primary reference in the review (Boesebeck 2002; Cascino 1996; Elsharkawy 2008b; Helmstaedter 2011; Kuzniecky 1996; Lachhwani 2003; Malla 1998; Weinand 2001). We found no papers from the same institutions reporting different factors (all reported either the same factors or factors outside the scope of our review). Characteristics of excluded studies tables present the relevant details. We excluded three studies in which fewer than 90% of participants had an MRI (Mohammed 2012; Wieser 2003a; Wieser 2003b), we excluded three studies which did not randomise surgical interventions (CTRI/2018/07/015007; NCT03643016; NCT03790280) and we excluded two studies that were not studies of surgery for epilepsy (one was a study of surgery for tumours (Grunert 2003), and the other was a study of the outcome of taking antiepileptic drugs after epilepsy surgery (Asadi-Pooya 2008)).

Risk of bias in included studies

As most of the studies in this review were not of a randomised design, we believe it would not be appropriate to judge the quality of each study on criteria of selection bias, performance and detection bias, attrition bias, and reporting bias. Instead, we employed the Effective Public Health Practice Project (EPHPP) tool, which is appropriate for the study designs included in this review (mostly retrospective case series). See Appendix 5 for the full tool, Table 2 for quality assessments for each study for each criterion of the tool (A to F) and an overall grading of quality for each study, and Table 3 for a summary of all components of the tool (A to G). We also note that the EPHPP tool is a tool for quality assessment rather than risk of bias, so we refer to 'quality assessment of included studies' throughout this section.

A. Selection bias

We judged that 129 of 182 studies (71%) recruited a sample of individuals that was 'very likely' to be representative of the target population. We made this judgement if the participants recruited were 'consecutive', or if all eligible participants undergoing surgery over a specific period of time were included. We also checked how reasonable inclusion criteria, exclusion criteria, and participant demographics in the study were for recruiting a sample very likely to be representative of the target population.

We judged that the remaining 53 studies (29%) recruited samples of individuals that were 'somewhat likely' to be representative of the target population. We made this judgement if participants were not consecutive, or if apparently eligible participants had been excluded. We also made this judgement if we were uncertain about where participants had been recruited from, if we were uncertain regarding inclusion or exclusion criteria, if we judged that inclusion and exclusion criteria were too specific or restrictive to recruit a sample representative of the target population (e.g. all participants had a very specific pathology for inclusion), or if we judged that the demographics of recruited participants were not representative of the target population.

We judged that if the sample recruited was based in any way on outcome (e.g. included only individuals with recurrence of seizures), then the study had recruited a sample of individuals 'not likely' to be representative of the target population. Such a study design met the exclusion criteria for this review (see Excluded studies). Therefore we judged all included studies in the review to have a sample of individuals 'very likely' or 'somewhat likely' to be representative of the target population.

For the 144 studies of a retrospective design, we were unable to judge the percentage of participants who agreed to take part in the study. Nine studies of a prospective design reported the percentage of eligible participants who agreed to take part in the study as 80% to 100% and one study reported that less than 60% of eligible participants had agreed to take part. For the remaining 28 studies, we could not tell how many participants agreed to take part in the study.

Overall we judged that 118 studies (65%) were of 'strong' quality in their selection criteria (i.e. the sample selected was very likely to be representative of the target population and the study was of a retrospective design, or 80% to 100% of participants agreed to take part for studies of a prospective design). We judged the remaining 64 studies (35%) to be of 'moderate' quality in their selection criteria (i.e. the sample selected was somewhat likely to be representative of the target population or the sample selected was very likely to be representative of the target population, but a large number of eligible participants had declined to participate in the study or we could not tell how many eligible participants had agreed to participate in the study).

B. Study design

Most of the included studies (144 of 182 studies; 79%) were of the design of a retrospective review of the clinical notes of a number of participants meeting specific inclusion criteria at a given centre over a specified time period (e.g. a clinical audit). We refer to this design in Table 2, in Table 3, and throughout this review as a 'retrospective case series' (one group before and after intervention), and we considered this design to be of 'moderate' quality as it is not

specifically referred to in the EPHPP tool. We made the judgement to avoid the design of the study alone dictating the overall quality rating (i.e. all retrospective designs are weak) to separate out the 144 retrospective studies based on other quality criteria.

We included nine studies of a randomised controlled design - a design judged by the EPHPP tool to be strong (Alonso-Vanegas 2018; Barbaro 2018; Ding 2016; Dwivedi 2017; Liang 2010; Schramm 2011; Vogt 2018; Wiebe 2001; Wyler 1995; see Included studies for additional details). We also used the Cochrane 'Risk of bias' tool for these six studies (Higgins 2011); see Table 4 for more information on the 'Risk of bias' criteria for these six studies. We preferred to present quality assessment data in Additional tables rather than in 'Risk of bias' tables in Characteristics of included studies, as the domains considered in these tables are not appropriate for most of the included studies.

Table 4 shows that only four of the nine RCTs described an adequate method of randomisation; Alonso-Vanegas 2018; Dwivedi 2017; Schramm 2011 and Vogt 2018 randomised participants by using a computer-generated randomisation list. Researchers described three studies as randomised but provided no details about the method used to generate the random list (Barbaro 2018; Wiebe 2001; Wyler 1995). Two studies described an inadequate method of quasi-randomisation (no allocation concealment in quasi-randomised studies); we judged these studies to be at high risk of bias (Ding 2016; Liang 2010). Three studies did not provide any information on concealment of treatment allocation (Alonso-Vanegas 2018; Barbaro 2018; Wyler 1995), and three studies described adequate methods of allocation concealment: sealed, opaque, and sequentially numbered envelopes prepared outside the treatment centre (Dwivedi 2017; Schramm 2011; Vogt 2018; Wiebe 2001). Three studies did not provide any information on blinding of participants, personnel, and outcome assessors (Ding 2016; Liang 2010; Vogt 2018); and for two studies that randomised participants to surgical or medical treatment, blinding was not possible by design (Dwivedi 2017; Wiebe 2001). One of these studies reported that outcome assessors were blinded (Dwivedi 2017), and for the other study, it is unclear if outcomes were affected by this design (Wiebe 2001). Two studies reported blinding of participants and outcome assessors, with only the surgeon remaining unblinded to allocation of treatment (Schramm 2011; Wyler 1995), one study reported that outcome assessors only were blinded (Barbaro 2018) and one study reported that there was no blinding (Alonso-Vanegas 2018). Five studies reported that no losses to follow-up occurred and/or included all randomised participants in the analysis (Alonso-Vanegas 2018; Barbaro 2018; Liang 2010; Schramm 2011; Wyler 1995). Three studies reported complete attrition rates and followed an intention-to-treat approach (Ding 2016; Dwivedi 2017; Wiebe 2001), so we judged these studies to be at low risk of attrition bias. One study reported excluded 13% of randomised participants from analysis who did not complete neuropsychological assessments at one year (Vogt 2018); this is not an intention-to-treat approach so we judged this study to be at high risk of attrition bias A protocol available as an online supplement for one study reported all pre-specified outcomes (Dwivedi 2017). We did not have access to study protocols for comparison of outcomes defined a priori for the remaining eight studies, but all eight studies reported outcomes defined well in the methods section and consistently in the results section, so we judged all of the studies to be at low risk of reporting bias. We detected no other biases in any studies.

Two studies described a randomised design: Oertel 2005 randomised participants to waterjet dissection or ultrasonic aspirator during surgery, and Velasco 2011 randomised participants to presurgical evaluation with or without SPECT. As neither of these designs randomised the intervention, for the purposes of this review, we refer to these designs as 'cohort analytic' (two groups before and after intervention), and we considered this design to be of 'strong' quality according to the EPHPP tool.

We considered the remaining 27 studies (15 of a prospective design, three of a combination design, and nine with the method of identification of participants not stated) to be of a 'cohort' design (one group before and after intervention), and this design is considered to be of 'moderate' quality according to the EPHPP tool. Therefore, we judged that 11 of 182 studies (6%) used a 'strong' design, and 171 of 182 (94%) used a 'moderate' design.

C. Confounders

Given that the aim of our review was to identify prognostic factors associated with the outcome of surgery (essentially factors that confound the results of surgery), it was difficult to make a judgement on the presence of confounders. Therefore we did not class any of the pre-operative prognostic factors of interest in our review as confounders (see Data extraction and management). Furthermore, most studies (171 of 182 studies; 94%) were of a design that followed up one group of participants before and after the intervention (retrospectively or prospectively), rather than two groups that may differ in terms of demographics, so by this single-sample design, we deemed it more appropriate to judge the methods of selection of the sample (see "A. Selection bias") than to assess 'confounders'. For this reason, we judged these 171 studies to be of 'strong' quality, in the absence of confounding variables.

For the nine studies of a randomised controlled design (Alonso-Vanegas 2018; Barbaro 2018; Ding 2016; Dwivedi 2017; Liang 2010; Schramm 2011; Vogt 2018; Wiebe 2001; Wyler 1995), as well as the two studies of a cohort analytic design (Oertel 2005; Velasco 2011), with two groups before and after intervention (randomised and non-randomised, respectively), we made a judgement regarding potential confounding factors (other than prognostic factors) in the two groups. Ten of these studies presented demographics for the two participant groups and/or tested whether any significant differences were present between the groups (Alonso-Vanegas 2018; Barbaro 2018; Ding 2016; Dwivedi 2017; Liang 2010; Schramm 2011; Velasco 2011; Vogt

2018; Wiebe 2001; Wyler 1995). We found no significant differences in any of these studies; therefore we judged that groups were balanced and there was no evidence of confounders. One study reported very limited information on the demographics of the two groups, and it did not appear that the groups had been compared for differences that may have influenced the results of analysis (Oertel 2005); for this study, we could not tell if any confounders were present, or if any adjustments had been made to the analysis to account for confounders.

Therefore we judged that for 181 studies (99%), the quality of evidence was 'strong' (i.e. no confounders that may have influenced the results of analysis were present). For one study of a cohort analytic design (1% of total studies), the quality of evidence was 'moderate' (i.e. we were unable to judge whether any confounders that may have influenced the analysis were present) (Oertel 2005).

D. Blinding

In the context of surgical treatment, blinding is very difficult, as the operating surgeon is required to know the procedure being carried out and the participant will be aware that he/she is undergoing surgery. It may be possible, however, to blind participants and outcome assessors (other than the surgeon) to the specific surgical procedure being carried out, and researchers often blinded outcome assessors to pre-operative evaluation details while making judgements regarding outcomes following surgery. We believe that in the context of surgical treatment, where blinding usually is not feasible, study outcomes would not necessarily be influenced by this. However, for the purposes of this quality assessment, we followed the criteria specified by the EPHPP tool related to blinding of the intervention.

Question 2 of the EPHPP tool for the blinding component (see Appendix 5) is stated as follows: "Were the study participants aware of the research question?" We interpreted this to mean 'Were the study participants aware of the intervention allocated?' as we believe that awareness of the research question is not the same as blinding to allocation of the intervention, and it would be impossible to determine awareness of participants of a research question in a study of retrospective design.

For 176 of 182 studies (97%), we judged that outcome assessors and participants were aware of the intervention, and that these studies provided evidence of 'weak' quality due to high risk of bias from lack of blinding. The remaining six studies were randomised controlled trials. Four studies (2%) blinded participants (if possible), and all studies blinded outcome assessors; we considered these studies to provide evidence of 'strong' quality (Barbaro 2018; Dwivedi 2017; Schramm 2011; Wyler 1995). Two studies (1%) did not provide any information on blinding of participants or outcome assessors, so we judged this study to provide evidence of 'moderate' quality (Liang 2010; Vogt 2018).

E. Data collection methods

Our outcome of interest in this review was seizure freedom following surgery; therefore the data required for the outcome would include details of recurrence of participant seizures after surgery. Given that such data are recorded from participant reports, which may be prone to recall error, and that no validated tools (e.g. quality of life assessment tools) are available to record such data, for each study, given the information reported on outcome data collection, we made a judgement on whether methods used were adequate and reliable.

Overall, we accepted any method of seizure data collection that seemed reasonable (participant seizure diaries, clinical notes, interviews with participants and/or family members at clinic visits or over the phone, postoperative MRI or EEG) to be valid. We judged all these methods to be 'reliable', given that all methods are likely prone to error, as the outcome is somewhat subjective. Ninety-five of 182 studies (52%) reported a 'valid and reliable' data collection method, and we judged these studies to provide evidence of 'strong' quality.

The remaining 87 studies (48%) either did not provide any information at all on data collection methods or did not provide sufficiently clear information on data collection methods for us to judge whether they were valid and/or reliable. We judged these studies to provide evidence of 'weak' quality.

F. Withdrawals and dropouts

This criterion was not applicable to the 144 studies (79%) of a retrospective design. For the remaining 35 studies, we made a judgement on whether study authors adequately reported withdrawal information.

Seventeen studies (9%), all of a prospective design, reported the numbers of withdrawals/losses to follow-up in the study with reasons when applicable; at least 80% of participants in all 17 studies completed the study, and less than 20% withdrew from the study. We judged these studies to provide evidence of 'strong' quality (8% of total studies). The remaining 21 studies (nine of a prospective design, three of a combination design, and nine with design not stated) provided no information regarding participant withdrawal nor losses to follow-up; therefore we could not tell how many participants completed the study. We judged these studies to provide evidence of 'weak' quality (12% of total studies).

G. Intervention integrity

In the context of a surgical intervention, we judged that it was 'highly unlikely' that any participant received an unintended intervention. Within all 182 included studies, 80% to 100% of included participants received the surgical intervention. Several studies (particularly those aiming to identify criteria in presurgical evaluation that may be associated with outcome) specified the numbers of participants who underwent presurgical evaluation

and were not recommended for surgical intervention; however this proportion of participants was less than 20% for all studies, and we included in the results of this review only participants who underwent surgery.

We judged that researchers had measured 'consistency' of the intervention if a study reported at least details of all surgical techniques used for all participants; it was not necessary for the surgical intervention to be exactly the same for all participants in a study for the intervention to be considered consistent, as many participants required tailored resections based on pathology or aetiology of seizures. We also considered the intervention to be 'consistent' if investigators used the same surgical technique for all participants or used the same surgical protocol or if the same surgeon(s) performed all surgeries, and if any study authors reported specific differences in surgical technique. We judged that researchers had not measured the 'consistency' of the intervention if the details of surgical techniques were not reported or were not reported for all participants, or if the types of interventions performed were unclear. We judged that the intervention was 'consistent' for 164 studies (90%) and was 'inconsistent' for 18 studies (10%).

H. Analyses

All 182 studies included individual units of allocation and analysis by design; in other words, all studies performed a surgical intervention on each individual and analysed each individual for the seizure outcome. We identified no studies of a cluster (randomised) design for this review. We judged that all studies performed analysis by intervention allocation status (intention-to-treat) rather than by the actual intervention received; for studies of a retrospective design, it was difficult to discern whether a different type of surgical intervention had been 'allocated', as the only information provided by a retrospective study is the intervention received. We judged that all studies of a prospective or combination design had taken an intention-to-treat approach to analysis.

Of 182 studies, 159 (87%) performed statistical analysis, and the remaining 23 studies (13%) reported only observational results without performing analysis. The statistical author of this review (SN) judged that all statistical analyses performed in the 156 studies were appropriate for the study design.

Overall rating

The global quality rating is based on components A to F of the EPHPP tool. We judged a study that had no components judged as 'weak' was 'strong' overall, a study with one 'weak' component was 'moderate' overall, and a study that had two or more 'weak' components was 'weak' overall.

We judged the global quality rating to be 'strong' for five studies (3% of total studies; all randomised controlled trials; Dwivedi 2017; Liang 2010; Wyler 1995), 'moderate' for 79 studies (43% of total studies), and 'weak' for 98 studies (54% of total studies).

Adequacy of EPHPP quality assessment tool

Based on the work of Tonini 2004 related to this review, we knew that most studies identified via searches for this review were likely to be of a non-randomised and retrospective design. At the initiation of the protocol for this review in 2012, a 'Risk of bias' tool for assessment of randomised controlled trials had been developed and was recommended by the *Cochrane Handbook for Systematic Reviews of Interventions* (Chapter 8, Higgins 2011); however we were not aware of a specific tool for assessment of studies of a non-randomised and/or retrospective design as recommended by the *Cochrane Handbook for Systematic Reviews of Interventions* (Chapter 13, Higgins 2011). Therefore two review authors (SN and JW) with methodological experience in quality assessment reviewed the existing literature at this time for a quality assessment tool and judged that the EPHPP tool, intended for the quality assessment of all study designs including non-randomised and retrospective, would be the most appropriate tool to use for this review.

Given that the tool was used by five authors of the 182 included studies, we now believe that this tool has not provided a fully accurate assessment of the quality of included studies. It is assumed that a randomised controlled trial provides evidence of the highest quality for the efficacy of an intervention (Mann 1996); 79% of the studies included in this review were of a retrospective, single-group design, which could be considered as providing evidence of the poorest quality in the hierarchy of evidence about an intervention. Therefore we needed a tool to separate the different levels of 'poor' evidence, and the EPHPP tool did not do this.

Despite the described applicability of this tool to all quantitative study designs, many criteria are not appropriate for studies of a retrospective design (e.g. withdrawals from the study, proportion of participants agreeing to take part in the study) nor for studies of a single-group design (confounders). Also in the context of surgical studies for epilepsy, where blinding of participants and outcome assessors is often impossible and only objective, non-validated methods for collection of seizure outcome data exist, the global quality rating of the study was influenced by two components (D and E) for most studies. Only five of the RCTs included in this review attempted blinding; therefore we automatically assigned the judgement for 175 of 182 studies (97%) as 'weak' according to the definition provided in the tool. On the basis of global rating, this meant that we could judge 97% at the most to be of 'moderate' quality due to lack of blinding alone. Then the difference between a 'moderate' and a 'weak' global rating was dictated by component E ('strong' or 'weak'). Essentially, the global rating reflects the quality of data collection methods rather than overall quality.

Furthermore, for the component "B. Study design", we made an assumption that the study design of 144 'retrospective case series' (one group before and after intervention) not specifically referred to in the EPHPP tool was of 'moderate' quality - the same quality assigned to a prospective cohort study. We made this judgement to avoid the design of the study alone dictating the overall quality

rating (i.e. all retrospective designs are 'weak') to separate out the 144 studies based on other quality criteria. If instead, more fitting with National Institute for Health and Care Excellence (NICE) guidelines (Mann 1996), we had assumed all retrospective designs to be of 'weak' quality, the global rating would have been as follows: 'strong': five studies; 'moderate': six studies; and 'weak': 171 studies. Such ratings would not have provided us with any useful information regarding the relative quality of included studies.

In hindsight, given the context of surgery for epilepsy and our prior knowledge of the likely design of included studies based on the Tonini 2004 review, it would have been more appropriate for us to design our own quality assessment tool for the review based on what we know to be clinically important in studies of surgical interventions. Given our lack of confidence in the global ratings assigned to included studies by the EPHPP tool, we believe it would be inappropriate to conduct sensitivity analyses based on the global quality assessments (see Effects of interventions for subgroup and sensitivity analyses performed).

Assessment of risk of bias in studies reporting multivariable prognostic models according to the Quality in Prognostic Studies (QUIPS) tool

Twenty-eight studies reported a multi-variable prognostic model including one or more of the factors of interest to us (Althausen 2013; Boesebeck 2007; Cossu 2005; Cossu 2008; Elsharkawy 2008a; Elsharkawy 2009a; Gelinas 2011; Janszky 2003a; Jennum 1993; Kim 2009; Kim 2010a; Lopez-Gonzalez 2012; Madhavan 2007; McIntosh 2012; O'Brien 2000; Paolicchi 2000; Phi 2009; Radhakrishnan 1998; Rossi 1994; Sagher 2012; Sarkis 2012; Schramm 2011; Spencer 2005; Tezer 2008; Theodore 2012; Walz 2003; Wyler 1995; Yang 2011) (see "Multi-variable analyses" in Effects of interventions below for additional details of these results and reported results).

The QUIPS tool considers six domains (see Table 5 for judgements for each domain for each study).

1. Study participation: judge risk of selection bias (likelihood that the relationship between prognostic factor (PF) and outcome is different for participants and eligible non-participants)

We judged 11 of 28 studies to be at 'low' risk of selection bias; the population of interest and the method of sample recruitment are well described and the samples seem to match the characteristics of the source population. We judged 15 of the 28 studies to be at 'moderate' risk of selection bias due to uncertainties or limited information regarding the population of interest or the method of sample recruitment, or both, to enable judgement on whether the sample matched the source population. We judged two studies to be at 'high' risk of selection bias: one due to a selective sample that is unlikely to represent the source population (Janszky 2003a), and one due to very limited information regarding the population of interest, the method of sample recruitment, and the characteristics of the sample (Rossi 1994).

2. Study attrition: judge risk of attrition bias (likelihood that the relationship between PF and outcome is different for completing and non-completing participants)

Twenty-two of the 28 studies were of a retrospective design, so this domain was not applicable. Six studies were of a prospective design. We judged that two of these studies were at 'low' risk of attrition bias, as intention-to-treat analyses were planned in the case of withdrawals or losses to follow-up, so all participants contributed to outcome assessment (Schramm 2011; Wyler 1995). We judged three to be at 'moderate' risk of attrition bias due to lack of information reported about withdrawals and losses to follow-up (Spencer 2005; Theodore 2012; Walz 2003), and one study to be at 'high' risk of attrition bias due to exclusion of participants with missing data and uncertainty over whether participants were recruited prospectively or retrospectively (Radhakrishnan 1998).

3. Prognostic factor measurement: judge risk of measurement bias related to how PF was measured (differential measurement of PF related to level of outcome)

We judged 22 of the 28 studies to be at 'moderate' risk of measurement bias due to unclear definitions of prognostic factors and limited information regarding how data were collected. Four studies judged to be at 'low' risk of measurement bias provided detailed definitions of prognostic factors and methods of measurement and data collection (Cossu 2008; McIntosh 2012; Sagher 2012; Sarkis 2012). We judged two studies to be at 'high' risk of measurement bias; in one multi-centre study, it is likely that researchers collected data using different methods across centres (Madhavan 2007), and in the other study, a large proportion of prognostic factor data was missing, which is likely to have had an impact on analyses (Rossi 1994).

4. Outcome measurement: judge risk of bias related to measurement of outcome (differential measurement of outcome related to baseline level of PF)

Recurrence of seizures in outpatients is generally patient-reported and therefore difficult to measure in a valid and reliable way; validated scales such as the Engel Class Scale as described above exist for assessment of post-surgical outcome.

We judged 18 of 28 studies to be at 'moderate' risk of bias; it is unclear exactly how and/or when outcome data had been collected and/or how outcome was defined. We judged two studies to be at 'high' risk of bias: in Althausen 2013, researchers measured outcome in variable ways (taken only from patient reports for some participants, and using supplementary data from medical records for other participants); Kim 2009 did not measure the

outcome according to a known scale such as the Engel Class Scale and provided no information on when study authors recorded outcome. We judged the remaining eight studies to be at 'low' risk of bias: investigators reported clear information about how they collected outcome data; they measured outcome according to a known scale such as the Engel Class Scale; and they recorded this information at the same time for all participants.

5. Study confounding: judge risk of bias due to confounding (i.e. the effect of PF is distorted by another factor that is related to PF and outcome)

Twenty of the 28 studies were of a single-group design, so this domain was not applicable. We judged one RCT, Wyler 1995, to be at 'low' risk of bias due to confounding, as the randomised design should remove confounding and it is confirmed in the study that groups were balanced at baseline. We judged seven studies to be at 'moderate' risk of bias of confounding: one study of an RCT design did not demonstrate whether groups were balanced at baseline and which variables of interest were prognostic factors and which were confounders (Schramm 2011); another study made reference to confounders and interactions in a generalised estimating equations model but did not specify which variables of interest were prognostic factors and which were confounders (Sagher 2012); and the remaining five studies made reference to "confounders" but did not adequately define the variables and/or did not specify which variables of interest were prognostic factors and which were confounders (Althausen 2013; Cossu 2008; Elsharkawy 2008a; Gelinas 2011; Janszky 2003a).

6. Statistical analysis and reporting: judge risk of bias related to statistical analysis and presentation of results

We judged only one study to be at 'low' risk of bias because researchers described statistical analysis well, performed modelling based on clinical relevance, and did not selectively report results (O'Brien 2000). We judged the other 27 studies to be at 'moderate' or 'high' risk of bias (13 'moderate' and 14 'high') due to use of unclear or inappropriate statistical methods, selection of variables based on statistical significance, and selective reporting of results. We have further discussed these issues and their likely impact on the analyses under "Multi-variable analyses" in Effects of interventions (below).

Overall, we judged one study to be at 'high' risk of bias in three domains (Rossi 1994), three studies to be at 'high' risk of bias in two domains (Althausen 2013; Janszky 2003a; Madhavan 2007), and 11 studies to be at 'high' risk of bias in one domain (Cossu 2008; Elsharkawy 2008a; Elsharkawy 2009a; Jennum 1993; Kim 2009; Paolicchi 2000; Radhakrishnan 1998; Sarkis 2012; Spencer 2005; Tezer 2008; Theodore 2012). The remaining 13 studies were not judged to be at 'high' risk of bias in any domain (Boesebeck 2007; Cossu 2005; Gelinas 2011; Kim 2010a; Lopez-Gonzalez 2012; McIntosh 2012; O'Brien 2000; Phi 2009; Sagher 2012; Schramm 2011; Walz 2003; Wyler 1995; Yang 2011).

Effects of interventions

See: **Summary of findings for the main comparison**; **Summary of findings 2**

Overall outcome of surgery compared to medical treatment

Two studies randomised participants to a surgical or control (medical) intervention (Dwivedi 2017; Wiebe 2001).

Dwivedi 2017 randomised 116 participants aged 18 years or younger to receive either appropriate brain surgery or continuing medical therapy.

All 57 allocated to the surgical intervention completed 12-month follow-up. One of the 59 allocated to continuing medical treatment was lost to follow-up. Researchers used an intention-to-treat approach to analysis and analysed all randomised participants in the allocated groups, regardless of the intervention received. Serious adverse events occurred in 19 participants (33%) in the surgery group and in none in the medical therapy group. These events included monoparesis in two participants (following temporal lobectomy or resection of parietal focal cortical dysplasia); hemiparesis in 15 (following hemispherotomy); and generalized hypotonia and language deficits in one (following frontal lobectomy). Study authors provided details on outcome at 12-month follow-up. None of these events appears to have been transient.

Wiebe 2001 randomised 40 participants to each intervention group and followed them up for 12 months for assessment of outcome.

Four participants allocated to the surgery group did not undergo surgical intervention (one declined surgery, two were deemed not eligible for surgery based on pre-operative testing, and one did not have seizures during pre-operative testing). Researchers took an intention-to-treat approach to analysis and analysed all randomised participants in the allocated groups, regardless of the intervention received.

Four participants experienced adverse events from surgery: one had a small thalamic infarct causing sensory abnormalities in the thigh, one had a wound infection, and two had decline in verbal memory that interfered with their occupations at one year. In addition, 22 participants in the surgery group experienced asymptomatic, superior sub-quadrantic visual field defects; seven experienced depression; and one developed transient psychosis. The only adverse event reported in the medical treatment group was depression (eight participants).

Primary outcome: seizure outcome

(See also Summary of findings for the main comparison.)

At one year, in Wiebe 2001, 23 of 40 (58%) participants in the surgery group were free from seizures impairing awareness compared to 3 of 40 (8%) in the medical treatment group (risk ratio (RR) 7.67, 95% confidence interval (CI) 2.50 to 23.51; P = 0.0004; Analysis 1.1), and in Dwivedi 2017, 44 of 57 (77%) participants in the surgery group were free from seizures (ILAE Class 1) compared to 4 of 59 (7%) in the medical treatment group (RR 11.33, 95% CI 4.37 to 29.64; P < 0.00001; Analysis 1.1). Pooling of data from the two studies showed that the RR of seizure freedom in the surgery group compared to the medical group was 9.78 (95% CI 4.73 to 20.21; P < 0.00001; Analysis 1.1; low-certainty evidence). No heterogeneity was present between studies (I^2 = 0%).

Also at one year in Wiebe 2001, 15 of 40 (38%) participants in the surgery group were free from all seizures including auras compared to 1 of 40 (3%) in the medical treatment group (RR 15.00, 95% CI 2.08 to 108.23; P = 0.007; Analysis 1.2; very low-certainty evidence). The median percentage improvement in monthly seizure frequency impairing awareness was 100% in the surgery group compared to 34% in the medical treatment group.

Secondary outcome: seizure outcome according to prognostic factors of interest

Neither Dwivedi 2017 nor Wiebe 2001 reported any univariate or multi-variable analyses that investigated the influence of any prognostic factors on the seizure outcome (including prognostic factors of interest to us).

Overall outcome according to surgical techniques

Six studies randomised the type of surgical intervention (Alonso-Vanegas 2018; Barbaro 2018; Ding 2016; Liang 2010; Vogt 2018; Wyler 1995) and one trial randomised the length of surgical intervention (Schramm 2011).

One study randomised 43 adult participants to anterior temporal lobectomy (ATL), selective amygdalohippocampectomy (SAH) or parahippocampectomy (PHC) (Alonso-Vanegas 2018). No participants died and in the PHC group, one participant had venous thrombosis of the arm, which resolved, in the ATL group, two participants developed mastoiditis, one had a transient oculomotor nerve palsy, and one presented with an internal cerebral spinal fluid fistula and in the SAH group, one participant developed acute transient hypoacusia. Participants in the PHC group did not have any postoperative visual field deficits whereas the outcome in the ATL and SAH groups was 85.7% and 46.7%, respectively, which was statistically significant (P <0.001).

One study randomised 63 adult participants who had been recommended for ATL to stereotactic radiosurgery (SRS) or ATL (Barbaro 2018). Five participants withdrew before surgery and were not included in analysis. Two participants withdrew from the study, one in each group. The participant in the SRS group withdrew early for ATL due to continued focal seizures and participant in the ATL group was lost to follow-up. There were 14 adverse events definitely related to treatment (5 serious and 9 non-serious) in 12 (39%) SRS patients and 5 events (2 serious and 3 non-serious) in 3 (11%) ATL patients. Events were cerebral edema, new neurological deficit, seizure exacerbation, pin-site infection, subdural hematoma, deep venous thrombosis, wound dehiscence and infection and psychiatric, with no overlap across treatment groups. Twenty SRS participants (65%) and seven (26%) ATL participants were treated with steroids during follow-up, there were no complications relating to steroids. 49 out of 54 participants (91%) who completed visual field defect testing experienced some visual field defects; 27 (93%) participants in the SRS group and 22 (88%) participants in the ATL group.

One study enrolled 68 children with Lennox-Gastaut syndrome who had no focal lesion on brain MRI, 25 of whom were in a continuing medical treatment group and 43 of whom underwent surgery (Ding 2016). This group allocation was not randomised. Within the surgery group, 20 had exclusively resective surgery and 23 had resective surgery combined with corpus callosotomy. Researchers randomised children to either of these two surgical subgroups and followed up on all children for three to five years. No postoperative death or permanent complications occurred. Investigators encountered transient complications in four participants, including two with urinary incontinence, one of whom had hemiplegia; one with aphasia; and one with apraxia. All transient complications resolved within three weeks.

One study randomised participants to anterior temporal lobectomy with or without anterior corpus callosotomy (ATL vs aCCT) (Liang 2010). Researchers randomised 30 participants to each group and followed them up for two years for assessment of outcome. Study authors reported transient complications of surgery in nine participants in total. The aCCT group included two cases of urinary incontinence, one case of aphasia, and two cases of apraxia. The ATL group comprised two cases of aphasia and two cases of apraxia.

One study randomised 54 adult participants who had been recommended for SAH to a subtemporal or transsylvian approach to surgery (Vogt 2018). Seven participants who did not complete neuropsychological follow-up at 12 months were excluded. One year after surgery, there were no permanent neurological deficit except for visual field defects; three participants in the transsylvian group showed no visual field defects compared to 11 participants in the subtemporal group. Severe deterioration of memory functions was shown in three participants in the subtemporal group and one participant in the transsylvian group. Postoperative MRIs of six participants showed vascular events (infarctions in four participants in the transsylvian group and transient postsurgical aphasia in one participant in each group).

One study randomised 34 participants to partial hippocampectomy (removal of hippocampus en bloc to the anterior margin of the cerebral peduncle) and 36 to total hippocampectomy (removal of hippocampus en bloc to the level of the colliculi) and followed

up participants for 12 months for assessment of outcome (Wyler 1995). Study authors reported complications in five participants: two participants with partial hippocampectomy (one subgaleal cerebrospinal fluid fistula and one temporary diplopia) and three participants with total hippocampectomy (one temporary nerve paresis and two cerebrospinal fluid subgaleal fistula).

One study randomised participants to a 2.5-cm or 3.5-cm tailored temporal lobe resection (i.e. intended minimum resection length of 25 vs 35 mm for hippocampus and parahippocampus) (Schramm 2011). Researchers randomised 104 participants to 2.5-cm resection and 103 to 3.5-cm resection and followed them up for 12 months for assessment of outcome. Results show no significant differences between 2.5-cm and 3.5-cm resection groups concerning neurological complications (P < 0.605), visual field defects (P < 0.856), or surgical complications (P < 0.875). Study authors provided no details of surgical complications.

Primary outcome: seizure outcome

(See also Summary of findings 2.)

In Alonso-Vanegas 2018, at one year, 11 out of 14 (79%) participants in the parahippocampectomy (PHC) group, 13 out of 14 (93%) in the anterior temporal lobectomy (ATL) group and 14 of 15 (93%) in the selective amygdalohippocampectomy (SAH) group had a good outcome according to Engel Class Scale 1 and 6 out of 14 (43%) participants in the PHC group, 10 out of 14 (71%) in the ATL group and 9 of 15 (60%) in the SAH group were seizure free according to Engel Class Scale 1A.

At 5 years, 50%, 64% and 67% of participants in the PHC, ATL and SAH groups respectively were seizure free according to Engel Class Scale 1 and 29%, 50% and 53% of participants in the PHC, ATL and SAH groups respectively were seizure free according to Engel Class Scale 1A. There were no statistically significant differences between any of the pairs of treatments at 1 year or at 5 years, or according to either definition of the Engel Class Scale (low-certainty evidence, Analysis 2.1, Analysis 2.2, Analysis 2.3).

In Barbaro 2018, between 25 and 36 months, 16 out of 31 (52%) participants in the stereotactic radiosurgery group achieved remission of seizures (at least Engel Class IB) which was statistically significantly less compared to 21 out of 27 (78%) participants in the ATL group (RR 0.66, 95% CI 0.45 to 0.99; P = 0.04; low-certainty evidence; Analysis 2.4).

In Ding 2016, at one year, 17 of 23 (74%) participants in the resection with CCT group were free from seizures (Engel Class 1) compared to 13 of 20 (65%) in the resection only group (RR 1.14, 95% CI 0.76 to 1.70; P = 0.53; low-certainty evidence; Analysis 2.5). The RR of seizure freedom for the resection with CCT group compared to the resection only group at three years was 1.19 (95% CI 0.72 to 1.95; P = 0.50; intention to treat approach; Analysis 2.5), and at five years was 1.09 (95% CI 0.53 to 2.21; P = 0.82; intention-to-treat approach; Analysis 2.5).

In Liang 2010, at two years, 18 of 30 (60%) participants in the ATL group were free from seizures (Engel Class 1) compared to 22 of 30 (73%) participants in the aCCT group (RR 1.22, 95% CI 0.85 to 1.76; P = 0.28; moderate-certainty evidence; Analysis 2.6).

In Vogt 2018, at 1 year, 13 out of 22 (59%) participants in the subtemporal SAH group were free from all seizures including auras (ILAE 1a) compared to 16 out of 25 (64%) participants in the transsylvian group (RR 0.92, 95% CI 0.59 to 1.46; P = 0.73; low-certainty evidence; Analysis 2.7).

In Wyler 1995, at one year, 25 of 36 (69%) participants in the total hippocampectomy group were free from all seizures including auras compared to 13 of 34 (32%) participants in the partial hippocampectomy group (RR 1.82, 95% CI 1.12 to 2.93; P = 0.01; low-certainty evidence; Analysis 2.8). Wyler 1995 also reported time to first seizure: seizure recurrence occurred earlier in the partial hippocampectomy group than in the total hippocampectomy group (at 1.3 vs 1.9 years, respectively).

In Schramm 2011, at one year, 77 of 104 (74%) participants in the 2.5-cm resection group were free from seizures (Engel Class 1) compared to 75 of 103 (73%) participants in the 3.5-cm resection group (RR 1.02, 95% CI 0.86 to 1.20; P = 0.84; moderate-certainty evidence; Analysis 2.9).

Secondary outcome: seizure outcome according to prognostic factors of interest

Ding 2016 reported univariate analyses contributing to 'MRI results', 'Presence of encephalomalacia', and 'Presence of focal cortical dysplasia (FCD)/malformation of cortical development (MCD)'.

Schramm 2011 reported univariate analyses contributing to 'Extent of resection', 'Presence of mesial temporal sclerosis (MTS)', and 'Side of surgical resection' (see below). Study authors presented results of these univariate analyses for all participants in the study who underwent a surgical procedure and did not report them separated by randomised group. They also reported a multivariable regression model of prognostic factors (see "Multi-variable analyses" below).

The randomised comparison in Wyler 1995 (partial vs total hippocampectomy) contributed to the univariate analysis of 'Extent of resection' (see Analysis 2.8 and "Extent of resection" below). Study authors also reported a multi-variable regression model of prognostic factors (see "Multi-variable analyses" below).

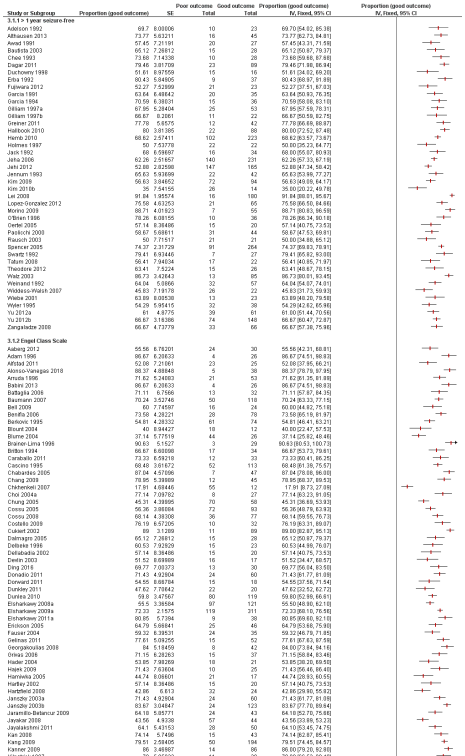
Alonso-Vanegas 2018, Barbaro 2018, Dwivedi 2017, Liang 2010, Vogt 2018, and Wiebe 2001 did not report any univariate or multivariable analyses that investigated the influence of any prognostic factors of interest to us for the seizure outcome.

Overall outcome of surgery according to all randomised and non-randomised evidence

Of 16,756 participants who underwent surgery for epilepsy included in the 182 studies, satisfactory seizure outcome data were

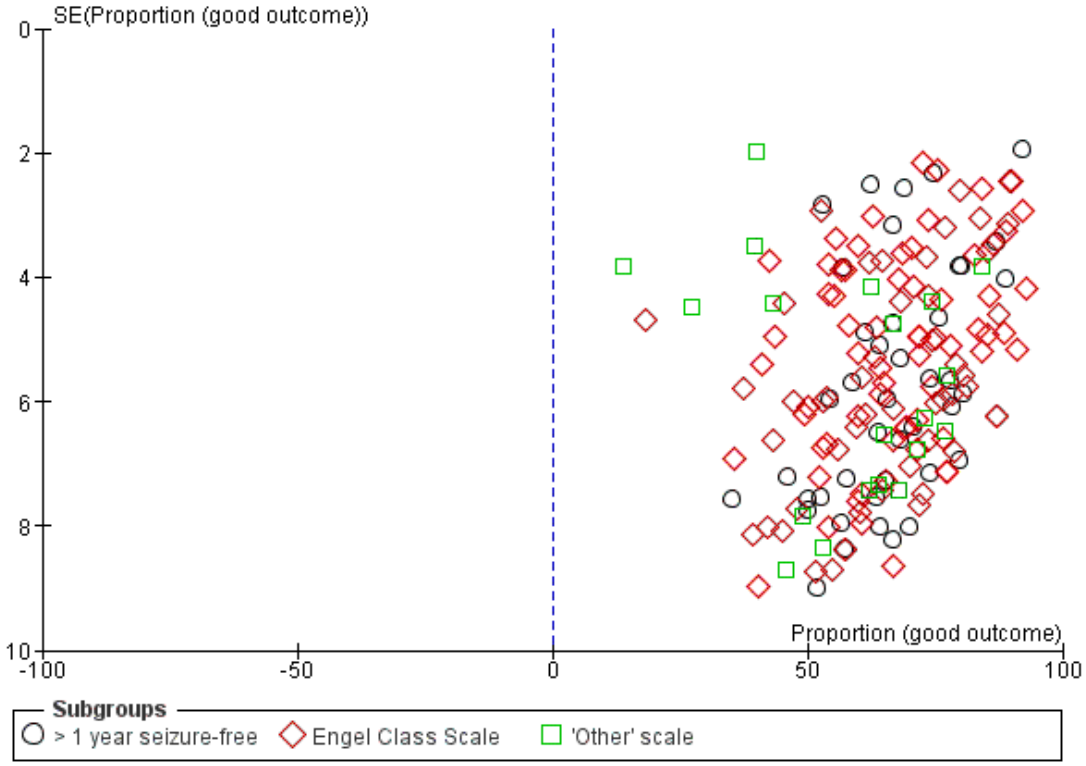
available for 16,501 from 178 studies. Among these 16,501 participants, 10,696 achieved a good outcome (65%), defined as Engel Class 1 - more than one year seizure-free - or a good outcome measured on another scale that satisfied our definition of a good outcome (see Primary outcomes and Included studies). Figure 3 shows the proportion of participants with a good outcome in each study (by outcome scale), ranging from 13.5% to 92.5% of participants with a good outcome. We note that Figure 3 is for illustrative purposes only, and the proportion of participants with a good outcome is not pooled in meta-analysis in Analysis 3.1 nor Figure 3.

Figure 3. Forest plot of comparison: 1 Surgery for Epilepsy, outcome: 1.1 Proportion with a good outcome of surgery.



See Figure 4 for the funnel plot of the outcome 'Proportion with a good outcome of surgery' for 178 included studies.

Figure 4. Funnel plot of comparison: 1 Surgery for epilepsy, outcome: 1.1 Proportion with a good outcome of surgery.



Further examination of overall post-surgery seizure outcome according to site of surgery (169 studies reported these data) revealed that 722 of 1253 participants from 14 studies in which participants underwent extratemporal lobe surgery achieved a good outcome of surgery (62%), 4558 of 6638 participants from 78 studies in which participants underwent temporal lobe surgery achieved a good outcome of surgery (69%), and 5016 of 7654 participants from 77 studies in which participants underwent temporal or extratemporal lobe surgery achieved a good outcome of surgery (66%). Data show a statistically significant association between site of surgery and outcome of surgery (Chi² test P < 0.001).

For 255 participants from four studies (1.5% of the total 16,756 participants undergoing surgery), we did not deem the seizure outcome scale to be satisfactory for the outcomes of this review, and we did not include these participants in any meta-analyses (see Primary outcomes and Included studies). Under the definition of 'good' outcome in these four studies, 142 of 255 (56%) participants achieved a 'good outcome'. We did not consider these four studies further in this review (Krsek 2013; Kuzniecky 1993; Kwan 2010; Ure 2009).

Recording of adverse events in all included studies

In all, 79 of the 182 (43%) included studies reported adverse events or complications of surgery. Details were highly variable; the RCTs reported the most details, see 'Overall outcome of surgery compared to medical treatment' and 'Overall outcome according to surgical techniques' for a summary of the surgical complications

and adverse events in the RCTs.

In the non-randomised studies, some studies reported deaths only, including those occurring many years later from unrelated causes. Study authors often did not state the timing of events and provided no clarity around what was perioperative, what was a transient event (some included persistence of a feature up to 12 months as transient), and what was a permanent deficit. The overall quality of these data is therefore very poor. Few studies included any reference to postoperative cognition or mental state.

Notwithstanding these constraints, study authors recorded adverse events in 1331 of the 9599 (13.8%) participants involved in these 76 studies. By taking data from studies that specified the number with transient adverse events (282 (21%)) and adding to this the number of events that we can assume to be transient (i.e. short-lived and treatable, to include infection/fever, cerebrospinal fluid (CSF) leak/collection, haemorrhage, deep venous thrombosis, status epilepticus, and cerebral oedema), we found that the total number with a transient adverse event is 618 (6%). This leaves us 713 of the 9599 (7.4%) participants with a permanent adverse event. It is highly likely that this represents an overestimation of a prevalence figure for 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.

Recorded adverse events include the following.

- Adverse events were undefined in 98 (7.5%) participants and included infection/fever (difficult to differentiate infective causes from autonomic dysfunction) in 251 (19.2%); motor impairment (to include monofacial and hemifacial pareses, along with cranial nerve involvement) in 220 (16.8%); visual field defect in 173 (13.2%); haemorrhage in 56 (4.3%); language impairment in 42 (3.2%); CSF leak or collection (e.g. subgaleal) in 36 (2.8%); cognitive impairment to include memory loss in 34 (2.6); hydrocephalus in 24 (1.8%); and miscellaneous (to include deep venous thrombosis (associated in three with pulmonary embolism), status epilepticus, cerebral oedema, and urinary incontinence in 10 (0.8%).
- Study authors recorded altered mental state in 118 (9%) participants. They did not define duration. It is notable that one study contributed 65 of this number as the result of a detailed psychiatric assessment included in its post-surgery follow-up protocol (Suppiah 2009). A new episode of psychological symptoms occurred in 52% of 114 participants assessed in this way during the first year after surgery. Sixty-six of these people had a lifetime prevalence of anxiety or depression or another axis I disorder. Supplementary publications sometimes reported on mental state. For example, Cleary 2012 analysed psychiatric diagnoses in 280 of 615 participants reported in de Tisi 2011, showing that 38% of 280 had significant psychiatric problems within four years following temporal lobe surgery.

The figures given here in parentheses are percentages of 1308 - the overall number of recorded adverse events.

Prognostic factors of a good outcome of surgery in all included studies

Univariate analyses

Of 175 studies reporting seizure outcome data on a satisfactory scale, 119 contributed data towards at least one of our pre-specified prognostic factors of interest for univariate analysis (i.e. the independent, unadjusted effect of each of these factors on outcome; see Data extraction and management). Twenty-nine studies reported one prognostic factor, 20 reported two prognostic factors, 28 three prognostic factors, 17 four prognostic factors, 12 five prognostic factors, seven six prognostic factors, two seven prognostic factors, and four nine prognostic factors. See Table 6 for full details of the prognostic factors recorded in each study.

Analyses 4.1 to 4.14 show the univariate risk ratio (RR) and 95% confidence interval (CI) of good outcome for each prognostic factor. All analyses are subgrouped according to the outcome scales 'more than one year seizure-free', 'Engel Class Scale', or 'other' scale, and an overall pooled RR and 95% CI adjusted for outcome scale are reported for each factor. All analyses were performed with a fixed-effect model unless otherwise stated.

We intended to compare the results of pooling unadjusted univariate analyses versus the results of pooling adjusted multi-variable analyses for each prognostic factor, under the assumption that it is likely that our pre-specified factors of interest do not act completely independently of outcome and do in fact interact with each other as well as with the outcome. However, due to limited information from adjusted multi-variable analyses reported as aggregate data, we were unable to perform any analyses in this review using adjusted results, and we have described below the multi-variable adjusted models including our pre-specified variables of interest (see "Multi-variate analyses").

We emphasise that the univariate RRs presented in Analyses 4.1 to 4.14 assume that each factor acts independently on seizure outcome, which, in reality, is unlikely to be the case. Therefore we have discussed only the direction of the analyses rather than the numerical magnitude, and we do not encourage use of these results in future research.

Pre-operative *f*actors

Results of pre-operative MRI

Forty-three studies with 3999 participants reported pre-operative MRI results (normal vs abnormal, where abnormal is defined within individual studies) as a prognostic factor for seizure outcome of surgery. Seventeen studies reported seizure outcome according to a more than one year seizure-free scale, 22 according to the Engel Class Scale, and four according to 'other' scales

(see Included studies for definitions of 'other' scales). A total of 1271 participants had normal MRI results, 700 of whom (55%) achieved a good outcome of surgery; and 2728 participants had abnormal MRI results, 1833 of whom (67%) achieved a good outcome of surgery.

Analysis 4.1 shows that participants with abnormal pre-operative MRI results are significantly more likely to have a good outcome of surgery than those with normal pre-operative MRI results (pooled RR for normal vs abnormal MRI, 95% CI adjusted for outcome scale 0.78 (0.73 to 0.83); P < 0.00001). Results according to outcome scale are very similar: more than one year seizure-free pooled RR for normal versus abnormal MRI 0.82 (95% CI 0.74 to 0.90; P < 0.0001); Engel Class Scale pooled RR for normal versus abnormal MRI 0.76 (95% CI 0.69 to 0.81; P < 0.00001); and 'other' scale pooled RR for normal versus abnormal MRI 0.84 (95% CI 0.53 to 1.32; P = 0.45). We found no evidence of a difference between outcome scales for this prognostic factor (Chi² test for subgroup differences P = 0.35).

A moderate amount of heterogeneity is present between studies in each of the subgroups and in the overall analysis (I^2 value ranges from 20% to 65% in subgroup analyses and is 39% overall). When the analysis is repeated for subgroups and overall analysis with a random-effects model, pooled results are similar and conclusions remain unchanged. The largest amount of heterogeneity is present between studies using 'other' scales; therefore the variability of results here is likely to be due to the different outcome scales used (see Included studies). Also one study in this subgroup shows a large effect in favour of an abnormal MRI for a good outcome of surgery (RR 0.17, 95% CI 0.01 to 2.38), as only 4 of 36 participants in this study had a normal pre-operative MRI, and none of these participants achieved a good outcome of surgery (Sakamoto 2009).

Further subgroup analysis separating site of surgery of participants in the study (temporal only, extratemporal only, both temporal and extratemporal) and study design (prospective or retrospective identification of participants) shows no significant differences between these subgroups, and this could be contributing to heterogeneity (analyses not shown but available from study authors). We therefore deduce that variability between studies may originate from slightly different definitions of pre-operative MRI abnormality across studies; for example, some studies defined only 'abnormalities' on MRI, and other studies defined specific abnormalities such as 'lesions on MRI'. Further, small participant numbers and unbalanced participant numbers with normal and abnormal MRIs leading to large, imprecise results may have contributed to variability between studies (e.g. in Adam 1996, of 30 participants, 1 had an abnormal MRI and 29 had a normal MRI).

Use of pre-operative intracranial (invasive) monitoring

Twenty-one studies with 1547 participants reported data on use of intracranial monitoring (used vs not used) as a prognostic factor for seizure outcome of surgery. Six studies reported seizure outcome according to a more than one year seizure-free scale, 14 studies according to the Engel Class Scale, and one study according to some 'other' scale (see Included studies for definitions of 'other' scales). A total of 762 participants underwent intracranial monitoring, 448 of whom (59%) achieved a good outcome of surgery; and 785 did not undergo intracranial monitoring, 564 of whom (72%) achieved a good outcome of surgery.

Analysis 4.2 shows that participants who do not undergo intracranial monitoring are significantly more likely to have a good outcome of surgery than those who do undergo intracranial monitoring (pooled RR for intracranial monitoring used vs not used 0.85, 95% CI adjusted for outcome scale 0.78 to 0.93; P = 0.0002). Results according to outcome scale include the following: more than one year seizure-free pooled RR for intracranial monitoring used versus not used 0.88 (95% CI 0.76 to 1.02; P = 0.10); Engel Class Scale pooled RR for intracranial monitoring used versus not used 0.85 (95% CI 0.77 to 0.94; P = 0.004); and 'other' scale pooled RR for intracranial monitoring used versus not used 0.53 (95% CI 0.28 to 0.98; P = 0.04). We found no evidence of a difference between outcome scales for this prognostic factor (Chi² test for subgroup differences P = 0.39).

A moderate amount of heterogeneity is present between studies in each of the subgroups and in overall analysis (I^2 value ranging from 37% to 46% in subgroup analyses and 37% overall). When analysis is repeated with a random-effects model, pooled results are similar and conclusions remain unchanged. We assume it is likely that the small amount of heterogeneity present between studies is due to small participant numbers, unbalanced participant numbers, and using or not using intracranial monitoring, leading to large, imprecise results that may have contributed to variability between studies.

Mesial temporal sclerosis (MTS) on MRI or pathology

Forty-six studies with 4354 participants reported data on mesial temporal sclerosis on pathology (present vs absent) as a prognostic factor for seizure outcome of surgery. Nine studies reported seizure outcome according to a more than one year seizure-free scale, 30 studies according to the Engel Class Scale, and seven studies according to some 'other' scale (see Included studies for definitions of 'other' scales). A total of 1735 participants had confirmed MTS on pathology, 1287 of whom (74%) achieved a good outcome of surgery; and 2619 participants did not show MTS on pathology, 1609 of whom (62%) achieved a good outcome of surgery.

Analysis 4.3 shows that patients with MTS on pathology are significantly more likely to have a good outcome of surgery than those without MTS on pathology (pooled RR for presence vs absence of MTS 1.18 (95% CI adjusted for outcome scale 1.13 to 1.24; P < 0.00001). Results according to outcome scale include the following: more than one year seizure-free pooled RR for presence versus absence of MTS 1.25 (95% CI 1.13 to 1.39; P < 0.0001);

Engel Class Scale pooled RR for presence versus absence of MTS 1.13 (95% CI 1.07 to 1.20; P < 0.00001); and 'other' scale pooled RR for presence versus absence of MTS 1.31 (95% CI 1.14 to 1.51; P = 0.0002). We found no statistically significant evidence of a difference between outcome scales (Chi² test for subgroup differences P = 0.06).

Across subgroups, no heterogeneity was present between studies classifying seizure outcome as more than one year seizure-free (I^2 = 0%). Some heterogeneity was present between studies classifying seizure outcome by Engel Class Scale (I^2 = 30%) and by 'other' scales (I^2 = 17%), so overall heterogeneity between all included studies was quite low (I^2 = 28%). As in previous examples, it is likely that the small amount of heterogeneity present between studies is due to many studies having small sample sizes and unbalanced numbers of participants with and without MTS. This has led to several large, imprecise results, which may have contributed to variability between studies.

Concordance of pre-operative MRI and EEG

Concordance is seen when results of two investigations - usually an MRI scan and an EEG - localise the likely source of epilepsy to the same lobe. Twenty-three studies with 1778 participants reported data on concordance of pre-operative MRI and EEG (concordant vs discordant) as a prognostic factor for seizure outcome of surgery. Eight studies reported seizure outcome according to a more than one year seizure-free scale, 12 studies according to the Engel Class Scale, and three studies according to some 'other' scale (see Included studies for definitions of 'other' scales). A total of 1200 participants had concordant pre-operative MRI and EEG, 824 of whom (69%) achieved a good outcome of surgery; and 578 participants had discordant pre-operative MRI and EEG, 313 of whom (54%) achieved a good outcome of surgery.

Analysis 4.4 shows that participants with concordant pre-operative MRI and EEG are significantly more likely to have a good outcome of surgery than those with discordant pre-operative MRI and EEG (pooled RR for concordant vs discordant 1.25, 95% CI adjusted for outcome scale 1.15 to 1.37; P < 0.00001). Results according to outcome scale include the following: more than one year seizure-free pooled RR for concordant versus discordant 1.21 (95% CI 1.07 to 1.37; P = 0.003); Engel Class Scale pooled RR for concordant versus discordant 1.27 (95% CI 1.11 to 1.46; P = 0.0005); and 'other' scale pooled RR for concordant versus discordant 1.40 (95% CI 1.02 to 1.93; P = 0.04). We found no evidence of a difference between outcome scales for this prognostic factor (Chi² test for subgroup differences P = 0.65).

No heterogeneity is present between studies classifying seizure outcome according to the Engel Class Scale (I^2 = 0%). A moderate amount of heterogeneity is present between studies in other subgroups (I^2 = 50% to 56% and I^2 = 26% overall). When analysis is repeated with a random-effects model, the pooled RR for concordant versus discordant is no longer significant in the subgroups on a more than one year seizure-free scale (RR 1.24, 95% CI 0.97 to 1.59; P = 0.08) and on another scale (RR 1.46, 95% CI 0.89 to 2.39; P = 0.14). However, overall pooled results adjusted for outcome scale are similar and conclusions remain unchanged (pooled RR for concordant vs discordant 1.20, 95% CI 1.08 to 1.34; P = 0.0009).

Heterogeneity present between three studies using 'other' scales is likely due to the different outcome scales used by the these studies (Holmes 2000; Rossi 1994; Yang 2011; see Included studies). From inspection of studies that classified seizure outcome as more than one year seizure-free, small participant numbers and unbalanced participant numbers with concordant and discordant pre-operative MRI and EEG leading to large, imprecise results may have contributed to variability between studies. Further, three studies show particularly variable results. Tatum 2008 shows a large significant effect in favour of concordance, with wide confidence intervals; participants in this study had a normal MRI for inclusion; therefore concordance with MRI was determined operatively rather than pre-operatively. Kim 2010b also showed a large effect in favour of concordance, with wide confidence intervals; all participants in this study had dual pathology of MTS and focal cortical dysplasia (FCD) for inclusion. Kim 2009 is the only study to show an effect in favour of discordance; all participants in this study had FCD for inclusion. Other studies in this subgroup, all showing moderate, non-significant effects in favour of concordance, had no specific inclusion criteria based on imaging or pathology. It is feasible that specific study inclusion criteria based on how pathological lesions are sited may in turn influence classification of the pre-operative MRI and therefore concordance with the pre-operative EEG (see below for the apparent disadvantage of retrospective design in this respect).

Further subgroup analysis separating the site of surgery of participants in the study (temporal only, extratemporal only, both temporal and extratemporal) shows no significant differences between these subgroups that could be contributing to heterogeneity (analyses not shown but available from study authors). Subgroup analysis according to study design (prospective or retrospective identification of participants) shows a larger advantage for concordant pre-operative MRI and EEG in the three studies of a prospective design than in the 20 studies of a retrospective design (prospective pooled RR for concordant vs discordant 1.91, 95% CI 1.06 to 3.44; P = 0.03; retrospective pooled RR for concordant vs discordant 1.21, 95% CI 1.10 to 1.33; P < 0.0001). We found no statistically significant evidence of differences between subgroups (Chi² test for subgroup differences P = 0.13); however, this trend may be contributing towards the heterogeneity. For example, for studies with a prospective design, determining concordance of tests performed during the study may be easier and more reliable than determining concordance of medical records of tests that have been previously performed in a study of a retrospective design. In summary, it is likely that study characteristics such as design, inclusion criteria, and outcome scale may have contributed to variability in

this prognostic factor.

History of febrile seizures

Fifteen studies with 1368 participants reported data on history of febrile seizures (history vs no history) as a prognostic factor for post-surgery seizure outcome. Five studies reported seizure outcome according to a more than one year seizure-free scale, nine studies according to the Engel Class Scale, and one study according to some 'other' scale (see Included studies for definitions of 'other' scales). A total of 440 participants had a history of febrile seizures, 343 of whom (78%) achieved a good outcome of surgery; and 928 participants had no history of febrile seizures, 615 of whom (66%) achieved a good outcome of surgery.

Analysis 4.5 shows that participants with a history of febrile seizures were significantly more likely to have a good outcome of surgery than those without a history of febrile seizures (pooled RR for history vs no history of febrile seizures 1.09, 95% CI adjusted for outcome scale 1.01 to 1.17; P = 0.002). Results according to outcome scale include the following: more than one year seizure-free pooled RR for history versus no history of febrile seizures 1.18 (95% CI 1.05 to 1.32; P = 0.006); Engel Class Scale pooled RR for history versus no history of febrile seizures 1.01 (95% CI 0.92 to 1.11; P = 0.83); and 'other' scale (one study) RR for history versus no history of febrile seizures 1.11 (95% CI 0.90 to 1.37; P = 0.32). We found no evidence of a difference between outcome scales for this prognostic factor (Chi² test for subgroup differences P = 0.14).

A substantial amount of heterogeneity is present between studies that classified seizure outcome according to more than one year seizure-free (I^2 = 70%), and no heterogeneity is present between the other outcome scales (I^2 = 0%), which leads to an overall moderate amount of heterogeneity in the overall analysis (I^2 = 32%). When analysis is repeated with a random-effects model, the pooled RR remains unchanged in subgroups without heterogeneity between studies, but in the subgroup more than one year seizure-free, and now in the overall analysis, the advantage for participants with a history of febrile seizures is no longer statistically significant (more than one year seizure-free pooled RR for history vs no history of febrile seizures 1.23, 95% CI 0.96 to 1.57; P = 0.10; overall pooled RR for history vs no history of febrile seizures 1.07, 95% CI 0.98 to 1.17; P = 0.12).

From inspection of studies that classified seizure outcome as more than one year seizure-free, small participant numbers and unbalanced participant numbers with and without a history of febrile seizures, leading to large, imprecise results, may have contributed to variability between studies as in previous analyses, particularly the two smallest studies showing the two largest effects in favour of a history of febrile seizures (Holmes 1997; Kim 2010b).

A potential association between febrile seizures and MTS, particularly whether prolonged febrile seizures are a risk factor for febrile seizures, is well documented (Davis 1996; Maher 1995; Sarkisian 1999; Scott 2002; Szabo 1999). Therefore as we have already noted in this review a good outcome associated with the presence of MTS on pathological examination (see Analysis 4.3), it is intuitive that we should also observe a good outcome of surgery for participants with a history of febrile seizures. Seven studies have recorded data on the presence of both MTS on pathological examination and a history of febrile seizures: two show a significant advantage for participants with MTS (Radhakrishnan 1998; Spencer 2005), three show a non-significant advantage for MTS (Jeong 1999; Perry 2010; Terra-Bustamante 2005a), and two show a small non-significant advantage for no MTS on pathological examination (Chabardes 2005; Grivas 2006). The same trends are evident in the analysis of febrile seizures as a prognostic factor: the five studies that show an advantage for MTS on pathological examination (significant or non-significant) also show an advantage for a history of febrile seizures in relation to a good post-surgery outcome; and the two studies that show small advantages for no MTS also show small advantages for no history of febrile seizures (see Analysis 4.5).

Given this apparent association between febrile seizures and MTS pathology, as in Analysis 4.4, specific inclusion criteria of studies based on pathology may be contributing to the variability observed in the subgroup of studies that classified seizure outcome by a more than one year seizure-free scale (see Analysis 4.5). Two studies in this subgroup included only participants with a diagnosis of MTS - in Walz 2003 - or a diagnosis of dual pathology MTS and FCD - in Kim 2010b, and one study excluded participants with any pathology other than FCD including MTS (Kim 2009). The two remaining studies had no specific inclusion criteria based on pathological findings (Holmes 1997; Spencer 2005).

History of head injury

Seven studies with 551 participants reported data on history of head injury (history vs no history) as a prognostic factor for post-surgery seizure outcome. Two studies reported seizure outcome according to a more than one year seizure-free scale, three studies according to the Engel Class Scale, and two studies according to some 'other' scale (see Included studies for definitions of 'other' scales). A total of 159 participants had a history of head injury, 100 of whom (63%) achieved a good outcome of surgery, and 392 participants had no history of head injury, 242 of whom (62%) achieved a good outcome of surgery.

Analysis 4.6 shows that there is no significant difference between history and no history of head injury for the outcome of surgery (pooled RR for history vs no history of head injury, 95% CI adjusted for outcome scale 0.99, 95% CI 0.86 to 1.13; P = 0.85). Results according to outcome scale are as follows: more than one year seizure-free pooled RR for history versus no history of head injury 0.87 (95% CI 0.72 to 1.05; P = 0.14); Engel Class Scale pooled RR for history versus no history of head injury 1.17 (95% CI 0.99 to 1.37; P = 0.06); and 'other' scale pooled RR for history

versus no history of head injury 0.83 (95% CI 0.51 to 1.33; P = 0.43).

Here, evidence shows a difference between outcome scales (Chi² test for subgroup differences P = 0.05), revealing the trend that studies classifying outcome on the Engel Class Scale favour a history of head injury for a good outcome of surgery, and studies classifying outcome on a more than one year seizure-free scale or 'other' scale favour no history of head injury. Heterogeneity is present only between studies using 'other' scales to classify seizure outcome (I^2 = 71%), which is the source of moderate heterogeneity in the analysis overall (I^2 = 46%). When analysis is repeated for subgroups and the overall analysis uses a random-effects model, pooled results are similar and conclusions remain unchanged. It is likely that this variation is due to the two different 'other' scales used by these studies. Holmes 2000 classified more than two years seizure-free as a good outcome, and Yang 2011 categorised ILAE Classes 1 and 2 as a good outcome.

Encephalomalacia on pathology

Five studies with 317 participants reported data on encephalomalacia on pathological examination (present vs absent) as a prognostic factor for seizure outcome of surgery. Four studies reported seizure outcome according to the Engel Class Scale, and one study according to some 'other' scale (see Included studies for definitions of 'other' scales). A total of 45 participants had encephalomalacia, 16 of whom (36%) achieved a good outcome of surgery; and 272 participants did not have encephalomalacia, 113 of whom (42%) achieved a good outcome of surgery.

Analysis 4.7 shows that there is no significant difference between the presence or absence of encephalomalacia for the outcome of surgery (pooled RR for presence vs absence of encephalomalacia 0.78, 95% CI adjusted for outcome scale 0.52 to 1.17; P = 0.23). In other words, the presence of encephalomalacia on pathology is not a significant independent predictor of seizure outcome of surgery. Results according to outcome scale include the following: Engel Class Scale pooled RR for presence versus absence of encephalomalacia 0.89 (95% CI 0.60 to 1.33; P = 0.58); and 'other' scale (one study) RR for presence versus absence of encephalomalacia 0.28 (95% CI 0.04 to 1.87; P = 0.19). We found no evidence of a difference between outcome scales for this prognostic factor (Chi² test for subgroup differences P = 0.24), nor did we find evidence of heterogeneity between studies in any of the subgroup analyses or overall (I^2 = 0%).

Focal cortical dysplasia/malformation of cortical development on pathology

Forty-six studies with 3572 participants reported data on FCD/malformation of cortical development (MCD) on pathological examination (present vs absent, with defect generally defined as FCD or MCD) as a prognostic factor for seizure outcome of surgery. Nine studies reported seizure outcome according to a more than one year seizure-free scale, 33 studies according to the Engel Class Scale, and five studies according to some 'other' scale (see Included studies for definitions of 'other' scales). A total of 1205 participants showed FCD/MCD, 687 of whom (57%) achieved a good outcome of surgery; and 2367 participants did not show FCD/MCD, 1599 of whom (68%) achieved a good outcome of surgery.

Analysis 4.8 shows that participants without FCD/MCD were significantly more likely to have a good outcome of surgery than those with FCD/MCD on pathology (pooled RR for presence vs absence of FCD/MCD 0.90, 95% CI adjusted for outcome scale 0.85 to 0.95; P = 0.0005). Results according to outcome scale include the following: more than one year seizure-free pooled RR for presence versus absence of FCD/MCD 0.92 (95% CI 0.84 to 1.02; P = 0.11); Engel Class Scale pooled RR for presence versus absence of FCD/MCD 0.89 (95% CI 0.82 to 0.96; P = 0.003); and 'other' scale pooled RR for presence versus absence of FCD/MCD 0.91 (95% CI 0.73 to 1.13; P = 0.39). We found no evidence of a difference between outcome scales for this prognostic factor (Chi² test for subgroup differences P = 0.83).

A moderate amount of heterogeneity is present between studies in each of the subgroups and in the overall analysis: I^2 value ranges from 28% to 41% in subgroup analyses and is 28% overall. When analysis is repeated with a random-effects model, pooled results are similar and conclusions remain unchanged. As in previous analyses, we assume it is likely that the small amount of heterogeneity present between studies is due to small participant numbers and unbalanced participant numbers with and without FCD/MCD, leading to large, imprecise results that may have contributed to variability between studies. Furthermore, variability across studies in the exact definition of FCD/MCD (focal cortical dysplasia or malformation of cortical development of varying severities) may have contributed to variability in study results.

Tumour on pathology

Forty-one studies with 3357 participants reported data on tumour as a pathological finding (present vs absent, with specific tumour types defined in some included studies) as a prognostic factor for seizure outcome of surgery. Seven studies reported seizure outcome according to a more than one year seizure-free scale, 28 studies according to the Engel Class Scale, and six studies according to some 'other' scale (see Included studies for definitions of 'other' scales). A total of 806 participants had a confirmed tumour, of whom 595 (74%) achieved a good outcome of surgery; and 2551 participants did not show a tumour, of whom 1512 (59%) achieved a good outcome of surgery.

Analysis 4.9 shows that participants with a tumour were significantly more likely to have a good outcome of surgery than those without a tumour (pooled RR for presence vs absence of tumour 1.21, 95% CI adjusted for outcome scale 1.15 to 1.28; P

< 0.00001). Results according to outcome scale are very similar: more than one year seizure-free pooled RR for presence versus absence of tumour 1.16 (95% CI 1.03 to 1.31; P = 0.02); Engel Class Scale pooled RR for presence versus absence of tumour 1.20 (95% CI 1.13 to 1.29; P < 0.00001); and 'other' scale pooled RR for presence versus absence of tumour 1.34 (95% CI 1.12 to 1.60; P = 0.001). We found no evidence of a difference between outcome scales for this prognostic factor (Chi² test for subgroup differences P = 0.41).

A moderate amount of heterogeneity is present between studies in each of the subgroups and in the overall analysis: I² value ranges from 34% to 54% and is 41% overall. The largest amount of heterogeneity is present between studies classifying seizure outcome by more than one year seizure-free (I² = 54%); however variability is greatly influenced by a single study in this subgroup with a large effect size due to all participants in this study with a tumour achieving a good outcome of surgery (Duchowny 1998). When analysis is repeated with a random-effects model in this subgroup, the pooled RR for presence versus absence of tumour is no longer statistically significant at 1.17 (95% CI 0.97 to 1.41; P = 0.10). Within other subgroups and in the overall analysis, pooled results are similar and conclusions remain unchanged. As in the previous analyses, we assume it is likely that the small amount of heterogeneity present between studies is due to small participant numbers and unbalanced participant numbers with and without tumours, leading to large, imprecise results and contributing to variability between studies. Furthermore, variability in the type of tumour observed across studies (i.e. some studies recorded specific types of tumours observed (e.g. dysembryoplastic neuroepithelial tumour (DNET), ganglioglioma, oligodendroglioma), and other studies reported that non-specific 'tumours' were observed) may have contributed to variability in study results.

Vascular malformation on pathology

Nineteen studies with 1488 participants reported data on vascular malformations (present vs absent, with specific malformations defined in some included studies) as a prognostic factor for post-surgery outcome. One study reported seizure outcome according to a more than one year seizure-free scale, 13 studies according to the Engel Class Scale, and five studies according to some 'other' scale (see Included studies for definitions of 'other' scales). A total of 139 participants had a confirmed vascular malformation, 89 of whom (64%) achieved a good outcome post surgery; and 1349 participants did not show a vascular malformation, 785 of whom (58%) achieved a good post-surgery outcome.

Analysis 4.10 shows there is no significant difference between presence and absence of vascular malformation for the outcome of surgery (pooled RR for presence vs absence of vascular malformation 1.07, 95% CI adjusted for outcome scale 0.94 to 1.21; P = 0.34). In other words, the presence of a vascular malformation on pathology is not a significant independent predictor of seizure outcome of surgery. Results according to outcome scale are very similar: more than one year seizure-free pooled RR for presence versus absence of vascular malformation 1.06 (95% CI 0.62 to 1.79; P = 0.84); Engel Class Scale pooled RR for presence versus absence of vascular malformation 1.14 (95% CI 0.98 to 1.34; P = 0.09); and 'other' scale pooled RR for presence versus absence of vascular malformation 1.07 (95% CI 0.94 to 1.21; P = 0.64). We found no evidence of a difference between outcome scales for this prognostic factor (Chi² test for subgroup differences P = 0.42) and no evidence of heterogeneity between studies in any subgroup analyses or overall (I² = 0%).

Distribution of interictal spikes

Eighteen studies with 1404 participants reported data on distribution of interictal spikes (unilateral vs bilateral spikes, also defined as lateralising vs non-lateralising spikes, focal vs non-focal spikes, or localising vs non-localising spikes) as a prognostic factor for seizure outcome of surgery. Seven studies reported seizure outcome according to a more than one year seizure-free scale, six studies according to the Engel Class Scale, and five studies according to some 'other' scale (see Included studies for definitions of 'other' scales). A total of 722 participants had unilateral spikes, of whom 504 (70%) achieved a good outcome of surgery; and 682 participants had bilateral spikes, of whom 406 (59%) achieved a good outcome of surgery.

Analysis 4.11 shows that participants with unilateral interictal spikes are significantly more likely to achieve a good outcome of surgery than those with bilateral interictal spikes (pooled RR for unilateral vs bilateral spikes 1.14, 95% CI adjusted for outcome scale 1.05 to 1.24; P < 0.0001). Results according to outcome scale include the following: more than one year seizure-free pooled RR for unilateral versus bilateral spikes 1.08 (95% CI 0.94 to 1.24; P = 0.72); Engel Class Scale pooled RR for unilateral versus bilateral spikes 1.19 (95% CI 1.04 to 1.36; P = 0.009); and 'other' scale pooled RR for unilateral versus bilateral spikes 1.16 (95% CI 0.97 to 1.39; P = 0.11). We found no evidence of a difference between outcome scales for this prognostic factor (Chi² test for subgroup differences P = 0.58).

A substantial amount of heterogeneity is present in the analysis overall (I² = 67%) and between studies that classified seizure outcome according to the Engel Class Scale (I² = 84%) and 'other' scales (I² = 82%). No heterogeneity is present between studies that classified seizure outcome according to a more than one year seizure-free scale (I² = 0%). When analyses were repeated with a random-effects model for studies that classified seizure outcome according to the Engel Class Scale, the pooled RR for unilateral versus bilateral spikes was no longer statistically significant at 1.33 (95% CI 0.88 to 2.00; P = 0.17). Results for other subgroups and for the overall analysis are similar, and conclusions remain unchanged.

As in previous analyses, a large amount of heterogeneity is present between studies using 'other' scales. Therefore the variability of results may be due to the different outcome scales used (see Included studies). Small participant numbers and unbalanced participant numbers with unilateral and bilateral spikes leading to large, imprecise results may have contributed to variability between studies. Further subgroup analysis separating the site of surgery for study participants (temporal only, extratemporal only, both temporal and extratemporal) and study design (all studies are of a retrospective design) shows no significant differences between these subgroups that could be contributing to heterogeneity (analyses not shown but available from study authors).

We note that data on interictal spikes are defined in slightly different ways across studies: two studies defined lateralising versus non-lateralising or contralateral spikes (Boshuisen 2010; Greiner 2011), three studies defined localised versus non-localised spikes (Dalmagro 2005; Lee 2008; Tatum 2008), four studies defined focal versus non-focal spikes (Jayakar 2008; Kim 2010b; Kim 2009; Rossi 1994), and nine studies defined unilateral versus bilateral spikes (Chee 1993; Erickson 2005; Goldstein 1996; Holmes 2000; Lee 2006; Madhavan 2007; Remi 2011; Walz 2003; Weinand 1992). Data based on these differing definitions as subgroups include the following: lateralising spikes pooled RR for lateralising versus non-lateralising spikes 1.05 (95% CI 0.85 to 1.31; P = 0.65; I^2 = 11%); localising spikes pooled RR for localised versus non-localised spikes 1.08 (95% CI 0.81 to 1.44; P = 0.59; I^2 = 0%); focal spikes pooled RR for focal versus non-focal spikes 1.05 (95% CI 0.85 to 1.30; P = 0.65; I^2 = 11%); and unilateral spikes pooled RR for unilateral versus bilateral spikes 1.22 (95% CI 1.10 to 1.34; P < 0.00001; I^2 = 76%). We found no statistically significant evidence of a difference between these subgroups (Chi^2 test for subgroup differences P = 0.39); however a trend is apparent for a larger effect in favour of unilateral spikes when compared with bilateral spikes as opposed to the other definitions of data related to the distribution of interictal spikes. We deduced that the definition of the prognostic factor was likely to have influenced this analysis; therefore we recommend caution when results of this analysis are interpreted.

Operative factors

Extent of surgical resection

Forty studies with 3013 participants reported data on 'Extent of surgical resection' (complete vs less complete, with completeness defined in individual studies) as a prognostic factor for seizure outcome of surgery. Nine studies reported seizure outcome according to a more than one year seizure-free scale, 28 studies according to the Engel Class Scale, and three studies according to some 'other' scale (see Included studies for definitions of 'other' scales). A total of 1716 participants underwent complete surgical resection, of whom 1277 (74%) achieved a good outcome of surgery; and 1297 participants underwent a less complete surgical resection, of whom 725 (56%) achieved a good outcome of surgery.

Analysis 4.12 shows that participants with complete surgical resection were significantly more likely to achieve a good outcome of surgery than those with a less complete resection (pooled RR for complete vs incomplete resection 1.41, 95% CI adjusted for outcome scale 1.32 to 1.50; P < 0.00001). Results according to outcome scale include the following: more than one year seizure-free pooled RR for complete versus incomplete resection 2.00 (95% CI 1.66 to 2.41; P < 0.00001); Engel Class Scale pooled RR for complete versus incomplete resection 1.29 (95% CI 1.21 to 1.39; P < 0.00001); and 'other' scale pooled RR for complete versus incomplete resection 1.59 (95% CI 1.15 to 2.20; P = 0.005). We found highly significant evidence of a difference between outcome scales for this prognostic factor (Chi^2 test for subgroup differences P < 0.0001), and we noted a larger advantage for studies that classified studies using a more than one year seizure-free scale compared with the other two outcome scales.

A substantial amount of heterogeneity is present between all subgroups and overall in the analysis (I^2 value ranges from 67% to 86% in subgroups and is 77% in the overall analysis). When analyses were repeated with a random-effects model for studies that classified seizure outcome according to 'other' scales, the pooled RR for complete versus incomplete resection was no longer statistically significant at 1.15 (95% CI 0.44 to 3.00; P = 0.78). Results for the 'other' outcome scale and in the overall analysis are similar and conclusions remain unchanged.

As in previous analyses, some of the variability evident between studies using the Engel Class Scale may be due to small participant numbers and unbalanced participant numbers, with unilateral and bilateral spikes leading to large, imprecise results. Also, some of the heterogeneity between studies using 'other' scales may be due to the different outcome scales used (see Included studies): two studies in this subgroup, which classified participants according to the ILAE scale (Lackmayer 2013; Sakamoto 2009), show a non-significant trend in favour of less complete resection, and the other study shows a large effect in favour of complete resection, classified according to more than three years of seizure freedom (Rossi 1994).

We carried out further subgroup analysis by separating the site of surgery of participants in the study (temporal only (13 studies), extratemporal only (one study), both temporal and extratemporal (24 studies); site of surgery not available for Dalmagro 2005 and Raabe 2012) and obtained the following results (see Analysis 4.13): extratemporal only RR 2.00 (95% CI 0.76 to 5.29; P = 0.16); temporal only pooled RR for complete versus incomplete resection 1.11 (95% CI 1.03 to 1.20; P = 0.006; I^2 = 31%); temporal and extratemporal pooled RR for complete versus incomplete resection 1.98 (95% CI 1.77 to 2.23; P < 0.00001; I^2 = 75%); and overall pooled RR 1.48 (95% CI 1.38 to 1.58; P < 0.00001; I^2 = 78%). We found highly significant evidence of a difference between the

site of surgery and the outcome of surgery (Chi² test for subgroup differences P < 0.00001) and less of an advantage for complete surgical resection for studies in which participants had temporal lobe surgery only compared to the study in which all participants had extratemporal lobe surgery or studies in which participants had either temporal or extratemporal lobe surgery.

Furthermore, most of the heterogeneity in this analysis can be seen between studies in which participants had either temporal or extratemporal lobe surgery. This could be due to the association we observed between site of surgery and seizure outcome of surgery (see "Overall outcome of surgery" above). In other words, the difference in site of surgery across studies is confounding the analysis of extent of resection. Analysis 4.13 could also suggest that there may be a difference in the feasibility of performing a complete or less complete resection for temporal or extratemporal lobes; therefore it would be expected that results would be variable between studies that include a mixture of temporal lobe and extratemporal lobe surgery candidates, and that outcomes may be dependent on the proportion of participants receiving each type of surgery.

In addition, we noted that the definition of a 'complete' or 'less complete' resection was variable across studies. Most studies defined the extent of resection by the type of surgery performed (e.g. anterior temporal lobectomy or extended resection is complete resection, but selective amygdalohippocampectomy or lesionectomy is less complete resection; Lackmayer 2013; Sakamoto 2009). Other studies defined complete or incomplete resection postoperatively by MRI (e.g. O'Brien 2000; Zentner 1996), or operatively by subdural EEG (e.g. Widdess-Walsh 2007). Other studies confirmed the completeness of tailored resection by the surgical team at the time (e.g. Hamiwka 2005). These differences in definition are also likely to have contributed to substantial variability in this analysis.

Side of surgical resection

Thirty-seven studies with 2976 participants reported data on side of surgical resection (left- vs right-sided resection) as a prognostic factor for post-surgery seizure outcome. Five studies reported seizure outcome according to a more than one year seizure-free scale, 27 studies according to the Engel Class Scale, and five studies according to some 'other' scale (see Included studies for definitions of 'other' scales). A total of 1749 participants underwent left-sided surgical resection, of whom 1302 (67%) achieved a good outcome of surgery; and 1476 participants underwent a right-sided surgical resection, of whom 1056 (72%) achieved a good outcome of surgery.

Analysis 4.14 shows that participants with right-sided resection are significantly more likely to achieve a good outcome of surgery than those with left-sided resection (pooled RR for left- vs right-sided resection 0.94, 95% CI adjusted for outcome scale 0.90 to 0.98; P = 0.008). Results according to outcome scale include the following: more than one year seizure-free pooled RR for left versus right-sided resection 1.01 (95% CI 0.90 to 1.13; P = 0.90); Engel Class Scale pooled RR for left- versus right-sided resection 0.93 (95% CI 0.88 to 0.98; P = 0.01); and 'other' scale pooled RR for left- versus right-sided resection 0.92 (95% CI 0.79 to 1.07; P = 0.27). We found no evidence of a difference between outcome scales for this prognostic factor (Chi² test for subgroup differences P = 0.47).

No heterogeneity is evident between studies classifying seizure outcome according to a more than one year seizure-free scale or 'other' scales (I^2 = 0%); however some heterogeneity is present between studies classifying seizure outcome according to the Engel Class Scale (I^2 = 43%) and in the overall analysis (I^2 = 28%). When analyses were repeated with a random-effects model for studies that classified seizure outcome according to the Engel Class Scale, the pooled RR and the overall pooled RR were no longer statistically significant: Engel Class Scale pooled RR for left- versus right-sided resection was 0.96 (95% CI 0.89 to 1.02; P = 0.19); and overall pooled RR for left- versus right-sided resection 0.96 (95% CI 0.91 to 1.01; P = 0.14). We found no evidence of a difference between outcome scales for this prognostic factor (Chi² test for subgroup differences P = 0.60).

As in previous analyses, the heterogeneity that is evident between studies using the Engel Class Scale may be due to small participant numbers and unbalanced participant numbers, with left- and right-sided resections leading to large, imprecise results.

We carried out further subgroup analysis by separating the site of surgery of participants in the study (temporal only (30 studies), extratemporal only (two studies), both temporal and extratemporal (four studies); site of surgery not available for Dalmagro 2005). This approach yielded the following results (see Analysis 4.15): extratemporal only pooled RR for left- versus right-sided resection 1.03 (95% CI 0.76 to 1.39; P = 0.84; I^2 = 85%); temporal only pooled RR for left- versus right-sided resection 0.93 (95% CI 0.89 to 0.98; P = 0.006; I^2 = 30%); temporal and extratemporal pooled RR for left- versus right-sided resection 0.98 (95% CI 0.84 to 1.14; P = 0.77; I^2 = 0%); and overall pooled RR for left- versus right-sided resection 0.94 (95% CI 0.90 to 0.98; P = 0.009; I^2 = 28%). We found no statistically significant difference between sites of surgery for this prognostic factor (Chi² test for subgroup differences P = 0.68); however this subgroup analysis shows that the significant advantage of right-sided resection for good outcome of surgery is found only in studies in which all participants had temporal lobe surgery. Further, this subgroup analysis shows that the two studies with the largest effects favouring left and right resection, respectively (Lee 2008; Liava 2012), which contributed to most of the variability in this analysis, are the only studies in which all participants had extratemporal lobe surgery.

In summary, results of this analysis suggest that there is likely to be an association between side of surgery and outcome of surgery (right-sided resection is associated with good outcome); however these results may have been confounded by the site of surgery, and this association may exist only for participants undergoing

temporal lobe surgery. We require more evidence on the side of extratemporal surgery related to seizure outcome before we can provide conclusions regarding side of resection as a prognostic factor for outcome.

Postoperative factors

Postoperative discharge

Six studies with 542 participants reported data on postoperative discharge (present vs absent) as a prognostic factor for post-surgery seizure outcome. Two studies reported seizure outcome according to a more than one year seizure-free scale, four studies according to the Engel Class Scale, and one study according to some 'other' scale (see Included studies for definitions of 'other' scales). A total of 200 participants had postoperative discharge, of whom 132 (66%) achieved a good outcome of surgery; and 342 participants did not have postoperative discharge, of whom 262 (77%) achieved a good outcome of surgery.

Analysis 4.16 shows that there is no significant difference between presence or absence of postoperative discharge in the outcome of surgery (pooled RR for presence vs absence of postoperative discharges 0.91, 95% CI adjusted for outcome scale 0.79 to 1.04; P = 0.16). In other words, the presence of postoperative discharge is not a significant independent predictor of seizure outcome of surgery. Results according to outcome scale include the following: more than one year seizure-free pooled RR for presence versus absence of postoperative discharge 1.19 (95% CI 0.82 to 1.73; P = 0.36); and Engel Class Scale pooled RR for presence versus absence of postoperative discharge 0.85 (95% CI 0.74 to 0.98; P = 0.03). We found no evidence of a difference between outcome scales for this prognostic factor (Chi² test for subgroup differences P = 0.10).

A substantial amount of heterogeneity is present in the analysis overall (I^2 = 73%) and between the two studies that classified seizure outcome according to a more than one year seizure-free scale (Jennum 1993; Widdess-Walsh 2007) (I^2 = 90%); these two studies showed the largest effects in favour of discharges present and absent, respectively. Further, some heterogeneity is present between studies that classified seizure outcome according to the Engel Class Scale (I^2 = 34%). Analyses repeated with a random-effects model yielded the following results: overall pooled RR adjusted for outcome scale 0.91 (95% CI 0.68 to 1.22; P = 0.52); more than one year seizure-free pooled RR for presence versus absence of postoperative discharges 0.97 (95% CI 0.24 to 3.93; P = 0.97); and Engel Class Scale pooled RR for presence versus absence of postoperative discharge 0.85 (95% CI 0.70 to 1.03; P = 0.09).

Further subgroup analysis separating the site of surgery for study participants (temporal only in Janszky 2003b, Miserocchi 2013, and Radhakrishnan 1998, vs both temporal and extratemporal in Jennum 1993, Widdess-Walsh 2007, and Wray 2012) shows a significant difference between these subgroups (Chi² test for subgroup differences P = 0.02; see Analysis 4.17). Within the three studies in which researchers performed temporal lobe surgery on participants, the pooled RR for presence versus absence of postoperative discharge was 0.81 (95% CI 0.70 to 0.94; P = 0.006; I^2 = 0%), indicating that for temporal lobe surgery only, participants without postoperative discharge were significantly more likely to achieve a good outcome of surgery than those with postoperative discharge. However, within the three studies that performed a mixture of temporal and extratemporal lobe surgeries on participants, the pooled RR for presence versus absence of postoperative discharge was 1.20 (95% CI 0.89 to 1.61; P = 0.23; I^2 = 81%). This shows a non-significant trend in favour of the presence of postoperative discharge for a good outcome of surgery, and all of the heterogeneity noted in the analysis is seen between these three studies. These three studies are the smallest in this analysis, and all show large, imprecise effect sizes due to small participant numbers. Further, the mixture of participants undergoing temporal lobe and extratemporal lobe surgery in these studies is likely to have contributed to the variability. The difference between subgroups also may suggest a difference between the presence of postoperative discharge in participants undergoing temporal or extratemporal surgery and in the prognosis of the two surgery types.

Results of these further analyses and our observation of an association between site of surgery and outcome of surgery (see "Overall outcome of surgery" above) show that absence of postoperative discharge may be a predictor of good outcome of surgery. However, this analysis is likely to have been confounded by differing sites of surgery across the included studies, and we require more evidence on this prognostic factor specific to the site of surgery before presenting any conclusions. We note the limitation in this analysis that the factor 'postoperative discharge' may be related to and may be influenced by other pre-operative and postoperative factors and potentially by outcome (e.g. whether or not a postoperative EEG is obtained), which may be more likely if an individual has experienced a possible postoperative seizure. Furthermore, clinicians may be more likely to perform postoperative EEG after a long interval following surgery to inform decisions such as antiepileptic drug tapering. Selective use of postoperative EEG and therefore selective participants contributing to this factor may have introduced selection bias into this analysis; we recommend extreme caution when results of this analysis are interpreted.

Multi-variable analyses

Summary of studies reporting multi-variable models

In an additional post hoc analysis, we screened all 174 studies reporting seizure outcome data on a satisfactory scale. This revealed whether a multi-variable prognostic regression model had been

fitted to assess the adjusted influence of independent prognostic factors of interest in this review (see Secondary outcomes) on the dependent variable of seizure outcome (defined as the proportion of individuals experiencing a good outcome of surgery; see Primary outcomes for further details on this definition).

Twenty-nine of 174 studies (17%) performed no statistical analysis at all and reported only proportions/percentages. For 72 of 174 studies (41%), researchers described only univariate analyses. For 19 of 174 studies (11%), study authors did not report seizure outcome according to our definitions of a 'good' seizure outcome for analyses involving prognostic factors. In 16 of 174 studies (9%), investigators described a multi-variable model but did not include any of our pre-specified factors.

In total, 29 studies described a multi-variable prognostic model including one or more of the factors of interest to us (Althausen 2013; Boesebeck 2007; Cossu 2005; Cossu 2008; Elsharkawy 2008a; Elsharkawy 2009a; Gelinas 2011; Grivas 2006; Janszky 2003a; Jennum 1993; Kim 2009; Kim 2010a; Lopez-Gonzalez 2012; Madhavan 2007; McIntosh 2012; O'Brien 2000; Paolicchi 2000; Phi 2009; Radhakrishnan 1998; Rossi 1994; Sagher 2012; Sarkis 2012; Schramm 2011; Spencer 2005; Tezer 2008; Theodore 2012; Walz 2003; Wyler 1995; Yang 2011). The authors of two studies described two separate multi-variate models for seizure outcome, with different combinations of variables entered into the two models (McIntosh 2012; O'Brien 2000).

We extracted data from all 29 studies regarding variables entered into the multi-variable model, statistical methods used, and results of multi-variable modelling; we performed an additional risk of bias assessment of each of the 29 studies using a tool for prognostic studies (see Risk of bias in included studies). Overall, we judged one study to be at 'high' risk of bias in three domains (Rossi 1994), three studies to be at 'high' risk of bias in two domains (Althausen 2013; Janszky 2003a; Madhavan 2007), and 11 studies to be at 'high' risk of bias in one domain (Cossu 2008; Elsharkawy 2008a; Elsharkawy 2009a; Jennum 1993; Kim 2009; Paolicchi 2000; Radhakrishnan 1998; Sarkis 2012; Spencer 2005; Tezer 2008; Theodore 2012); The remaining 13 studies were not judged to be at 'high' risk of bias in any domain (Boesebeck 2007; Cossu 2005; Gelinas 2011; Kim 2010a; Lopez-Gonzalez 2012; McIntosh 2012; O'Brien 2000; Phi 2009; Sagher 2012; Schramm 2011; Walz 2003; Wyler 1995; Yang 2011).

In the 29 studies, 2311 of 3564 individuals who underwent surgery (65%) experienced a good outcome of surgery. Five studies identified participants according to a prospective design (Radhakrishnan 1998; Schramm 2011; Spencer 2005; Theodore 2012; Wyler 1995), two of which used a randomised design (Schramm 2011; Wyler 1995). In one study, it was not clear if participants were identified according to a prospective or retrospective design (Walz 2003); the remaining 23 studies identified participants according to a retrospective design.

It is unclear from the information reported in one study whether the dependent variable of seizure outcome was analysed as 'good' (Engel Class 1) or 'favourable' (Engel Classes 1 and 2) (Grivas 2006). Furthermore, it is unclear whether this study entered variables into the model, and study authors provided very little information regarding the results of modelling. Due to these issues, we have not considered this study any further in the narrative review of multi-variable models.

Given the variability of statistical regression models used (logistic regression, Cox proportional hazards regression, generalised estimating equations, etc.) and the combinations of variables entered into prognostic models, as well as the level of detail reported regarding results of prognostic models, combining adjusted results in meta-analysis was impossible in this review. Instead we provide below a narrative summary of the multi-variable models fitted. Furthermore, we have identified several issues that arose when we considered the multi-variable models reported in 28 studies (minus Grivas 2006; see "Adjusted results" below for further details).

- For 13 of 28 studies (46%), it is not clear exactly which variables had been entered into the model.
- For 13 of 28 studies (46%), researchers seem to have entered variables into the model according to statistical significance rather than clinical relevance (i.e. only variables showing a statistical association with outcome in univariate analyses were considered for multi-variable modelling).
- For 13 of 28 studies (46%), study authors reported no adjusted treatment effect sizes (revealed only P values or whether results that were 'significant' were reported).
- For 15 of 28 studies (54%), researchers selectively reported results of the multi-variate model or did not report them fully (e.g. numerical results reported only for variables shown to be statistically significant in multi-variable analysis).

One study did not report adjusted results for the Cox proportional hazards model fitted to a wide range of prognostic variables considered in the study (including extent of surgical resection, history of febrile seizures, history of initial precipitating insult, distribution of interictal spikes, and side of surgery of interest to us); study authors reported only 'crude' unadjusted hazard ratios from the model (Walz 2003).

One study described a multi-variable logistic regression analysis for a wide range of prognostic variables (including extent of surgical resection of interest to us); however, study authors referred to 'univariate conditions' when describing results of the model (Paolicchi 2000). Therefore, it is unclear whether presented results reflect adjusted or unadjusted values.

Adjusted results

The other 26 studies presented adjusted results for a multi-variable model. We have summarised these results below according to the level of detail reported (least detailed to most detailed) and the type of regression model fitted.

Four studies reported only the significance of results (Cossu 2005; Elsharkawy 2008a; Elsharkawy 2009a; Theodore 2012). For all

four studies, it is clear which variables had been entered into the model; however two studies - Elsharkawy 2008a and Elsharkawy 2009a - entered variables into the multi-variable model based on statistical significance in univariate analyses, and all four studies selectively reported 'significant' and 'non-significant' results.

- Cossu 2005 entered a large range of variables into a stepwise multi-variable logistic regression analysis: discrete numerical variables (age at seizure onset, illness duration before surgery, monthly seizure frequency) and categorical variables (sex, presence of lesion on MRI, presence of MTS on MRI, side of stereoelectroencephalography, site of epileptogenic zone (EZ), site of resection, type of resection, completeness of lesionectomy, reason for incomplete lesionectomy, histological diagnosis, presence of MTS at histological analysis on resected mesial temporal specimens). Most variables are not mentioned in the results (including presence of MTS on MRI and presence of MTS at histological analysis of interest to us) and therefore are assumed to be not significantly associated with seizure outcome. It is stated that completeness of lesionectomy shows "statistically significant association with outcome at univariate and multivariate analysis", but no P value, treatment effect size, or direction of effect is mentioned.
- Elsharkawy 2008a entered the following variables (significant in univariate analyses) into multi-variable logistic regression analysis: well-circumscribed lesion on the pre-operative MRI scan, short duration of epilepsy, early surgical interference, a neoplasm in the resected specimen, a psychic aura, versive seizures, tonic-clonic seizures, history of previous surgery, and focal cortical dysplasia in the resected specimen. The only variable of interest to us is "presence of focal cortical dysplasia in the resected specimen", which was "unable to provide predictive value for the outcome".
- Elsharkawy 2009a entered the following variables (significant in univariate analyses) into multi-variable stepwise Cox proportional hazards regression analysis: presence of regional hippocampal atrophy on pre-operative MRI, history of febrile seizure, EEG unilateral seizure onset, age under 30 years at surgery, exclusively unilateral sharp waves, right-sided resection, short epilepsy duration, family history of epilepsy, bilateral sharp waves, seizure onset bilateral, versive seizures, somatosensory aura, EEG at six months with interictal epileptiform discharges (IEDs), and EEG at two years with IEDs. The variables of interest to us (history of febrile seizures, EEG unilateral seizure onset, EEG with IED at two years, and right-sided resection) "did not retain significance in [the] stepwise model".
- Theodore 2012 entered three variables into a multi-variable stepwise logistic regression analysis: MRI, 18-(fluorodeoxyglucose)F-trans-4-fluoro-N-2-[4-(2-methoxyphenyl) piperazin-1-yl]ethyl-N-(2-pyridyl)cyclohexane carboxamide (FCWAY) positron emission tomography (PET), and 18F-FDG PET. The only variable of interest to us (MRI) "was not selected as being predictive of outcome".

Six studies reported only P values for results (Althausen 2013; Jennum 1993; Madhavan 2007; Rossi 1994; Sarkis 2012; Schramm 2011). Three studies entered variables into the multi-variable model based on statistical significance in univariate analyses (Madhavan 2007; Rossi 1994; Sarkis 2012), and four studies selectively reported multi-variable model results based on statistical significance (Althausen 2013; Jennum 1993; Sarkis 2012; Schramm 2011).

- Althausen 2013 specified in the methods section that age at surgery, side of surgery, aetiology (acquired, developmental, progressive), pre-operative intelligence, age at epilepsy onset, and duration of epilepsy would be entered into a stepwise logistic regression, but reported results suggest that hemispherectomy technique or completeness of hemispheric disconnection has also been entered into the model. Among the variables of interest to us, neither completeness of hemispheric disconnection nor side of surgery showed "significant effect on postoperative outcome" ($P > 0.1$). It is unclear if any other variables of interest to us were included in the model.
- Jennum 1993 entered the following variables into multiple regression analysis: age, sex, duration of epilepsy, MRI, structural lesion (tumour, arteriovenous malformation, or hamartoma) versus normal or localised atrophy, extent of temporal resection, temporal versus extratemporal focus, ictal focus completely resected, interictal focus completely resected, and presence of post-resection spikes in operative electrocorticography. Among the variables of interest to us, study authors did not report structural lesions on MRI in the results of factors strongly associated with good outcome. P values < 0.01 and < 0.04 were reported for complete resection of ictal focus and presence of post-resection spikes in operative electrocorticography, respectively, with no further discussion of the association between these variables and outcome.
- Madhavan 2007 entered the following variables (significant in univariate analyses) into the multi-variate analysis (details of multi-variate model not specified): age at seizure onset, presence/prior history of infantile spasms, ictal and interictal focality (unilateral vs bilateral), extent of surgical procedure (corpus callosotomy, lesionectomy, lobar resection, lesionectomy, lobar resection), and presence of residual dominant tube. Among the variables of interest to us, "there was a trend toward better seizure outcome in those patients that had more extensive procedures ($p = 0.86$)", and interictal focality was not associated with seizure outcome ($P = 0.42$).
- Rossi 1994 entered the following variables (significant in univariate analyses) into multi-variate logistic regression: spatial arrangement of electrocerebral epileptiform interictal and ictal activities, extent of resection of the structural lesion, and that of the epileptogenic zone. Among the variables of interest to us, extent of resection of the structural lesion and prevalence of interictal epileptiform activity were 'significantly associated with surgical outcome' ($P < 0.001$ and $P = 0.013$, respectively);

however researchers did not specify the direction of association for either variable.

- Sarkis 2012 entered the following variables (significant in univariate analyses) into multi-variate Cox proportional hazards regression: type of resection, pre-operative auras, incomplete resection, presence of postoperative spikes, age at seizure onset, and prior epilepsy surgery. Among the variables of interest to us, incomplete surgical resection and presence of postoperative spikes are "correlated with seizure recurrence" (P = 0.03 and P = 0.0003, respectively).
- Schramm 2011 presented unclear information on which variables from a list of "confounders" researchers entered into multi-variable logistic regression analysis. Study authors stated, "Extent of resection and surgery type interacted, as did extent of resection and centre (p = 0.073)"; however they did not discuss any association between extent of resection and seizure outcome. It remains unclear whether any other variables of interest to us were included in the model.

Three studies reported P values plus regression coefficients (Boesebeck 2007; Kim 2010a; Sagher 2012). None of these studies seemed to enter variables into the multi-variable model based on statistical significance; however it is unclear for all three studies exactly which variables researchers had entered into the models. Regression coefficients could not be converted to treatment effects (e.g. odds ratios) in any of the three studies.

- In Boesebeck 2007, details are unclear regarding which 'demographic' and 'histological' data had been entered into a backward stepwise multi-variable logistic regression. Among the variables of interest to us, tumour on histology was significantly associated with a good outcome (regression coefficient 1.358; standard error (SE) 0.67; P = 0.044), and vascular lesions and malformation of cortical development (MCD) on histology were not significantly associated with outcome (regression coefficient 0.40; SE 0.94; P = NS; and regression coefficient 0.39, SE 0.62; P = NS, respectively).
- Kim 2010a entered extent of resection, EEG findings, MRI findings, and pathology findings (not further defined) into multi-variate logistic regression analysis. Among the variables of interest to us, visible lesion on MRI and extent of resection of electrodes were significantly associated with outcome (P < 0.001, likelihood ratio 12.7; and P = 0.008, likelihood ratio 7.1, respectively); however study authors did not specify the direction of association. It also appears that researchers entered presence of tumour and presence of cortical dysplasia on pathology into the model, but they mentioned no numerical results for these variables.
- Sagher 2012 analysed the following variables via generalised estimating equations: type of operation, extent of resection of mesial temporal structures, sex, participant age at operation, handedness, pre-operative secondary generalisation, age at onset of epilepsy, duration of epilepsy, dual pathology, complications, and grid implantation. Among the variables of interest to us, increasing percentage of various mesial temporal structures (amygdala, hippocampus, entorhinal cortex, total) was significantly associated with good outcome, and implantation of grids and/or depth of electrodes was significantly associated with poor outcome (coefficient 0.12; SE 0.06; P = 0.05).

Two studies reported a mixture of P values and treatment effect sizes (Janszky 2003a; Spencer 2005).

- Janszky 2003a entered the following variables into stepwise logistic regression analyses (variables not selected based on statistical significance): complex febrile seizures (CFCs), unilateral interictal epileptiform discharges, tonic-clonic seizures, perinatal insult, or side of surgery. Researchers reported numerical results only for variables that were significant in multi-variable analysis; among the variables of interest to us, results showed that history of CFC (odds ratio (OR) 5.9, 95% CI 1.26 to 27.7; P = 0.023), where OR > 1, was associated with a good surgical outcome. Study authors also stated that history of perinatal insult, unilateral epileptiform discharges concordant with the operated side, and side of surgery had "no influence on post-operative outcome".
- For Spencer 2005, it is unclear which of the variables from a long list of 'independent variables' researchers had entered into the multi-variable proportional hazards model; variables did not seem to be entered based on statistical significance. Study authors reported numerical results only for variables that were significant in multi-variable analysis. Among the variables of interest to us, results showed that presence of hippocampal atrophy on MRI (RR 1.58, 95% CI 1.13 to 2.21; P = 0.007), where RR > 1, is a predictor of two-year remission. Study authors also stated that a history of febrile seizures did not "approach significance"; it is unclear whether investigators included in the model any other variables of interest to us.

Three studies reported risk ratios (RRs) or hazard ratios (HRs) from multi-variable Cox proportional hazards models (Lopez-Gonzalez 2012; McIntosh 2012; Phi 2009). All three studies entered variables into multi-variable analysis based on statistical significance at univariate analysis, but none of these studies seemed to selectively report the results of multi-variable analysis based on statistical significance.

- Lopez-Gonzalez 2012 entered the following variables (significant in univariate analyses) into multi-variable analysis: side of surgery (left), number of antiepileptic drug trials (more than four), tumour aetiology, and extensive surgical resection (lesionectomy plus cortico-amygdalohippocampectomy). Among the variables of interest to us, tumour aetiology and right side of resection were not significant predictors of seizure freedom (RR 0.72, 95% CI 0.30 to 1.48; and RR 1.59, 95% CI 0.92 to 2.76, respectively), but extensive surgical resection was a significant predictor of seizure freedom (RR 0.13, 95% CI 0.007 to 0.64; P = 0.007).
- McIntosh 2012 conducted two multi-variable analyses.

Study authors entered the following variables into the first model: pathology (lesion (tumour), acquired insult, cortical dysplasia, non-specific) and extent of resection. For the second model, they entered the variables that were significant in the first multi-variable analysis plus presence or absence of early postoperative seizures. Among the variables of interest to us, model one shows that incomplete resection was a significant risk factor for seizure recurrence (HR 1.71, 95% CI 1.06 to 2.76; P = 0.028), but model two shows that incomplete resection was no longer a significant risk factor (HR 0.98, 95% CI 0.59 to 1.63; P = 0.95). Also, in both models one and two, pathology of FCD compared to other pathologies is a significant risk factor for seizure recurrence (model one: HR 1.90, 95% CI 1.08 to 3.34; P = 0.025; model two: HR 1.54, 95% CI 0.87 to 2.42; P = 0.014).

- In Phi 2009, it is unclear which variables from a long list of "patient-related factors" and "treatment-related factors" were significant at univariate analysis and had been entered into analysis. Among the variables of interest of us, failure of macroscopic total resection was significantly associated with poor outcome (RR 18.22, 95% CI 3.81 to 87.09; P < 0.001). It is unclear if any other variables of interest to us were included in the model.

The remaining eight studies reported odds ratios from multi-variable logistic regression models (Cossu 2008; Gelinas 2011; Kim 2009; O'Brien 2000; Radhakrishnan 1998; Tezer 2008; Wyler 1995; Yang 2011). Four studies entered variables into the multi-variable model based on statistical significance in univariate analyses (Cossu 2008; Kim 2009; Radhakrishnan 1998; Tezer 2008); for five studies, it is not clear exactly which variables researchers had entered into multi-variable analysis (Gelinas 2011; Kim 2009; Radhakrishnan 1998; Tezer 2008; Yang 2011); and three studies selectively reported multi-variable model results based on statistical significance (Cossu 2008; Kim 2009; Tezer 2008).

- Cossu 2008 entered the following variables (significant in univariate analysis) into multi-variable analysis: sex, neurological status, age at seizure onset, duration of epilepsy, seizure frequency, MRI findings, use of video EEG and stereoelectroencephalography, age at surgery, type of surgery, side and site of surgery, extent of lesion resection, histology of resected tissue, length of follow-up. Among the variables of interest to us, results show that complete lesionectomy and histological diagnosis of neuronal/glial-neuronal tumour were significantly associated with surgical outcome (OR 0.40, 95% CI 0.23 to 1.01; P = 0.05; and OR 0.19, 95% CI 0.05 to 0.53; P = 0.004, respectively).
- For Gelinas 2011, it is unclear which of the variables from 'clinical characteristics' researchers had entered into analysis. Among the variables of interest to us, use of ECoG (intracranial monitoring) was not associated with seizure freedom at one year or at most recent follow-up (OR 0.71, 95% CI 0.21 to 2.43; P = 0.59; and OR 0.44, 95% CI 0.14 to 1.34; P = 0.15, respectively). It is unclear whether any other variables of interest to us were included in the model.
- For Kim 2009, it is unclear which of the variables from a long list of 'clinical characteristics' and 'prognostic factors' were significant variables at univariate analysis and had been entered into analysis. Among the variables of interest to us, results show that complete resection of the epileptogenic area was associated with seizure outcome (OR 4.94, 95% CI 2.41 to 10.14; P < 0.001). It is unclear whether any other variables of interest to us were included in the model.
- O'Brien 2000 conducted two multi-variable analyses. For the first model, researchers entered the following variables: subtraction ictal SPECT co-registered with MRI (SISCOM) regional localisation (concordant vs non-concordant/non-localising), pre-operative MRI findings (lesional vs non-lesional), and ictal scalp EEG findings (localising vs non-localising). For the second model, researchers entered the following variables: extent of excision of the SISCOM focus, pre-operative MRI findings, and ictal scalp EEG findings. Neither model showed the presence of focal structural lesions to be a significant predictor of surgical outcome (OR 2.3, P = 0.32; and OR 4.7, P = 0.28, respectively). The second model showed complete excision of SISCOM focus to be a significant predictor of surgical outcome (OR 201.0, P = 0.03).
- For Radhakrishnan 1998, it is unclear which of the variables were significant variables at univariate analysis and had been entered into analysis. Among the variables of interest to us, results show that the presence of MRI-detected unilateral hippocampal formation atrophy "is a predictor of excellent seizure control" (OR 3.7, 95% CI 1.2 to 11.71; P = 0.024). It is unclear whether any other variables of interest to us were included in the model.
- For Tezer 2008, it is unclear which 'continuous' and 'categorical' variables were significant variables at univariate analysis and had been entered into analysis. From the variables of interest to us, results show that the presence of history of trauma was "predictive for worsening of outcome" (OR 0.33, 95% CI 0.003 to 0.38; P = 0.05). It is unclear whether any other variables of interest to us were included in the model.
- Wyler 1995 entered the following variables into multi-variable analysis: extent of resection (partial vs total hippocampectomy), age at surgery, age at onset of epilepsy, laterality of surgery, gender, and presence/absence of hippocampal sclerosis. Among the variables of interest to us, results show that total hippocampectomy (compared to partial hippocampectomy) was associated with seizure freedom (OR 4.2, P = 0.02), but the presence of hippocampal sclerosis was not associated with seizure freedom (OR 2.0, P = 0.32).
- For Yang 2011, it is unclear which of the variables from 'data collected' researchers had entered into analysis. Among the variables of interest to us, results show that concordance of MRI with EEG and presence of hippocampal sclerosis were

significantly associated with outcome (OR 6.33, 95% CI 1.44 to 27.81; P = 0.015; and OR 18.06, 95% CI 4.48 to 72.88; P < 0.001, respectively), but complete resection and use of subdural electrodes were not significantly associated with outcome (OR 0.60, 95% CI 0.06 to 5.76; P = 0.659; and OR 0.61, 95% CI 0.14 to 2.68; P = 0.52, respectively).

Summary of adjusted analyses

It is difficult to summarise the adjusted results of the 26 studies described above due to different statistical methods used, different variables entered into the models chosen according to different criteria, and variable levels of detail in the reporting of multi-variable results.

Overall, none of the reported prognostic models included encephalomalacia as a factor; one included vascular malformations; two included concordance of MRI and EEG, head injury, and distribution of interictal spikes; three included focal cortical dysplasia, febrile seizures, and use of intracranial monitoring; four included MRI results, tumour, and postoperative discharge; five included side of resection; six included mesial temporal sclerosis; and 18 included extent of resection.

Due to the different combinations of variables entered into multi-variable models and therefore lack of adjustment of adjusted results for the same factors, direct comparison of the multi-variate analysis versus the univariate meta-analysis reported in this review is difficult.

Generally the direction of association of variables with outcome was the same in multi-variable analyses as in univariate meta-analyses. The only differences of note were that no multi-variable models found an association between side of surgery and outcome (the significant advantage for right-sided resection in Analysis 4.14), or between distribution of interictal spikes and outcome (the significant advantage for unilateral spikes in Analysis 4.11).

However, we note that for all but one study (O'Brien 2000), we had judged statistical analysis and reporting of multi-variable models to be at moderate or high risk of bias; therefore we recommend caution when any numerical results from multi-variable models are interpreted. Many of the multi-variable models included only variables that were significant at univariate analysis, or for which some variables did not retain significance in adjusted analysis (in other words, the aim of the model may have been to investigate which variables would not retain significance). This approach to multi-variable analysis may explain why no significant association was found between certain variables and outcomes in some studies, whereas a univariate association was shown in this review. Furthermore, many studies reported results only for variables that showed a statistically significant association with outcome. Therefore, there might have been more instances in which a factor of interest to us was shown not to be associated with outcome by a multi-variable model, but this information is not provided in the published study paper.

In several instances, researchers reported that variables were associated with outcome (particularly extent of resection) but did not specify the direction of the association (variably associated with good or poor outcome); reporting an association without a direction is of little clinical utility for practice.

ADDITIONAL SUMMARY OF FINDINGS [Explanation]

Comparison of surgical interventions for epilepsy

Patient or population: adults and children with drug-resistant epilepsy suitable for surgical intervention
Settings: outpatients (following surgery in hospital)
Intervention: experimental surgical intervention (see comments)
Comparison: control surgical intervention (see comments)

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control surgical intervention (see comments)	Experimental surgical intervention (see comments)				
Proportion free from seizures (Engel Class 1 or 1A) at 1 year and at 5 years	There were no clear differences between the ATL, SAH and PHC groups in terms of seizure freedom (by either Engel Class definition) at 1 year or at 5 years		NA	43 (1 study)	⊕⊕◯◯ **low** [a,b]	Interventions are anterior temporal lobectomy (ATL), selective amygdalohippocampectomy (SAH) or parahippocampectomy (PHC). All pairs of interventions were compared
P roportion with remission of seizures (at least Engel Class IB) between 25 and 36 months	**778 per 1000**	**513 per 1000** (350 to 770 per 1000)	**RR 0.66** (0.45 to 0.99)	58 (1 study)	⊕⊕◯◯ **low**[b,c]	Experimental Intervention is Stereotactic radiosurgery (SRS) Control intervention is anterior temporal lobectomy (ATL) RR > 1 indicates advantage for SRS

Proportion free from seizures (Engel Class 1) at 1 year	**650 per 1000**	**741 per 1000** (494 to 1000 per 1000) [d]	**RR 1.14** (0.76 to 1.70)	43 (1 study)	⊕⊕◯◯ **low**[e,f]	Experimental Intervention is resection with corpus callosotomy (CCT) Control intervention is resection only RR > 1 indicates advantage for resection with CCT The RR of seizure freedom for the resection with CCT group compared to the resection only group at 3 years was 1.19 (95% CI 0.72 to 1.95; P = 0.50) and at 5 years was 1.09 (95% CI 0.53 to 2.21; P = 0.82)
Proportion free from seizures (Engel Class 1) at 2 years	**600 per 1000**	**732 per 1000** (510 to 1000 per 1000) [d]	**RR 1.22** (0.85 to 1.76)	60 (1 study)	⊕⊕⊕◯ **moderate**[e]	Experimental Intervention is anterior temporal lobectomy with corpus callosotomy (aCCT) Control intervention is anterior temporal lobectomy without corpus callosotomy (ATL) RR > 1 indicates advantage for aCCT
Proportion free from all seizures (including auras, ILAE 1a) at 1 year	**640 per 1000**	**589 per 1000** (378 to 934 per 1000)	**RR 0.92** (0.59 to 1.46)	47 (1 study)	⊕⊕◯◯ **low**[b,g]	Experimental intervention is Subtemporal selective amygdalohippocampectomy (SAH) Control intervention is Transsylvian SAH

						RR > 1 indicates advantage for Subtemporal SAH
Proportion free from all seizures (including auras) at 1 year	**382 per 1000**	**695 per 1000** (428 to 1000 per 1000) [d]	**RR 1.82** (1.12 to 2.93)	70 (1 study)	⊕⊕◯◯ **low**[b,c]	Experimental intervention is total resection Control intervention is partial resection RR > 1 indicates advantage for total resection
Proportion free from seizures (Engel Class 1) at 1 year	**728 per 1000**	**743 per 1000** (626 to 874 per 1000)	**RR 1.02** (0.86 to 1.2)	207 (1 study)	⊕⊕⊕◯ **moderate**[b]	Experimental Intervention is a 2.5-cm resection Control intervention is 3.5-cm resection RR > 1 indicates advantage for 2.5-cm resection

*The basis for the **assumed risk** is the event rate in the control group (medical treatment). The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
aCCT: anterior temporal lobectomy with corpus callosotomy; ATL: anterior temporal lobectomy without corpus callosotomy; CCT: corpus callosotomy; CI: confidence interval; RR: risk ratio; parahippocampectomy (PHC); selective amygdalohippocampectomy (SAH)

GRADE Working Group grades of evidence.
High certainty (quality): further research is very unlikely to change our confidence in the estimate of effect.
Moderate certainty (quality): further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low certainty (quality): further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low certainty (quality): we are very uncertain about the estimate.

[a] Downgraded due to risk of bias: outcome assessors of the study were not blinded
[b] Downgraded for indirectness: results are applicable to adults (18 years and over only), with children excluded from the study.
[c] Downgraded due to insufficient information regarding methods of randomisation and allocation concealment in the study.
[d] Upper bounds of corresponding risk interval revised to their maximum to align with the upper bound of the confidence interval of the relative effect.
[e] Downgraded due to risk of bias: inadequate method of quasi-randomisation used (allocation based on odd and even participant ID numbers) and unclear if participants/personnel/outcome assessors were blinded.

[f] Downgraded for indirectness: results are applicable to children and adolescents (under 18 years only), with adults excluded from the study.
[g] Downgraded due to risk of bias: participants not completing one year of follow-up measures were excluded from the study and an intention to treat approach was not taken

DISCUSSION

Summary of main results

We have identified 182 studies investigating the outcome of surgery for epilepsy. These 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. These studies carried out a wide range of surgical techniques and used different scales to measure the outcome of surgery.
Nineof the 182 studies used a randomised controlled trial (RCT) design: two that randomised surgery and medical treatment, six that randomised types of surgical technique (i.e. anterior temporal lobectomy (ATL) with or without corpus callosotomy (CCT), partial or total hippocampectomy, ; resection of the epileptogenic region with or without CCT in children with Lennox-Gastaut syndrome, stereotactic radiosurgery (SRS) or ATL, subtemporal or transsylvian approach to selective amygdalohippocampectomy (SAH), and ATL, SAH or parahippocampectomy (PHC)), and one that randomised length of surgical resection (2.5-cm vs 3.5-cm resection).
The two RCTs that randomised surgery and medical treatment found surgery to be superior to medical treatment in terms of freedom from seizures at one year (risk ratio (RR) 9.78, 95% confidence interval (CI) 4.73 to 20.21; P < 0.00001), and one of the these RCTs found surgery to be superior to medical treatment in terms of freedom from all seizures including auras at one year (RR 15.00, 95% CI 2.08 to 108.23; P = 0.007). Results show no statistically significant differences between ATL with or without CCT in terms of seizure freedom at two years (RR 1.22, 95% CI 0.85 to 1.76; P = 0.28), between subtemporal and transsylvian SAH (RR 0.92, 95% CI 0.59 to 1.46; P = 0.73), or between 2.5-cm and 3.5-cm ATL resection (RR 1.02, 95% CI 0.86 to 1.20; P = 0.84) in terms of seizure freedom at one year, respectively. Data also show no statistically significant differences between resection with CCT and resection only at one year (RR 1.14, 95% CI 0.76 to 1.70; P = 0.53), at three years (RR 1.19, 95% CI 0.72 to 1.95; P = 0.50), or at five years (RR 1.09, 95% CI 0.53 to 2.21; P = 0.82) or between any pair of ATL, SAH and PHC at 1 year or at 5 years in terms of seizure freedom. Results show a statistically significant advantage of total over partial hippocampectomy in terms of seizure freedom at one year (RR 1.82, 95% CI 1.12 to 2.93; P = 0.01) and for ATL over SRS (RR 0.66, 95% CI 0.45 to 0.99; P = 0.04) in terms of seizure remission between 25 months and 36 months after surgery.
The 182 studies included in this review included 16,501 participants with adequate data relating to outcomes of surgery, 10,696 (65%) of whom achieved a good outcome of surgery, ranging across studies from 13.5% to 92.5% of participants. We found reporting of related adverse events to be sparse and very poor; less than half of included studies reported complications and/or surgery-related deaths, often lacking specific details of the nature and consequences of the event (transient or permanent) and event timing. Few studies contained any reference to postoperative cognition or mental state.
A total of 119 studies examined between one and nine factors of interest for this review in univariate relation to outcome of surgery. We found abnormal pre-operative magnetic resonance imaging (MRI), no use of intracranial monitoring, complete surgical resection, presence of mesial temporal sclerosis, concordance of pre-operative MRI and electroencephalography (EEG), history of febrile seizures, absence of focal cortical dysplasia/malformation of cortical development, presence of tumour, right-sided resection, and presence of unilateral interictal spikes to be independently associated with a good outcome of surgery. We found no evidence that history of head injury, presence of encephalomalacia, presence of vascular malformation, and presence of postoperative discharges were independent, univariate prognostic factors for outcome of surgery. We observed variability between studies in many of our analyses, likely due to small study sizes with unbalanced group sizes, variation in the definition of the seizure outcome, definition of the prognostic factor (e.g. the definition of a 'complete' resection varied across studies), and the influence of the site of surgery, which we have observed to be related to postoperative seizure outcome.
Twenty-nine studies presented multi-variable prognostic models, and 26 of these provided clear adjusted results for the association of independent variables with the dependent variable of seizure freedom. None of the studies included encephalomalacia as a factor; one included vascular malformations; two included concordance of MRI and EEG, head injury, and distribution of interictal spikes; three included focal cortical dysplasia, febrile seizures, and use of intracranial monitoring; four included MRI results, tumour, and postoperative discharge; five included side of resection; six included mesial temporal sclerosis; and 18 included extent of resection. Generally the direction of association of variables with outcome was the same in multi-variable analyses as in univariate meta-analyses. However, due to different combinations of variables entered into the multi-variable models, different (often inappropriate) statistical approaches used to modelling, and selective reporting of results, meaningful comparison of multi-variate analysis versus the univariate meta-analysis reported in this review is difficult. We recommend caution when results of the univariate meta-analysis and the narratively reported multi-variable analyses are interpreted.

Overall completeness and applicability of evidence

Completeness of evidence

We were aware that most of the evidence for this review was likely to be derived from non-randomised studies; however no Cochrane-approved or -recommended search filter is available for

non-randomised studies. The Trial Search Co-ordinators for the Cochrane Epilepsy Group chose the search strategies implemented and did not subject the resulting search filters to any systematic testing before use. We do believe that our systematic electronic searches identified the vast majority of relevant evidence for this review, and given the large number of studies included in this review, it is unlikely that any evidence not identified by the electronic searches would change the review conclusions.

We were able to extract data for 16,756 participants from 182 eligible studies who had surgery, and the large number of participants that we included in this review is reflected in the precision of our results. However, we believe that some of the studies we had to exclude from the review (see Excluded studies) could possibly have been included if additional information regarding follow-up had been available, or if study authors had presented data in an extractable way. For example, several studies reported only percentages, P values, or coefficients of regression models for prognostic factors related to outcome, and we were unable to extract raw data for the number of participants with and without the prognostic factor achieving good or poor outcome of surgery for inclusion in our univariate analyses; other researchers provided insufficient detail regarding multi-variable analyses of prognostic factors to allow for meaningful comparison with univariate analyses.

Furthermore, several studies reported outcome as 'favourable' (usually Engel Classes 1 and 2 combined) versus 'unfavourable' (Engel Classes 3 and 4 combined) rather than as 'good' versus 'poor' (Engel Class 1 vs Engel Classes 2 to 4). We strongly believe there is a large difference between a 'good' outcome and a 'favourable' outcome of surgery for epilepsy. Therefore we believe it was not appropriate to extract data on prognostic factors expressed as 'favourable' versus 'unfavourable.' However, if the data had been presented in a different way, for example, if each Engel Class 1 to 4 had been presented by the prognostic factor of interest, we would have been able to include this information, further improve the precision of our results, and possibly reduce variability between studies in our results.

Applicability of our results

The potential efficacy of temporal and extratemporal resection for people with a focal epilepsy uncontrolled by antiepileptic medication is undisputed (Engel 2003), and our review, which showed that about two-thirds of patients have a good surgical outcome, has confirmed this. For temporal resection, Engel's practice parameter focuses on the single intention-to-treat RCT of surgery for mesial temporal lobe epilepsy (Wiebe 2001), which found that 58% of participants randomised to be evaluated for surgical therapy (64% of those who received surgery) were free of disabling seizures at one year, compared with 8% free of disabling seizures in the group randomised to continued medical therapy. The recent consensus from the International League Against Epilepsy proposes that treatment success should be defined by sustained freedom from seizures (Kwan 2010b), as this is the only efficacy outcome that is 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 in this review on at least 12 months of seizure freedom. Using this measure, Costa 2011 showed in a meta-analysis that the overall weighted pooled risk difference in favour of newer antiepileptic drugs compared with placebo for freedom from seizures during limited study periods was only 6% (95% confidence interval (CI) 4% to 8%; number needed to treat in terms of freedom from seizures with newer drugs as add-on therapy ranged from 9 to 19 (mean 11.3)). The message for the clinician facing a person with intractable epilepsy in consultation is therefore clear. The chance of helping with the next antiepileptic drug is 1 in 11, and the chance of helping with surgery is 2 in 3, if selection criteria are met.

Furthermore, we have observed that overall surgical procedures have a low rate of complications, and this finding is consistent with other reports showing that less than 5% of patients have permanent postoperative neurological deficits secondary to accidental damage of central nervous system (CNS) tissue (Engel 1996; Engel 2003). As stated, the figure given here for adverse events of 7.3% is highly likely to represent an overestimation of prevalence for 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. Having said this, very few studies address the important issue of formally reassessing any postoperative impairment of cognition, speech and language, and social functioning or altered mental state (all linked to quality of life). Researchers should write this aspect into research protocols.

The poor recording of adverse event data in the included studies is lamentable. Most studies recorded no data at all. No significant improvement has occurred over the past 10 years since the Tonini 2004 review. When any intervention study is carried out, researchers should provide detailed assessments of both risks and benefits. We are surprised how journal editors continue to accept papers for publication without requiring adverse event reporting. The required standard should be to report how many events are recorded in how many participants, and to make it clear which are postoperative complications, which are transient events (within a set period), and which are permanent new impairments. Protocols should include pre-operative and postoperative measures of speech and language function, cognition, and social functioning, along with a mental state assessment.

The criteria adopted to identify indications and applications of epilepsy surgery are constantly evolving. Continuing attempts must be made to define patient- and procedure-related prognostic indicators. Our systematic review shows that the strongest predictors of success of surgery include, in decreasing order, extent of resection (especially for extratemporal surgery), an abnormal MRI finding, concordance between neuroimaging and EEG findings, tumour, mesial temporal sclerosis, unilateral EEG discharges especially when extratemporal, a history of febrile seizures, and vascular malformations. By contrast, adverse prognostic factors include

the need for intracranial monitoring and the presence of postoperative discharges (particularly those seen extratemporally).

The extent of resection, particularly with extratemporal surgery, was the strongest determinant of outcome in our review. 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. It is clear that this is one area in which further RCTs may inform future practice with good effect. We identified two trials using this design - Schramm 2011 (with Helmstaedter 2011 reporting on a sub-set from Schramm 2011) and Wyler 1995. The primary intention-to-treat analysis did not show benefit for the seizure freedom rate in the more extensive resection group in Schramm 2011 but did demonstrate benefit in Wyler 1995.

Tumours carry a higher chance of seizure remission at 12 months when compared with other CNS disorders (risk ratio (RR) present vs absent for 12-month remission 1.23, 95% CI 1.14 to1.32). This finding is readily understood in that the epileptogenic area is more easily detectable and defined both on neuroimaging and at operation. Non-tumoural lesions often have a more diffuse pathology; many of these are less easily resectable, resulting in a poor surgical outcome. In this heterogeneous group, we observed inferior 12-month remission pooled risk ratios: encephalomalacia RR for present versus absent 0.67 (95% CI 0.37 to 1.21); neuronal migration disorders including focal cortical dysplasias RR for present versus absent 0.90 (95% CI 0.85 to 0.95); and vascular malformations RR for present versus absent 1.07 (95% CI 0.94 to 1.21). In these instances, the margin both on the MRI scan and at operation is often difficult to define.

The good outcome associated with the presence of any abnormal MRI findings is expected and probably largely reflects a variety of CNS conditions that we know are associated with a good prognosis, such as tumour, mesial temporal sclerosis (MTS), and many congenital malformations. These are discrete structural lesions that lend themselves to complete resection. We note moderate heterogeneity between studies, in part accounted for by the degree of definition of MRI abnormality in individual studies. So, non-specific or ill-defined white matter abnormalities described in one study may well dilute the benefit of a well-defined area of MTS or tumour noted in another study. A reasonable prospect of seizure freedom is not ruled out with a normal MRI. Bell 2009 reported an Engel Class 1 outcome at 12 months in 60% (24/40) of people following anterior temporal lobectomy for medically refractory temporal lobe epilepsy, but it should be noted that one of the inclusion criteria was subtle non-specific MRI findings in the mesial temporal lobe concordant with the area of resection. Jayakar 2008 reported on a cohort (predominantly of children) with non-lesional intractable focal epilepsy undergoing resective surgery. At two years' follow-up, 44 of 101 participants were seizure-free. Outcomes correlated with good outcome included the presence of convergent scalp EEG focal interictal spikes ($P < 0.005$) and completeness of resection ($P < 0.0005$). Dorward 2011 studied children with extratemporal, non-lesional epilepsy. Researchers classified outcome as Engel Class 1 or 2 in 54.5% of the children who underwent resection of the lesion or multiple sub-pial resections. Investigators obtained results by using invasive monitoring with grid/strip electrodes.

The association between MTS and a history of febrile seizures is strong. 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. Thom 2009 studied neocortical neuronal loss and gliosis (temporal lobe sclerosis (TLS)). Investigators identified TLS in 30 of 272 surgically treated cases of hippocampal sclerosis. A history of a febrile seizure was an initial precipitating injury in 73% of patients with TLS compared with 36% without TLS. A history of febrile status was noted in 27% of these cases. Changes in TLS may be due to enhanced vulnerability of superficial cortical neurons to an early cerebral event in the maturing neocortex 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 MTS.

Concordance of EEG/MRI findings is correlated with positive surgical outcome. It is clear that results obtained from individual studies will depend very much on the mix of associated pathologies underlying the epilepsy seen among participants. Studies containing a large number of participants 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 uncertainty surrounds the location and extent of an epileptogenic zone, often accompanied by indeterminate neuroimaging. The association between the need for neuroimaging and a poor outcome is therefore not surprising. In these cases, less than 50% of cases 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 discharge is likely to reflect these very same issues. Some units 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 inform the correct care pathway (see below).

We have already referred to the limitations of this review. We can summarise these as including the following: different criteria for seizure outcome; variable length of follow-up; forced dichotomisation of each putative prognostic predictor; retrospective design for most studies that enhances the risk of bias in data collection and presentation; and variables that were examined most often in univariate analyses without consideration of the role of combined effects of prognostic factors or of other (known or unknown) con-

founders, which may be the true prognostic predictors. We minimised bias in part by using restrictive criteria for study inclusion and by measuring the heterogeneity of study results. The predictive value of prognostic factors was usually higher when heterogeneity of study results was lower.

Despite these limitations, our results provide some clinical guidance for selection of the best surgical candidates. Engel 2003 identified major methodological deficiencies in the published studies on epilepsy surgery, which included retrospective design, scarcity of data on pre-operative seizures, and absence of blinding in seizure outcome assessment. We have to report no quality improvement in the vast majority of the body of literature reviewed here, published since Engel's comments 11 years ago. We would strongly advocate such an improvement and identification of better standards for assessment of surgical outcome in future studies. We would emphasise the need for a prospective design. Examples of this include Helmstaedter 2011, Schramm 2011, and Wyler 1995, already mentioned, which studied the extent of resection and the outcome of temporal lobe surgery; Liang 2010, which reported benefit in improved quality of life and performance IQ for anterior temporal lobectomy combined with anterior corpus callosotomy in people with temporal lobe epilepsy and mental retardation; Oertel 2005, which demonstrated that a waterjet dissector enables a significant reduction in intraoperative blood loss in epilepsy surgery; Velasco 2011, which showed that ictal-single-photon emission computed tomography (SPECT) did not add localising value beyond that provided by EEG-video telemetry and structural MRI that altered the surgical decision and outcome for patients with mesial temporal lob epilepsy with unilateral hippocampal sclerosis (MTLE-HS); and the sentinel work of Wiebe 2001, already referred to. 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 were when Victor Horsley helped the young Scot in 1886.

Many questions remain to be answered, but researchers 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 pre-operative selection, non-lesional focal epilepsy, bilateral and postoperative spikes, and when to stop antiepileptic drugs, among many others. Investigators should always record clear data on risks (adverse events, their nature and timing) and benefits. We are pleased to note that since this review was first published in 2015 (West 2015), RCTs are now being conducted and results published, addressing some of these questions. Outcomes are still not addressing all the issues important in a person's life. We suggest that protocols should include pre-operative and postoperative measures of speech and language function, cognition, and social functioning, along with a mental state assessment. Methodological difficulties and adequate powering will require multi-centre approaches. Researchers have achieved improvements in cancer care over the past three to four decades 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.

Quality of the evidence

Most of the evidence included in this review was of a non-randomised, retrospective design. As detailed in Assessment of risk of bias in included studies and Risk of bias in included studies, at the time of initiation of this review, we did not know of a tool recommended by Cochrane for assessment of the quality of studies using this design. After extensive review of the literature related to quality assessment tools for studies of a non-randomised design, we selected a tool that we believed to be appropriate a priori; however we discovered that it was not effective in separating differences in quality between studies. We also learned that several criteria were not applicable for most of the studies we identified, and that the overall quality rating was dictated by one or two criteria.

Currently, the certainty of evidence for outcomes addressing the primary objective of the review is moderate to very low. We downgraded the evidence due to indirectness, risk of bias, and imprecision arising from small sample sizes in these studies (Summary of findings for the main comparison; Summary of findings 2). Most of the relevant evidence for this review addresses the secondary objective of the review but comes from studies of a retrospective design and has not enabled us to explore the effects of multiple prognostic factors in a single analysis.

Surgical treatment for epilepsy is the only treatment option for a substantial proportion of individuals. Designing randomised trials in which participants could be randomised away from an effective treatment could be considered unethical (the two RCTs that randomised participants to surgical or medical treatment showed a large advantage for surgery over antiepileptic drugs - Dwivedi 2017; Wiebe 2001). Therefore, identifying prognostic factors that are associated with a good outcome of surgery is a very important goal of research.

Until higher-quality evidence becomes available, ideally from studies of a prospective cohort design that aim to examine differences in surgical approaches and specific prognostic factors of interest, it is important that we accurately judge differences in quality of evidence that currently exists. We established from this review that the Effective Public Health Practice Project (EPHPP) Quality Assessment Tool was not appropriate for assessing the quality of retrospective studies of surgery. After considering existing tools developed for risk of bias assessment of studies of a non-randomised design listed in Chapter 13 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), along with the ACROBAT-NRSI (A Cochrane Risk Of Bias Assessment Tool for Non-Randomised Studies of Interventions) tool recently de-

veloped by the methods groups at Cochrane (ACROBAT 2014), we were not able to identify any tool that would be appropriate for most of the studies of the design included in this review. Therefore it is essential that an appropriate tool is developed for assessment of non-randomised studies of all designs, including those without comparator control groups.

Potential biases in the review process

As we have stated, use of a retrospective design in the vast majority of the body of literature reviewed allows great scope for bias in study results with lack of standardisation in data collection, differing durations of follow-up, and lack of blinding for seizure assessment, as reflected by the significant heterogeneity of study results. We have also discussed at length in Overall completeness and applicability of evidence the limitations associated with the search strategy employed, the quality assessment tool used, and the restricted analyses we were able to perform, particularly in terms of multi-variable analyses.

Agreements and disagreements with other studies or reviews

Our results broadly concur with those presented in the Tonini 2004 review (of which RN was a co-author). We have reviewed a substantially larger body of literature. Often this led to identification of greater heterogeneity for studies related to specific ocutome predictors. Nonetheless, the general implications for clinical practice remain the same. This observation serves to emphasise the need for the clinical questions to be refined and for a new body of research with prospective and randomised controlled design to emerge, so that future clinical practice can be better informed by evidence of improved quality.

AUTHORS' CONCLUSIONS

Implications for practice

The poor quality of the data presented in most of the body of literature reviewed, for example, due to lack of uniformity regarding definitions of outcomes, prognostic factors, and measurement times; variable populations; retrospective designs; and inadequate reporting of analysis results means that our results provide limited clinical guidance for selection of the best surgical candidates. Assessment for surgical selection should be offered to all people with a focal epilepsy wherein the first two antiepileptic drugs have failed, and assessment for surgery must be tailored to the individual, with co-morbidities and the whole patient context considered. Given the results of the univariate analysis conducted in this review and supported by multi-variable analyses conducted in the included studies, by which a discrete lesion is identified on magnetic resonance imaging (MRI) and there is good concordance with seizure semiology and ictal electroencephalography (EEG) discharges, more sophisticated pre-operative investigation probably is not required. When one of these pointers is absent, more sophisticated imaging and EEG studies (which may include intracranial electrodes) are needed. Pre-operative assessment of memory function should be carried out on all candidates for temporal lobe surgery. The technology must be used in a setting that includes a good interdisciplinary team. Pre-operative and postoperative assessments should include cognition and mental state; neuropsychological and psychiatric evaluations are essential parts of presurgical evaluation and should also be scheduled after surgery, at a minimum at three to four months and at one year.

Implications for research

The case has already been made for surgical resection of the epileptogenic zone for intractable focal epilepsy in carefully selected cases. Future research should have a prospective cohort or randomised controlled trial (RCT) design, should be appropriately powered, and should focus on specific issues related to diagnostic tools, the site-specific surgical approach, and other issues such as extent of resection. Researchers should investigate prognostic factors related to the outcome of surgery via multi-variable statistical regression modelling, whereby variables are selected for modelling according to clinical relevance and all numerical results of prognostic models are fully reported. Protocols should include pre-operative and postoperative measures of speech and language function, cognition, and social functioning, along with a mental state assessment. Investigators must record adverse events; journal editors should not accept papers that report studies that did not record adverse events from a medical intervention. We found that the Effective Public Health Practice Project (EPHPP) Quality Assessment Tool was not appropriate for assessing the quality of retrospective studies of surgery, and to the best of the review authors' knowledge, an appropriate tool does not exist and needs to be developed. Researchers have achieved improvements in cancer care over the past three to four decades 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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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Aaberg 2012

Methods	Retrospective case series
Participants	54 children from a single Norwegian centre
Interventions	Lesionectomy or hemispherotomy; 44 had resective surgery, temporal and extratemporal
Outcomes	Assessed as Engel class at 12 and 24 months post surgery
Notes	-

Adam 1996

Methods	Prospective case series
Participants	30 adults aged 18 to 44 from a single French centre
Interventions	Anteromedial temporal lobe resections
Outcomes	Seizure outcome assessed by Engel class at a mean of 24 months and at least 12 months after surgery
Notes	-

Adelson 1992

Methods	Retrospective case series
Participants	33 children younger than 15 years of age at 1 American centre
Interventions	Temporal or extended temporal lobe resections
Outcomes	Seizure outcome assessed by the presence of seizure freedom at least 18 months after surgery
Notes	-

Alfstad 2011

Methods	Retrospective case series
Participants	48 patients - adults and children younger than 14 years old - who had had surgery for epilepsy
Interventions	Type of surgery: temporal and extratemporal

Alfstad 2011 (*Continued*)

Outcomes	Seizure outcome assessed at 2 years post surgery using Engel's classification
Notes	-

Alonso-Vanegas 2018

Methods	Pilot, unblinded randomised controlled trial conducted at a tertiary-care neurological center located in Mexico City,
Participants	Adult participants, over the age of 18 years of age, with medically refractory mesial temporal lobe epilepsy and hippocampal sclerosis (typical clinical seizures, mesial temporal lobe focal MRI findings, and concordant epileptiform activity with ILAE pathologic confirmation of HS,failure to acceptably control seizures with 2 to 3 antiepileptic drugs over 2 years)
Interventions	Randomisation to anterior temporal lobectomy (ATL, n = 14), selective amygdalohippocampectomy (SAH, n = 15) or parahippocampectomy (PHC, n = 14)
Outcomes	Freedom from seizures according to the Engel Class Scale at 1 year and 5 years after surgery
Notes	

Althausen 2013

Methods	Retrospective case series
Participants	61 children (aged 6 years and older) and adults from a single German centre
Interventions	Hemispherectomy
Outcomes	Reported as seizure-free at least 12 months after surgery
Notes	-

Arruda 1996

Methods	Retrospective case series
Participants	74 adults from a single Canadian centre
Interventions	Selective amygdalohippocampectomy or anterior temporal lobe resection
Outcomes	Seizure outcome assessed by Engel class at a mean of 33.1 months
Notes	Study of people with non-lesional temporal lobe epilepsy who had MRI volumetric studies

Awad 1991

Methods	Retrospective case series
Participants	47 children and adults from a single American centre
Interventions	Surgical objectives included biopsy of the structural lesion and maximum resection of the lesion as defined on neuroimaging studies and of the epileptogenic area when possible. Lesions were temporal and extratemporal
Outcomes	Seizure outcome assessed as seizure-free at 12 months
Notes	-

Babini 2013

Methods	Retrospective case series
Participants	30 participants, 3 to 18 years of age, from a single Italian centre, who underwent surgery for histopathologically confirmed low-grade tumours, in which seizures were the only clinical manifestation
Interventions	Lesionectomy or tailored lesionectomy (i.e. tumour plus neighbouring epileptogenic region)
Outcomes	Assessed as Engel class at least 12 months post surgery
Notes	-

Barbaro 2018

Methods	Randomised controlled trial conducted at 14 treatment centers based in the USA, UK, and India
Participants	Participants over the age of 18 years who were eligible for anterior temporal lobectomy (ATL) to treat pharmaco-resistant unilateral mesial temporal lobe epilepsy (MRI evidence of concordant unilateral hippocampal sclerosis without significant secondary cortical lesions and at least 3 focal-onset seizures with impairment of consciousness occurred during stable anticonvulsant administration documented over three months),
Interventions	Randomisation to stereotactic radiosurgery (SRS, n = 31 analysed) or anterior temporal lobectomy (ATL, n = 27 analysed); a total of 63 participants were randomised and five withdrew before surgery
Outcomes	Seizure remission outcome is defined by the seizure-free (defined as at least Engel scale IB) rate between 25 and 36 months Adverse events Verbal memory and quality of life (not relevant to this review)
Notes	

Battaglia 2006

Methods	Case series; unclear whether prospective or retrospective
Participants	45 children with refractory epilepsy operated on before 7 years from 1 Italian centre
Interventions	19 had hemispherectomy, 9 had multi-lobar resection, 17 had focal resection - 9 temporal, 4 frontal, 4 parieto-occipital
Outcomes	Seizure outcome at least 2 years after the time of surgery
Notes	Focus on neurocognitive outcome

Baumann 2007

Methods	Multi-centre retrospective case series
Participants	Participants were 168 consecutive children and adults with a single supratentorial cerebral cavernous malformation and symptomatic epilepsy. Centres in Switzerland, Italy, Germany, USA, and Canada
Interventions	Type of surgery: temporal and extratemporal
Outcomes	Seizure outcome by Engel class was determined in the first, second, and third postoperative years
Notes	-

Bautista 2003

Methods	Retrospective case series
Participants	55 patients aged 17 to 57 years with a histopathological diagnosis of focal cortical dysplasia
Interventions	Types of surgery - temporal and extratemporal
Outcomes	Seizure outcome after at least 12 months of follow-up from the time of surgery
Notes	-

Bell 2009

Methods	Retrospective case series
Participants	44 patients, 13 to 62 years of age, with a non-lesional modern "seizure protocol" MRI, who underwent anterior temporal lobectomy for treatment of medically refractory partial epilepsy
Interventions	Temporal lobe surgery
Outcomes	Seizure outcome measured using Engel's classification at least 1 year post surgery

Bell 2009 (*Continued*)

Notes	Study of people with "non-lesional MRIs"

Benifla 2006

Methods	Retrospective case series
Participants	126 children who had surgery at 1 Canadian centre over a 10-year period
Interventions	Anterior temporal lobectomy (ATL) with resection of mesiotemporal structures. The resection margin extended 5 to 6 cm from the temporal pole of the non-dominant hemisphere (and included the superior temporal gyrus) , and 4 to 5 cm in the dominant hemisphere, modified according to presentation, imaging findings, and lesion localisation. Patients with dorsal temporal or basal temporal lesions underwent lesionectomy or ATL without removal of mesiotemporal structures. Mesiotemporal structures were removed in certain cases, particularly if lesions impinged upon or involved the hippocampus or the amygdala. Intraoperative ECoG was performed in 94 patients
Outcomes	Seizure outcome assessed using Engel's classification at follow-up at least 24 months after surgery
Notes	-

Berkovic 1995

Methods	Retrospective case series
Participants	135 children and adults from a single Australian centre
Interventions	Standard anterior temporal lobectomy, including partial hippocampectomy, for dominant temporal lobe removal; 3. 5 cm of the lateral temporal lobe was excised; for non-dominant removals, 5.0 cm was excised. The hippocampus was excised microsurgically, usually to the level of the posterior midbrain. Foreign tissue lesions were completely excised when possible, and the anterior 2 cm of hippocampus was also removed. When the foreign tissue lesion was located in the lateral temporal region, the hippocampus was not resected unless it appeared abnormal on MRI
Outcomes	Seizure outcome assessed as Engel's class at last follow-up (after at least 18 months of follow-up) or as at least 2 years of seizure-free remission at last follow-up
Notes	-

Blount 2004

Methods	Retrospective case series
Participants	30 consecutive Canadian children from 1 centre followed for at least 30 months
Interventions	Multiple subpial transections
Outcomes	Seizure outcome by Engel class determined at mean follow-up of 3.5 years after surgery

Blount 2004 (*Continued*)

Notes	-

Blume 2004

Methods	Retrospective case series
Participants	70 participants with intractable focal epilepsy and no specific lesion, as determined by both MRI and histopathology; age ranged from 6 to 65 years, with a mean age of 31 years
Interventions	Temporal and extratemporal
Outcomes	Seizure outcome measured using Engel's classification at least 2 years post surgery
Notes	Study of non-lesional intractable epilepsy

Boesebeck 2007

Methods	Retrospective case series
Participants	81 patients, aged 16 to 53 years at surgery, from a single German centre, with lesional focal epilepsies of the extratemporal cortex with resistance to at least 2 antiepileptic drugs
Interventions	Extratemporal surgery
Outcomes	Seizure outcome measured using Engel's classification at 2-year follow-up post surgery
Notes	-

Boshuisen 2010

Methods	Retrospective case series
Participants	43 children from a single Dutch centre who had hemispherectomy for intractable hemispheric epilepsy
Interventions	Functional hemispherectomy
Outcomes	Seizure outcome by Engel class determined at least 12 months after surgery
Notes	-

Brainer-Lima 1996

Methods	Retrospective case series
Participants	32 children and adults from a single Brazilian centre with a tumour and intractable epilepsy
Interventions	Temporal corticectomy with amygdalo-hippocampectomy, temporal corticectomy, extratemporal corticectomy, posterior hippocampectomy, and lesionectomy with stereotactic guidance
Outcomes	Seizure outcome assessed by Engel class at a mean of 26.3 months
Notes	-

Britton 1994

Methods	Retrospective case series
Participants	51 children and adults from a single American centre with a tumour and intractable epilepsy
Interventions	Lesionectomy or lesion resection and corticectomy
Outcomes	Seizure outcome assessed by Engel class at least 24 months postoperatively
Notes	-

Caraballo 2011

Methods	Retrospective case series
Participants	45 children, aged 2 months to 18 years, from a single Argentinian centre, with a medically refractory epilepsy and hemispheric lesions
Interventions	Extratemporal
Outcomes	Seizure freedom assessed using Engel's classification at least 1 year post surgery
Notes	-

Cascino 1995

Methods	Retrospective case series
Participants	165 children and adults from a single American centre with intractable temporal lobe epilepsy
Interventions	Temporal lobe surgery
Outcomes	Seizure freedom assessed using Engel's classification at least 1 year post surgery

Cascino 1995 (*Continued*)

Notes	-

Chabardes 2005

Methods	Retrospective case series
Participants	48 consecutive adults from France and Italy with drug-refractory temporal lobe epilepsy
Interventions	All participants underwent tailored anterior temporal lobectomy that included the temporal pole, the hippocampus, the parahippocampal gyrus, and the anterior part of the lateral temporal cortex
Outcomes	Seizure outcome by Engel class determined at least 48 months after surgery and related to site relative to the pole of temporal lobe seizure onset
Notes	-

Chang 2009

Methods	Retrospective case series
Participants	Results on 57 of a total group of 164 American participants with cavernomas and epilepsy
Interventions	Microsurgical resection of supratentorial cerebral cavernous malformations
Outcomes	Seizure outcome by Engel class determined at 12 months after surgery
Notes	-

Chee 1993

Methods	Retrospective case series
Participants	40 adults from a single American centre with temporal lobe epilepsy
Interventions	Temporal lobectomy
Outcomes	Seizure outcome assessed by seizure freedom at least 12 months postoperatively
Notes	This was a study of non-lesional epilepsy with FDG-PET scanning

Chkhenkeli 2007

Methods	Retrospective case series
Participants	129 adults and children from Georgia and the USA with bitemporal epileptiform abnormalities in multiple scalp EEGs
Interventions	Temporal lobectomies were performed in 85 of 129 participants. Temporal lobe resections included 2 modifications of the surgery, depending on hemispheric dominance. The "standard temporal lobe resection" in "en block" modification was performed in the non-dominant hemispheres (29/67 participants). This resection usually included 6.0 to 6.5 cm of lateral cortex, uncus, amygdala, and 2 to 4 cm of the anterior hippocampus. In the dominant hemisphere (38/67 participants), extension of cortical resection was reduced to 3 to 4 cm and usually was performed as a modification named "anterior medial temporal lobectomy". This modification includes incision of the temporal lobe cortex for 3 to 3.5 cm from the temporal pole along the inferior surface of the superior temporal gyrus
Outcomes	Seizure outcome by Engel class determined at 24 months after surgery
Notes	-

Choi 2004a

Methods	Retrospective case series
Participants	35 Korean teenagers and adults with temporal lobe epilepsy associated with tumour
Interventions	Resection of epileptogenic area and tumour (guided by ECoG as required)
Outcomes	Seizure outcome by Engel class determined at a mean of 33 months and at least 15 months after surgery
Notes	-

Chung 2005

Methods	Retrospective case series
Participants	128 adults and children from a single Korean centre with epilepsy secondary to cortical dysplasia diagnosed postoperatively on histology
Interventions	Types of surgery: temporal and extratemporal
Outcomes	Seizure outcome by Engel class determined at least 48 months after surgery
Notes	-

Cossu 2005

Methods	Retrospective case series
Participants	174 children and adults from 1 Canadian centre and 1 Italian centre operated on over a 7-year period
Interventions	Temporal and extratemporal surgery: corticectomy, n = 58; corticectomy and lesionectomy, n = 112; lesionectomy, n = 3
Outcomes	Seizure outcome assessed using Engel's classification at follow-up at least 12 months after surgery
Notes	-

Cossu 2008

Methods	Retrospective case series
Participants	113 children from 1 Italian centre
Interventions	72 had a complete lesionectomy. Resection sites were as follows: 43 temporal, 32 frontal, 20 posterior, and 9 including central: 4 temporal plus and 5 wide multi-lobar
Outcomes	Seizure outcome assessed using Engel's classification at follow-up at least 24 months after surgery
Notes	-

Costello 2009

Methods	Retrospective case series
Participants	42 with disabling, medically refractory focal epilepsy operated on at 1 American centre
Interventions	11 participants underwent a standard left anterior-medial temporal lobectomy (including amygdalohippocampectomy); 17 a standard right anterior-medial temporal lobectomy; 3 a limited left frontal resection; 3 a limited right frontal resection; and 2 a left temporal lesionectomy (without removal of the amygdalohippocampal complex). The following operations were performed in single patients: right temporal neocortical resection of extensive malformation of cortical development, right posterior temporal resection, left posterior temporal resection, right temporal lesionectomy, corpus callosotomy, and left parietal lesionectomy. Intraoperative mapping of language was performed in 2 participants
Outcomes	Seizure outcome was assessed using Engel's classification at between 1 and 14.4 years postoperatively
Notes	Included only those 45 years of age or older

Cukiert 2002

Methods	Prospective case series
Participants	100 adults from a single Brazilian centre
Interventions	Corticoamygdalohippocampectomy on the side of the mesial temporal sclerosis, consisting of cortical resection, including superior, middle, and inferior temporal lobes; fusiform and parahippocampal gyri, with its posterior border at the level of the central artery; total hippocampectomy; and resection of the intratemporal portion of the amygdala. The central artery was used as the landmark for the posterior border of the cortical resection (a proportional method) , instead of distances measured from the tip of the temporal lobe (a quantitative method)
Outcomes	Seizure outcome assessed using Engel's classification at follow-up from 18 to 48 months after surgery
Notes	-

Dagar 2011

Methods	Retrospective case series
Participants	118 children from a single Indian centre, aged 0.3 to 18 years at the time of surgery, with a medically refractory epilepsy
Interventions	Temporal and extratemporal
Outcomes	Seizure outcome as measured using Engel's classification at least 12 months after surgery
Notes	-

Dalmagro 2005

Methods	Retrospective case series
Participants	44 children and adults from a single Brazilian centre with posterior cortex epilepsy
Interventions	Multi-lobar resection, lesionectomy, and lobectomy in 5 (11.63%). According to PO MRI, surgeries were considered complete in 16 (37.21%) and incomplete in 27 (62.79%) of 43 participants. However, completeness of the resection had no influence on surgical outcome
Outcomes	Assessed as Engel class at 12 months post surgery
Notes	-

de Tisi 2011

Methods	Retrospective cohort study
Participants	615 people from a single UK centre, aged 16 to 63 years at surgery, who had undergone surgery for epilepsy
Interventions	Temporal and extratemporal surgery
Outcomes	Seizure freedom assessed using ILAE outcome score at follow-up, at least 12 months from surgery
Notes	-

Delbeke 1996

Methods	Retrospective case series
Participants	38 participants aged 15 to 59 years from a single American centre with temporal lobe epilepsy, who had FDG-PET as part of their pre-operative assessment
Interventions	Lesionectomy with or without neocortical resection
Outcomes	Seizure outcome assessed by Engel class at least 18 months postoperatively
Notes	-

Dellabadia 2002

Methods	Retrospective case series
Participants	Initially 99 children and adults from an American centre admitted for surgical selection with a temporal or extratemporal lobe epilepsy
Interventions	Of 69 participants evaluated, 35 had a focal resection (33 temporal, 2 frontal)
Outcomes	Assessed as Engel class at least 22 months post surgery
Notes	Focus on which pre-operative tests are most discriminatory of good outcome

Devlin 2003

Methods	Retrospective case series
Participants	33 children who underwent hemispherectomy at a single UK centre between 1991 and 1997
Interventions	Functional hemispherectomy involving a modified approach with a limited suprasylvian window but a large temporal lobectomy; the insular cortex was undercut
Outcomes	Assessed as Engel class at least 12 months post surgery

Devlin 2003 (*Continued*)

Notes	-

Ding 2016

Methods	Prospective study with participants "randomly allocated" to either surgical treatment group
Participants	43 Chinese children aged 4 to 18 with Lennox-Gastaut syndrome submitted to surgery with a localised epileptogenic
Interventions	Randomisation to exclusive resective surgery (n = 20) or to resective surgery combined with CCT (n = 23)
Outcomes	Seizure outcome by Engel class determined at 12 months after surgery
Notes	Study conducted to compare the outcome of the 2 surgical approaches. 25 children recruited without a localised epileptogenic zone were enrolled into a 'medical therapy' group; however as this group was not randomised within the study (2018 update), these 25 children are not included within the review

Donadio 2011

Methods	Retrospective case series
Participants	110 participants, children and adults ranging in age from 1 year to 52 years, with a drug-resistant epilepsy
Interventions	Extratemporal and temporal surgery including lesionectomies, lobectomies, callostomies, multiple subpial transections, hemispherectomies, and insertion of vagal nerve stimulators
Outcomes	Assessed using Engel's classification at follow-up at least 12 months after surgery
Notes	-

Dorward 2011

Methods	Retrospective case series
Participants	33 children, aged 3 to 19 years at surgery, with an intractable epilepsy and no lesion on MRI scan, who had invasive EEG monitoring with subdural grid/strip electrodes
Interventions	Extratemporal resections or multiple subpial resections
Outcomes	Seizure outcome assessed using Engel's classification at follow-up at least 12 months after surgery
Notes	-

Duchowny 1998

Methods	Retrospective case series
Participants	31 young children from a single American centre
Interventions	Temporal and extratemporal lesionectomy
Outcomes	Seizure outcome assessed by seizure freedom at least 12 months postoperatively
Notes	-

Dunkley 2011

Methods	Retrospective case series
Participants	42 children younger than 36 months who had surgery for epilepsy
Interventions	Temporal and extratemporal surgery and hemispherectomies
Outcomes	Assessed using Engel's classification at follow-up at least 12 months after surgery
Notes	-

Dunlea 2010

Methods	Retrospective case series
Participants	199 Irish participants with at least 1-year follow-up who underwent resective surgery for refractory epilepsy since 1975
Interventions	Interventions included anterior temporal lobectomy, amygdalo-hippocampectomy, neocorticectomy, lesionectomy, and frontal lobe resection
Outcomes	Engel's criteria were used to classify seizure outcome at 1, 2, 5, 10, 15, and > 15 years of follow-up
Notes	-

Dwivedi 2017

Methods	Randomised controlled trial conducted at the All India Institute of Medical Sciences in New Delhi
Participants	Participants had to have "drug-resistant epilepsy", defined as failure of adequate trials of 2 appropriately chosen antiepileptic drug schedules with acceptable side effects and referred for surgery at the trial centre
Interventions	Randomisation to a resection (n = 57) OR medical therapy group (n = 59 remaining on the waiting list, with surgery planned for 1 year or longer after randomisation) Participants with concordance of video EEG localisation of the ictal-onset zone and location of the lesion on MRI underwent resection of that region of cortex or of the lesion or malformed cortex

Dwivedi 2017 (*Continued*)

	Participants with multiple, subtle, or no lesions underwent resection of the region that was concordant between video EEG results and localisation on PET, SPECT, or MEG Participants who had multiple seizure types and multiple bilateral lesions and seizure foci underwent corpus callosotomy Participants who had extensive lesions confined to 1 hemisphere with significant weakness of limbs (weak pincer grip or worse) opposite to the involved hemisphere underwent hemispherotomy
Outcomes	Primary outcome was freedom from seizures according to the ILAE Scale at 12 months Secondary outcomes were seizure severity scores and cognitive/quality of life measures (not relevant to this review)
Notes	

Elsharkawy 2008a

Methods	Retrospective case series
Participants	218 consecutive adults with extratemporal lesions from a single German centre who underwent resective surgical treatment for intractable focal epilepsy between 1991 and 2005
Interventions	Resection of epileptogenic zone: frontal lobe 95, posterior cortical 103, multi-lobar 20
Outcomes	Assessed as Engel class at least 12 months post surgery
Notes	-

Elsharkawy 2009a

Methods	Retrospective case series
Participants	434 German adults from 1 centre
Interventions	• Anterior temporal lobe resection included the pole of the temporal lobe. The laterodorsal resection line was delineated by EEG and abnormalities noted by MRI. The size of the resection ws 2.5 to 4 cm in the language-dominant hemisphere and 3 to 6 cm in the non-dominant hemisphere. The procedure included removal of the parahippocampal gyrus, hippocampus, and amygdala • Apical temporal resection: tailored resection of the lesion in the apex of the temporal lobe with amygdalectomy, and maximal 4 cm laterodorsal cortex from the pole; extension of the resection was guided by ECoG • Temporal lesionectomy included only a singular lesion resection as defined by EEG and MRI but saved the eloquent cortex. In the case of dual pathology a lesionectomy and a selective amygdalohippocampectomy were performed, and the dorsal resection was guided via intraoperative ECoG • Selective amygdalohippocampectomy included only a resection of the hippocampus or mesial structures based on MRI and intraoperative findings (5 people only)
Outcomes	Seizure outcome by Engel class determined at 24 months and 5, 10, and 16 years after surgery
Notes	-

Elsharkawy 2011a

Methods	Retrospective case series
Participants	61 patients ranging in age from 5 to 58 years at the time of surgery with a refractory temporal lobe epilepsy, with MRI showing a lesion in the apex of the temporal lobe but normal hippocampus and intact memory function
Interventions	All had apical temporal lobe resections
Outcomes	Seizure outcome measured at 2 years and 5 years of follow-up post surgery, measured according to Engel's classification
Notes	-

Engman 2004

Methods	Retrospective case series
Participants	54 patients
Interventions	Temporal lobectomy
Outcomes	Seizure outcome not the main focus but data show numbers of those who were seizure-free at 2 years of follow-up
Notes	-

Erba 1992

Methods	Retrospective case series
Participants	46 children and adults from a single American centre
Interventions	Standard or modified en bloc anterior temporal lobectomy. Depending on hemispheric dominance, 4 to 7 cm of lateral cortex of the temporal lobe was removed. Mesial structures (uncus, amygdala, hippocampus, and hippocampal gyrus) were not removed when assessment suggested bilateral involvement
Outcomes	Seizure outcome assessed by seizure freedom at least 24 months postoperatively
Notes	-

Erickson 2005

Methods	Retrospective case series
Participants	84 military beneficiaries at the only US military medical centre with a comprehensive epilepsy surgery programme
Interventions	Standard temporal lobectomy in the majority, including mesial temporal lobe structures; margins extended posteriorly 3.5 to 4.0 cm in the dominant lobe and 5 to 6 cm in the non-dominant lobes; 8 had amygdalohippocampectomies

Erickson 2005 (*Continued*)

Outcomes	Seizure outcome by Engel class determined at least 24 months after surgery
Notes	-

Fauser 2004

Methods	Retrospective case series
Participants	67 patients, aged 2 to 66 years, with histologically proven focal cortical dysplasias
Interventions	Temporal lobe
Outcomes	Seizure outcome measured using Engel's classification at least 12 months post surgery, with a mean follow-up period of 21.9 months
Notes	-

Fujiwara 2012

Methods	Retrospective case series
Participants	44 in 2 American centres operated after intracranial EEG over a 15-month period
Interventions	Lesionectomies - temporal and extratemporal
Outcomes	Reported as seizure-free at least 12 months after surgery
Notes	Focus was outcome related retrospectively to the presence of high-frequency oscillations on ICEEG

Garcia 1991

Methods	Retrospective case series
Participants	55 children and adults from a single American centre operated on over a 3-year period
Interventions	Temporal lobectomy
Outcomes	Seizure outcome assessed by seizure freedom at 12 months postoperatively and annually thereafter
Notes	Focus on postoperative seizures and outcome

Garcia 1994

Methods	Prospective case series
Participants	51 participants from a single American centre operated on over a 3-year period
Interventions	Anterotemporal resection including amygdala and hippocampus
Outcomes	Seizure outcome assessed by seizure freedom at least 12 months postoperatively
Notes	Focus on value of qualitative pre-operative MRI findings

Gelinas 2011

Methods	Single-centre retrospective case series
Participants	67 children between 3 months and 16 years of age with recurrent seizures attributable to a discrete lesion on neuroimaging
Interventions	Site of surgery was temporal and extratemporal
Outcomes	Seizure outcome was examined 1 year post surgery and at subsequent follow-ups using Engel's classification
Notes	-

Georgakoulias 2008

Methods	Retrospective case series
Participants	50 adult patients from a single UK centre - mean age 34 years - with medically intractable medial temporal lobe epilepsy
Interventions	Temporal
Outcomes	Seizure outcome measured using Engel's classification; intermediate-term and long-term with mean follow-up of 6. 2 years
Notes	-

Gilliam 1997a

Methods	Prospective case series
Participants	78 children and adults from a single American centre with mesial-basal temporal lobe epilepsy
Interventions	En bloc neocorticectomy of the anterior 4.5 to 5.5 cm of the temporal lobe, sparing the superior temporal gyrus
Outcomes	Seizure outcome assessed by seizure freedom at least 12 months after surgery

Gilliam 1997a (*Continued*)

Notes	Study focuses on concordance of MRI and EEG findings and outcome

Gilliam 1997b

Methods	Prospective case series
Participants	33 children from a single American centre
Interventions	Extratemporal and temporal lobe cortical resection for children with intractable epilepsy
Outcomes	Seizure outcome assessed by ILAE classification at a mean follow-up period of 2.7 years
Notes	-

Goldstein 1996

Methods	Retrospective case series
Participants	33 children from a single American centre
Interventions	Temporal lobe cortical resection for children with intractable epilepsy
Outcomes	Seizure outcome assessed by Engel classification at least 24 months post surgery
Notes	-

Greiner 2011

Methods	Retrospective case series from 2 centres in the USA
Participants	54 participants, aged 6 months to 40 years at the time of surgery, who had had a hemispherectomy
Interventions	Extratemporal (i.e. all had hemispherectomy)
Outcomes	Seizure freedom assessed using Engel's classification at least 1 year post surgery
Notes	-

Grivas 2006

Methods	Retrospective case series
Participants	52 patients older than 50 years from 1 German centre were operated on for intractable mesial or combined mesiolateral TLE

Grivas 2006 (*Continued*)

Interventions	Temporal lobe resections
Outcomes	Seizure outcome measured using Engel's classification with a mean follow-up period of 33 months
Notes	-

Gyimesi 2007

Methods	Retrospective case series; a German/Hungarian collaboration
Participants	130 adult patients (no age range provided) who had undergone epilepsy surgery for intractable medial temporal lobe epilepsy
Interventions	Temporal lobe surgery
Outcomes	Seizure freedom at 24 months after surgery compared with not seizure-free
Notes	-

Hader 2004

Methods	Retrospective case series from 1 centre in Canada
Participants	39 children, aged 2 months to 18.5 years, at surgery with a medically intractable epilepsy and focal cortical dysplasia on histology
Interventions	Temporal and extratemporal
Outcomes	Seizure outcome measured using Engel's classification at least 1.5 years after surgery
Notes	-

Hajek 2009

Methods	Retrospective case series
Participants	35 people from 1 Czech centre with mesial temporal lobe epilepsies, who had had MR spectroscopy before surgery
Interventions	Temporal lobe
Outcomes	Seizure outcome measured using Engel's classification at least 24 months after surgery
Notes	-

Hallbook 2010

Methods	Retrospective case series
Participants	110 children, 18 years or younger, from a single US centre, with severe refractory epilepsy
Interventions	Functional hemispherectomy
Outcomes	Seizure freedom at the time of follow-up, which was at least 12 months
Notes	-

Hamiwka 2005

Methods	Retrospective case series
Participants	38 children, with age at surgery ranging from 6 months to 18 years (mean, 9.6 years), with malformations of cortical development
Interventions	Temporal and extratemporal
Outcomes	Seizure outcome at 2, 5, and 10 years measured using Engel's classification
Notes	-

Hartley 2002

Methods	Retrospective case series from a single UK centre
Participants	35 children (24 females, 11 males; mean age 9.6 years; age range 11 months to 18 years) with a partial epilepsy, who had had a SPECT scan before surgery
Interventions	Temporal, extratemporal, and hemispherectomy
Outcomes	Seizure outcome measured using Engel's classification; range of follow-up since surgery was 3 to 6 years (mean 4.8 years)
Notes	-

Hartzfield 2008

Methods	Retrospective case series
Participants	57 patients from a single US centre operated on for post-traumatic medial temporal lobe epilepsy
Interventions	Temporal lobe surgery

Outcomes	Seizure outcome measured using Engel's classification with a mean follow-up of 4.84 years and a range of 0.5 to 9 years
Notes	-

Hemb 2010

Methods	Retrospective case review from a single US centre
Participants	192 children operated on before 1997 vs 397 children operated on from 1998 to 2008, all with a refractory epilepsy
Interventions	Extratemporal and temporal and hemispherectomies
Outcomes	Seizure freedom at time of follow-up, which was at least 12 months
Notes	-

Holmes 1997

Methods	Retrospective case series
Participants	44 teenagers and adults from a single American centre with bitemporal, independent, interictal epileptiform patterns
Interventions	Temporal lobectomy
Outcomes	Seizure outcome assessed by seizure freedom at least 12 months post surgery
Notes	-

Holmes 2000

Methods	Retrospective case series
Participants	126 children and adults from a single American centre with medically intractable extratemporal epilepsy
Interventions	Extratemporal cortical resections
Outcomes	Seizure outcome assessed by seizure freedom at least 24 months post surgery
Notes	-

Jack 1992

Methods	Retrospective case series
Participants	50 teenagers and adults from a single American centre with medically intractable temporal lobe epilepsy
Interventions	Anterior temporal lobectomy
Outcomes	Seizure outcome assessed by seizure freedom at least 12 months post surgery
Notes	-

Janszky 2003a

Methods	Retrospective case series from a single German centre
Participants	133 patients (aged 16 to 59 years) with hippocampal sclerosis-associated temporal lobe epilepsy
Interventions	Temporal lobe resections
Outcomes	Seizure outcome at 2 years post surgery (for 84 patients) measured using Engel's classification
Notes	-

Janszky 2003b

Methods	Retrospective case series from a single German centre
Participants	147 patients (range 16 to 59 years) with intractable medial temporal lobe epilepsy who underwent presurgical evaluation including high-resolution MRI and video-EEG monitoring with seizure registration
Interventions	Temporal lobe
Outcomes	Seizure outcome at 2 years post surgery measured using Engel's classification
Notes	-

Jaramillo-Betancur 2009

Methods	Retrospective case series; nested case-control study
Participants	89 teenagers and adults from Columbia
Interventions	Temporal lobectomies
Outcomes	Seizure outcome by Engel class determined at 12 and 24 months after surgery
Notes	-

Jayakar 2008

Methods	Retrospective case series
Participants	102 children with non-lesional intractable partial epilepsy
Interventions	Temporal and extratemporal
Outcomes	Seizure outcome measured according to Engel's classification at 2 years, 5 years, and 10 years post surgery
Notes	-

Jayalakshmi 2011

Methods	Retrospective case review
Participants	87 children with refractory partial epilepsy
Interventions	Temporal, extratemporal, and hemispherectomy
Outcomes	Seizure outcome by Engel class determined at least 12 months after surgery
Notes	-

Jeha 2006

Methods	Retrospective case series
Participants	371 patients who underwent anterior temporal lobectomy to treat pharmacoresistant epilepsy
Interventions	Temporal lobe
Outcomes	Seizure-free vs not seizure-free assessed at least 1 year after surgery
Notes	-

Jehi 2012

Methods	Retrospective case series from a single US centre
Participants	312 patients ranging in age from 2.5 to 74 years with an intractable temporal lobe epilepsy
Interventions	Temporal resections
Outcomes	Seizure freedom assessed using Engel's classification at least 1 year post surgery
Notes	-

Jennum 1993

Methods	Retrospective case series
Participants	64 children and adults from a single Danish centre with medically intractable temporal and extratemporal lobe epilepsy
Interventions	Tailored temporal or extratemporal lobe cortical resection
Outcomes	Seizure outcome assessed by seizure freedom at least 12 months post surgery
Notes	-

Jeong 1999

Methods	Retrospective case series
Participants	93 consecutive children and adults from a single Korean centre with medically intractable mesial temporal lobe epilepsy
Interventions	Temporal lobectomy
Outcomes	Seizure outcome assessed by seizure freedom at least 18 months post surgery
Notes	-

Kan 2008

Methods	Retrospective case series from a single US centre
Participants	58 children with an intractable localised epilepsy
Interventions	Temporal and extratemporal
Outcomes	Seizure outcome measured according to Engel's classification at least 1 year post surgery
Notes	-

Kang 2009

Methods	Retrospective case series from a single US centre
Participants	244 adult patients with a mean age at surgery of 35 years (range 18 to 68 years) with an intractable temporal lobe epilepsy, all of whom had BMI > 26 (i.e. overweight, obese, or morbidly obese)
Interventions	Temporal lobe surgery
Outcomes	Seizure outcome measured according to Engel's classification at least 1 year post surgery

Kang 2009 (*Continued*)

Notes	-

Kanner 2009

Methods	Retrospective case series from a single US centre
Participants	100 patients with a mean age of 31.2 years with temporal lobe epilepsy (TLE)
Interventions	Temporal lobe surgery
Outcomes	Seizure outcome at 2-year follow-up measured using Engel's classification
Notes	-

Kilpatrick 1997

Methods	Prospective case series
Participants	75 consecutive teenagers and adults from 2 Australian centres with medically intractable temporal lobe epilepsy
Interventions	Those with hippocampal sclerosis underwent a tailored anterior temporal lobectomy with en bloc excision of the neocortical structures followed by microsurgical resection of the amygdala and en bloc excision of the hippocampal formation and parahippocampal gyrus. On the non-dominant side, this included excision of 4 cm of the superior temporal gyrus and the middle temporal gyrus, and the inferior temporal gyrus to the vein of Labbe or 5 to 6 cm; in dominant lobectomy, the superior temporal gyrus was left intact, the middle temporal gyrus was excised for 4 to 5 cm or to the vein of Labbe, and the inferior temporal was excised for either 4.5 to 5.5 cm or to the vein of Labbe. Patients with foreign tissue lesions had an anterior temporal lobectomy, lesionectomy, or neocorticectomy
Outcomes	Seizure outcome assessed by Engel class at least 12 months post surgery
Notes	-

Kim 2009

Methods	Retrospective case series from a single Korean centre
Participants	166 patients aged 3 to 51 years with a mean age of 24.7 years with intractable epilepsy related to focal cortical dysplasia
Interventions	Temporal and extratemporal
Outcomes	Seizure outcome (i.e. freedom or not at follow-up); mean length of postoperative follow-up was 7.94 years
Notes	-

Kim 2010a

Methods	Retrospective case series from a single Korean centre
Participants	177 participants, between 11 and 51 years of age at the time of surgery, who had had resective surgery and intracranial EEG monitoring
Interventions	Temporal and extratemporal resections
Outcomes	Seizure outcome by Engel class determined at least 12 months after surgery
Notes	-

Kim 2010b

Methods	Retrospective case series from a single Korean centre
Participants	40 patients, aged 4 to 51 years, with refractory epilepsy
Interventions	Temporal and extratemporal surgery
Outcomes	Seizure-free (as opposed to not seizure-free) measured at least 2 years postoperatively
Notes	-

Kloss 2002

Methods	Retrospective and prospective case series
Participants	68 participants from 1 German centre younger than 18 years of age
Interventions	Types of resection included lesionectomy, lesion and corticectomy, lobectomy, and multi-lobar resection
Outcomes	Seizure outcome was assessed using Engel's classification at 2 years postoperatively
Notes	-

Knowlton 2008

Methods	Prospective case series from a single US centre
Participants	62 patients with mean age at surgery of 26 years (minimum age 1 year, maximum age 60 years), who required intracranial electroencephalography (ICEEG) because epileptic focus was not sufficiently localised with scalp EEG and MRI
Interventions	Temporal and extratemporal
Outcomes	Seizure outcome measured using Engel's classification at least 1 year post surgery; range of follow-up was 1.5 to 10. 5 years, with mean time of 4.2 years, and median of 3.5 years. Patients with < 1 year follow-up were excluded

Knowlton 2008 (*Continued*)

Notes	-

Kral 2007

Methods	Retrospective cases series from a single German centre
Participants	49 patients with mean age at surgery of 18 years (range 5 to 47 years) with focal cortical dysplasia
Interventions	Temporal and extratemporal
Outcomes	Seizure outcome measured using the ILAE classification with mean follow-up of 8.1 (SD 4.5) years
Notes	-

Krsek 2013

Methods	Retrospective case series
Participants	106 children from 1 American centre
Interventions	Resection of epileptogenic zone - temporal and extratemporal
Outcomes	Assessed as Engel class at 24 months post surgery
Notes	Focus was outcome related retrospectively to pre-operative SPECT findings

Kuzniecky 1993

Methods	Prospective case series
Participants	34 children and adults from 1 American centre with medically intractable temporal lobe epilepsy
Interventions	Temporal lobectomy
Outcomes	Seizure outcome assessed by modified Engel class at least 12 months post surgery
Notes	Focus on MRI findings and presence of febrile seizures

Kwan 2010

Methods	Retrospective cases series
Participants	41 Canadian children undergoing hemispherectomy
Interventions	Hemidecortication compared with peri-insular hemispherotomy

Kwan 2010 (*Continued*)

Outcomes	Seizure outcome by Engel class determined at least 24 months after surgery
Notes	-

Lackmayer 2013

Methods	Retrospective case series
Participants	45 consecutive patients from a single Austrian centre with medically refractory unilateral mesial temporal lobe seizures
Interventions	Selective amygdalohippocampectomy or anteromedial temporal lobectomy
Outcomes	Assessed as seizure freedom 1, 2, or 3 years post surgery
Notes	Focus of study was postoperative depression related to seizure outcome

Lee 2006

Methods	Retrospective cases series from a single Korean centre
Participants	51 patients with a mean age at surgery of 31.4 years (ranging from 16 to 50 years) with pathologically proven mesial temporal sclerosis
Interventions	Temporal lobe surgery
Outcomes	Seizure outcome measured using Engel's classification at follow-up, which lasted at least 4 years
Notes	-

Lee 2008

Methods	Not stated
Participants	71 participants from a single Korean centre with frontal lobe epilepsy and mean age at surgery of 26.2 years (ranging from 12 to 57 years)
Interventions	Extratemporal surgery
Outcomes	Seizure outcome at least 2 years after surgery with an unclassified scale
Notes	-

Lee 2010a

Methods	Retrospective case series from a single Korean centre
Participants	52 people with intractable temporal lobe epilepsy; 19 patients were classified as children (≤ 18 years old), and 33 patients were classified as adults (> 18 years old)
Interventions	Temporal lobe
Outcomes	Whether seizure-free or not at 2 years and 4 years post surgery
Notes	-

Lee 2011

Methods	Retrospective cases series
Participants	40 Korean participants treated for lesional mesial temporal lobe epilepsy between 1993 and 2008
Interventions	Intervention before 2006 was anterior temporal lobectomy, and from 2006, selective lesionectomy via a transsylvian-transcisternal approach
Outcomes	Seizure outcome by Engel class determined at least 12 months after surgery
Notes	-

Lei 2008

Methods	Retrospective case series from a single Korean centre
Participants	250 cases of epilepsy caused by cerebral schistosomiasis in patients 17 to 66 years of age (mean age 32.8 years)
Interventions	Temporal and extratemporal
Outcomes	Seizure outcome at follow-up 4 to 5 years after operation measured using Engel's classification
Notes	-

Li 1997

Methods	Retrospective case series
Participants	51 children and adults from Canadian, UK, and American centres with medically intractable temporal and extratemporal lobe epilepsy
Interventions	Lesionectomy, lesionectomy plus corticectomy or lobectomy, corticectomy without removal of the lesion, selective amygdalo-hippocampectomy, selective amygdalohippocampectomy, and lesionectomy
Outcomes	Seizure outcome assessed by modified Engel class at least 12 months post surgery

Notes	-

Li 1999

Methods	Case series; not clear whether retrospective or prospective
Participants	38 teenagers and adults from Canadian, UK, American, and Australian centres with medically intractable epilepsy associated with hippocampal sclerosis and an additional lesion, which could have been temporal or extratemporal
Interventions	Lesionectomy (removal of the extrahippocampal lesion); mesial temporal resection (removal of the atrophic hippocampus); and lesionectomy plus mesial temporal resection (removal of both the lesion and the atrophic hippocampus)
Outcomes	Seizure outcome assessed by modified Engel class at least 12 months post surgery
Notes	-

Liang 2010

Methods	Prospective study "randomly allocated" to either treatment group
Participants	60 Chinese participants with temporal lobe epilepsy and mental retardation
Interventions	Half had anterior temporal lobectomy, and half anterior corpus callosotomy combined with anterior temporal lobectomy
Outcomes	Seizure outcome by Engel class determined at 24 months after surgery
Notes	Study to compare the outcome of the 2 surgical approaches

Liang 2012

Methods	Retrospective case series
Participants	206 children from 4 Chinese centres undergoing surgical resection for epilepsy between 2001 and 2007
Interventions	Lesion resection, epileptogenic zone resection, anterior temporal lobectomy (involving resection of 3 to 3.5 cm of the neocortex and 2 to 2.5 cm of the mesial structure of the left anterior temporal lobe, or 3.5 to 4.5 cm of the neocortex and 2 to 3 cm of the mesial structure of the right anterior temporal lobe, and selective amygdalohippocampotomy using a trans-Sylvian approach
Outcomes	Assessed as seizure freedom at least 12 months post surgery
Notes	-

Liava 2012

Methods	Retrospective case series
Participants	53 children and young adults from 2 Italian centres with extratemporal lobe epilepsy
Interventions	Tailored resections with localisation: 5 frontomesial, 6 fronto-dorsolateral, 6 fronto-mesial + dorsolateral, 2 fronto-orbital, 5 fronto-operculo-insular, 1 fronto-central, 4 frontocentro-parietal, 3 fronto-centro-temporal, 5 parietal, 2 parietotemporal, 1 centro-parietal, 1 occipital, 7 occipito-temporal, and 5 temporo-parieto-occipital. In 5 cases, only partial excision of the EZ was performed because of its functional intersection with eloquent areas: 1 fronto-dorsolateral, 1 fronto-mesial + dorsolateral, 1 fronto-central, 1 parietal, and 1 temporo-parieto-occipital; the remaining resections were considered as complete
Outcomes	Assessed as Engel class at least 18 months post surgery
Notes	-

Lopez-Gonzalez 2012

Methods	Retrospective case series from a single US centre
Participants	130 children, aged 1 to 18 years at surgery, who had temporal lobe surgery
Interventions	Temporal lobe resections
Outcomes	Seizure outcome measured using Engel's classification at 1, 2, 5, and 12 years post surgery
Notes	-

Lorenzo 1995

Methods	Retrospective case series
Participants	48 participants (age not specified) from 1 American centre with medically intractable focal frontal lobe epilepsy
Interventions	Focal cortical resection (i.e. partial or complete frontal lobectomy with or without an identified mass lesion) and stereotactic resection of a frontal lobe MRI-identified epileptogenic lesion
Outcomes	Seizure outcome assessed by modified Engel class at least 12 months post surgery
Notes	-

Madhavan 2007

Methods	Retrospective case series from 5 centres: 1 French, 3 American, and 1 Canadian
Participants	70 patients with tuberous sclerosis complex and epilepsy; mean age at surgery 9.9 years
Interventions	Temporal and extratemporal
Outcomes	Seizure outcome at follow-up (time from surgery to evaluation was 5.2 (8.0) years) measured using Engel's classification
Notes	-

Mani 2006

Methods	Retrospective cases series from a single US centre
Participants	132 children (< 18 years) with intractable epilepsy; mean age at surgery was 8.17 years
Interventions	Extratemporal cortical resection and hemispherectomy
Outcomes	Seizure outcome at 12 and 24 months post surgery assessed using Engel's classification
Notes	-

Mathern 1999

Methods	Retrospective case series from a multi-centre Australian surgery for epilepsy programme
Participants	198 children from 1 American centre with medically intractable temporal and extratemporal lobe epilepsy
Interventions	The most common procedures were hemispherectomies, followed by lobar resections
Outcomes	Seizure outcome assessed by seizure freedom at least 12 months post surgery
Notes	-

McIntosh 2012

Methods	Retrospective case series from an Australian centre
Participants	81 patients - aged 4 to 60 years at the time of surgery with 12 people younger than 16 years - who had extratemporal resection
Interventions	Extratemporal resections
Outcomes	Seizure freedom measured at least 2 years post surgery
Notes	-

Mihara 2004

Methods	Retrospective case series from a Japanese centre
Participants	357 patients with a medically intractable epilepsy (mean age at surgery calculated as 24.7 years); temporal lobe group: 25.5 years (range 2 to 55 years); extratemporal group: 21.8 years (range 2 to 40 years)
Interventions	Temporal and extratemporal
Outcomes	Seizure outcome measured using Engel's classification at least 12 months post surgery
Notes	-

Miserocchi 2013

Methods	Retrospective case series
Participants	68 children from a single Italian centre with temporal lobe epilepsy, operated between 2001 and 2010
Interventions	Tailored microsurgical resections of epileptogenic zone
Outcomes	Assessed as Engel class at least 12 months post surgery
Notes	-

Morino 2009

Methods	Retrospective case series
Participants	62 people with temporal lobe seizures operated on at a single Japanese centre
Interventions	All participants underwent trans-sylvian selective amygdalohippocampectomy
Outcomes	Seizure freedom 12 months postoperatively
Notes	Study to determine effects of selective surgery on memory outcome

Morris 1998

Methods	Retrospective case series from a US centre
Participants	38 children and adults from 1 American centre with medically intractable epilepsy, who had had resection of a ganglioglioma in the temporal or extratemporal lobe over a 9-year period
Interventions	Tumour resection
Outcomes	Seizure outcome assessed by Engel class at least 12 months post surgery

Morris 1998 (*Continued*)

Notes	-

O'Brien 1996

Methods	Retrospective case series from an Australian centre
Participants	46 teenagers and adults from 1 Australian centre with medically intractable temporal lobe epilepsy over a 9-year period
Interventions	Standard anterior temporal lobectomy (4.5 to 5.5 cm lateral resection) with en bloc removal of the mesial temporal structures or lesionectomy
Outcomes	Seizure outcome assessed by seizure freedom at least 12 months post surgery
Notes	-

O'Brien 2000

Methods	Retrospective case series from an Australian centre
Participants	36 children at 1 American centre who had peri-ictal and interictal SPECT studies and extratemporal resective epilepsy surgery performed between June 1993 and June 1997
Interventions	Resection of epileptogenic zone
Outcomes	Seizure outcome assessed by seizure freedom at least 12 months post surgery
Notes	Study of whether subtraction ictal SPECT co-registered with MRI (SISCOM) is predictive of outcome

Oertel 2005

Methods	Prospective randomised study from a German centre
Participants	30 patients; mean age and range: waterjet group 35.5 (18 to 70), aspirator group 34.7 (20 to 57); mean age for all patients calculated as 35.1, with an intractable epilepsy
Interventions	Temporal lobe surgery
Outcomes	Seizure outcome with a mean follow-up period of 2.15 years (range 1 to 3.5 years), measured as seizure-free or not
Notes	-

Paglioli 2006

Methods	Prospective case series
Participants	161 consecutive Brazilian participants with MTLE/HS
Interventions	Anterior temporal lobectomy or a selective amygdalohippocampectomy
Outcomes	Seizure outcome by Engel class determined from 24 months after surgery onwards
Notes	-

Paolicchi 2000

Methods	Retrospective case series
Participants	75 children at 2 American centres with intractable temporal or extratemporal lobe epilepsy
Interventions	Cortical resections. None of the temporal resections were 'standard'; all included anterior neocortical and mesial limbic structures, tailored posteriorly according to EEG, lesional data, and location of language cortex. For seizures that originated posteriorly, resection of the temporal convexity and the basal neocortex was extended further posteriorly, with the vein of Labbe undercut if needed. Extratemporal resections consisted of complete removal of the lesion combined with corticectomy tailored to the epileptogenic region. Anterior frontal epileptogenic regions were often treated by medial or lateral wedge resections; posterior frontal, parietal, and occipital foci were more likely to be treated by tailored corticectomy alone
Outcomes	Seizure outcome assessed by seizure freedom at least 12 months post surgery
Notes	-

Park 2002

Methods	Retrospective case series from a US centre
Participants	148 participants younger than 18 years who underwent surgery for relief of medically intractable epilepsy, with mean age at surgery of 13.4 years (range 5 months to 18 years)
Interventions	Temporal and extratemporal
Outcomes	Seizure outcome measured using Engel's classification at least 12 months after surgery
Notes	-

Park 2006

Methods	Retrospective case series from a single Korean centre
Participants	30 patients with cortical dysplasia (CD) and epilepsy (age range 1.5 to 18.3 years)
Interventions	Temporal and extratemporal
Outcomes	Seizure outcome measured using Engel's classification with a mean follow-up period of 3.2 years and a minimum follow-up period of 12 months
Notes	-

Perego 2009

Methods	Retrospective case series
Participants	37 adults from 1 Spanish centre
Interventions	25 participants underwent anteromedial temporal lobe resection; 5 underwent temporal complete lobectomy; 6 underwent a lesionectomy with well-demarcated lesions; and 1 underwent selective transventricular amygdalohippocampectomy
Outcomes	Seizure outcome was assessed using Engel's classification at 1 and 3 years postoperatively
Notes	-

Perry 2010

Methods	Retrospective cases series
Participants	83 American participants younger than 18 years of age with incomplete resection (defined by intraoperative or extraoperative subdural EEG data and postoperative MRI when a lesion was present) for epilepsy, with 2 years of follow-up
Interventions	Lesional resection - excluding those who had corpus callosotomy, vagal nerve stimulator placement, multiple subpial transections as their sole procedure, and those who had a hemispherectomy
Outcomes	Seizure outcome by Engel class determined at least 24 months after surgery
Notes	Note: this is a follow-up study of participants with original incomplete resection

Phi 2009

Methods	Retrospective cases series
Participants	87 participants from a single Korean centre with tumour-related temporal lobe epilepsy
Interventions	Temporal lobe lesionectomy with or without hippocampectomy
Outcomes	Seizure outcome by Engel class determined at least 12 months after surgery
Notes	-

Phi 2010

Methods	Retrospective cases series
Participants	41 paediatric patients from a single Korean centre with focal cortical dysplasia
Interventions	Temporal or extratemporal lobe surgery
Outcomes	Seizure outcome by Engel class determined at least 12 months after surgery
Notes	-

Pinheiro-Martins 2012

Methods	Retrospective case series from a Brazilian centre
Participants	70 participants, aged 1 to 52 years at the time of surgery, with a refractory frontal lobe epilepsy
Interventions	Extratemporal resections
Outcomes	Seizure outcome measured according to Engel's classification at time of follow-up, which was at least 4 years after surgery
Notes	-

Prevedello 2000

Methods	Retrospective case series
Participants	84 adults from 1 German centre with intractable temporal lobe epilepsy
Interventions	Anterior temporal lobectomy
Outcomes	Seizure outcome assessed by Engel class at least 15 months post surgery
Notes	-

Raabe 2012

Methods	Retrospective case series from a German centre
Participants	80 patients with drug-resistant focal epilepsy and either a cavernous angioma or an arteriovenous malformation in underlying histology
Interventions	Not stated whether temporal or extratemporal resections
Outcomes	Seizure outcome measured using Engel's classification at follow-up at least 2 years post surgery
Notes	-

Radhakrishnan 1998

Methods	Prospective and retrospective case series
Participants	175 children and adults from 1 American centre with intractable temporal lobe epilepsy
Interventions	Anterior temporal lobectomy with amygdalohippocampectomy with resection of the lateral temporal cortex and the mesial temporal structures, which included the amygdala, the hippocampus, and the parahippocampal gyrus
Outcomes	Seizure outcome assessed by Engel class at least 24 months post surgery
Notes	-

Rausch 2003

Methods	Not stated - but a longitudinal study, possibly prospective
Participants	44 patients from a US centre who had a temporal lobe resection
Interventions	Temporal lobe resection
Outcomes	Seizure freedom at time of follow-up, which was at least 12 months
Notes	-

Remi 2011

Methods	Retrospective case study
Participants	154 German participants with a focal epilepsy, temporal and extratemporal
Interventions	Resections were tailored so as to encompass as much epileptogenic tissue as possible and as little eloquent cortex as possible
Outcomes	Seizure outcome by Engel class determined at least 22 months after surgery

Remi 2011 (*Continued*)

Notes	-

Roberti 2007

Methods	Retrospective case study
Participants	42 adults and children from a single US centre with non-lesional temporal lobe epilepsy
Interventions	All had anteromedial temporal lobectomy
Outcomes	Seizure outcome by Engel class at a median of 60 months but a minimum of 12 months of follow-up
Notes	-

Rossi 1994

Methods	Retrospective case series
Participants	138 children and adults from 1 Italian centre with intractable temporal and extratemporal lobe epilepsy
Interventions	Surgical procedures utilised were 17 hemispherectomies (children only), 67 anterior temporal lobectomies, and 54 extratemporal resections
Outcomes	Seizure outcome assessed by Engel class at least 24 months post surgery
Notes	-

Russo 2003

Methods	Retrospective case series from 1 Italian centre
Participants	126 participants - adults and children, with age at surgery ranging from 0 to 53 years - with intractable epilepsy and malformation of cortical development on histology
Interventions	Temporal and extratemporal resections
Outcomes	Seizure outcome by Engel class determined at least 12 months after surgery
Notes	-

Sagher 2012

Methods	Retrospective case series from a single US centre
Participants	96 patients with medically refractory mesial temporal lobe epilepsy
Interventions	Temporal lobe resections
Outcomes	Seizure outcome measured using Engel's classification at 3 months, 1 year, 2 years, and 3 years post surgery
Notes	-

Sakamoto 2009

Methods	Retrospective case series from a Japanese centre
Participants	36 participants, 12 years old and over, with intractable temporal lobe epilepsy
Interventions	Temporal lobe surgery - anterior temporal lobectomy with amygdalo-hippocampectomy or selective amygdalo-hippocampectomy with or without multiple subpial transection
Outcomes	Seizure outcomes evaluated according to ILAE classification at least 24 months after resection
Notes	-

Salanova 1994

Methods	Retrospective case series
Participants	98 children and adults from 1 American centre with intractable temporal lobe epilepsy
Interventions	Temporal lobectomy
Outcomes	Seizure outcome assessed by Engel class at least 12 months post surgery
Notes	-

Sarkis 2012

Methods	Retrospective case series from a US centre
Participants	63 participants, aged 1.6 to 56 years at time of surgery, who had a multi-lobar resection for a medically refractory epilepsy
Interventions	Multi-lobar surgical resections, classified based on the lobes involved (frontal, parietal, temporal, or occipital), then categorised into frontotemporal (FT), temporoparietal (TP), frontoparietal (FP), and occipital plus (temporoparieto-occipital (TPO), parieto-occipital (PO), or temporo-occipital (TO)). The occipital plus group represented extended posterior quadrant resections as opposed to more anterior resection subsets

Sarkis 2012 (*Continued*)

Outcomes	Seizure outcome measured using Engel's classification 1 year post surgery and annually thereafter
Notes	-

Schramm 2011

Methods	Randomised controlled trial
Participants	207 participants from 3 German centres with temporal lobe epilepsy
Interventions	Randomised to an intended minimum resection length of 25 mm or 35 mm for hippocampus and parahippocampus
Outcomes	Seizure outcome by Engel class determined at 12 months after surgery
Notes	-

Seymour 2012

Methods	Retrospective case series from a UK centre
Participants	306 adults and children operated on between 1975 and 1995
Interventions	Resection of either temporal lobe
Outcomes	Seizure outcome by Engel class determined at least 24 months after surgery
Notes	Report on mortality, after a longer interval, in a cohort treated by temporal lobe surgery between 1975 and 1995

Sinclair 2003

Methods	Retrospective case series from 1 Canadian centre
Participants	77 children with intractable epilepsy
Interventions	Extratemporal operations: 8 parietal, 12 frontal, 4 occipital, and 10 multi-lobar or hemispherectomy resections. One hypothalamic hamartoma and 4 callosotomies (reported separately), as well as 42 temporal lobectomies (method not defined in any detail)
Outcomes	Seizure outcome was assessed using Engel's classification at 1 year postoperatively and annually thereafter
Notes	-

Sindou 2006

Methods	Not stated - probably retrospective case series
Participants	100 people from a French centre with medically intractable temporo-mesial epilepsy
Interventions	Tailored temporal lobe resection
Outcomes	Seizure outcome was assessed using Engel's classification at least 1 year postoperatively up to 10 years of follow-up
Notes	-

Sola 2005

Methods	Retrospective case series; multi-centre study from Spain
Participants	137 teenagers and adults followed for 2 years postoperatively
Interventions	Temporal lobectomies
Outcomes	Seizure outcome by Engel class (1 and 2 combined) determined at 24 months after surgery
Notes	-

Spencer 2005

Methods	Prospective observational multi-centre American study of seizures, anxiety, depression, and quality of life (QOL) outcomes after resective epilepsy surgery
Participants	339 participants followed for at least 2 years
Interventions	Resective surgery: mesial temporal resection or resection in any neocortical region including temporal lobe
Outcomes	Any seizure at 12 months or 1 to 2 years postoperatively
Notes	-

Sperling 1992

Methods	Prospective case series
Participants	51 adults from 1 American centre with intractable temporal lobe epilepsy
Interventions	Standard anterior temporal lobectomy. In the non-dominant hemisphere, the resection line ran 5.0 to 5.5 cm from the temporal tip and 4.5 to 5.0 cm in the dominant hemisphere. The amygdala and 1.5 to 2.0 cm of the hippocampus were removed by suction in early participants and en bloc in later participants in the series
Outcomes	Seizure outcome assessed by Engel class at least 21 months post surgery

Sperling 1992 (*Continued*)

Notes	-

Stavrou 2008

Methods	Retrospective case series
Participants	53 children and adults from a single Austrian centre with a cavernoma and epilepsy
Interventions	58 microsurgical resections; 3 participants underwent several operations for multiple cavernomas; 1 underwent a second operation for remaining lesion 4 years after initial surgery
Outcomes	Seizure outcome by ILAE classification at least 2 years after surgery
Notes	-

Suppiah 2009

Methods	Retrospective case series
Participants	176 children and adults from New Zealand followed up for at least 12 months
Interventions	Temporal lobectomy
Outcomes	Seizure outcome by Engel class determined at 12 months after surgery
Notes	-

Swartz 1992

Methods	Prospective case series
Participants	34 adults from 1 American centre with intractable temporal lobe epilepsy
Interventions	Temporal lobe resection
Outcomes	Seizure outcome assessed by seizure freedom Engel class at least 20 months post surgery
Notes	-

Tanriverdi 2010

Methods	Retrospective case series
Participants	256 participants from Canada and France with mesial temporal lobe epilepsy
Interventions	Corticohippocampectomy or selective amygdalohippocampectomy
Outcomes	Seizure outcome by Engel class determined at 12 months after surgery
Notes	Comparison of surgical approach and IQ and memory outcomes at 1-year follow-up for people with medically refractory mesial temporal lobe epilepsy (MTLE) due to hippocampal sclerosis

Tatum 2008

Methods	Retrospective case series from 2 US centres
Participants	39 adults with intractable localisation-related epilepsy and a normal MRI scan
Interventions	Anterior temporal lobectomy
Outcomes	Participants were classified as seizure-free or not seizure-free at follow-up, which was at least 12 months after surgery
Notes	-

Terra-Bustamante 2005a

Methods	Prospective study from a Brazilian centre
Participants	107 patients, 18 years of age and younger, with medically intractable epilepsy
Interventions	Temporal and extratemporal resections
Outcomes	Seizure outcome was classified according to Engel's classification scheme and was assessed at least 12 months post-operatively
Notes	-

Terra-Bustamante 2005b

Methods	Prospective study from a Brazilian centre
Participants	35 children, 18 years and younger, with medically intractable temporal lobe epilepsy
Interventions	All had surgery on the temporal lobe
Outcomes	Seizure outcome was classified according to Engel's classification scheme and was assessed at least 12 months post-operatively

Notes	-

Tezer 2008

Methods	Retrospective case series from a Turkish centre
Participants	109 adults with mesial temporal lobe epilepsy and hippocampal sclerosis
Interventions	Anterior temporal lobectomy in all
Outcomes	Seizure outcome assessed using Engel's classification at least 12 months after surgery
Notes	-

Theodore 2012

Methods	Prospective case series
Participants	41 adults from 1 American centre
Interventions	All participants underwent anterior temporal lobectomy, tailored to individual pre-resection evaluations, and intra-operative electrocorticography. All resections included the temporal tip, a minimum of 1 cm of the anterior part of the superior temporal gyrus, and between 3 and 5 cm of the middle and inferior temporal gyri. Resection was extended to involve epileptogenic frontal regions identified on subdural electrode recording in 2 participants
Outcomes	Seizure outcome by Engel class determined at least 12 months after surgery
Notes	Objective of this study was to compare 5-hydroxytryptamine receptor 1A (5-HT1A) PET vs cerebral metabolic rate of glucose (CMRglc) PET for temporal lobectomy planning

Tigaran 2003

Methods	Retrospective case series from a US centre
Participants	65 adults who had surgery for intractable partial epilepsy
Interventions	All had frontal lobe cortical resections
Outcomes	Seizure outcome was classified according to Engel's classification scheme and was assessed at least 12 months post-operatively
Notes	-

Tripathi 2008

Methods	Retrospective cases series from an Indian centre
Participants	57 children and adults (61% younger than 18 years) with intractable epilepsy secondary to cortical dysplasia
Interventions	Temporal and extratemporal resections
Outcomes	Seizure outcome measured at least 12 months postoperatively and classified using Engel's scale
Notes	-

Trottier 2008

Methods	Retrospective case series
Participants	105 French adults (2 children) from 1 centre
Interventions	Lesionectomies defined by MRI/EEG concordance or by SEEG
Outcomes	Seizure outcome assessed using Engel's classification at follow-up at 12 months after surgery and annually thereafter
Notes	-

Urbach 2007

Methods	Retrospective case series from a German centre
Participants	42 adults and children with drug-resistant parietal and occipital lobe epilepsies
Interventions	Extratemporal surgery
Outcomes	Seizure outcome at 12 months was determined using Engel's classification
Notes	-

Ure 2009

Methods	Retrospective case series
Participants	77 participants from 1 Canadian centre aged 14 to 53 years with bitemporal lobe epilepsy
Interventions	Target temporal lobectomies
Outcomes	Seizure outcome was assessed using Engel's classification at 1 year
Notes	Study of the usefulness of intracranial electrical stimulation in identifying the temporal lobe to be targeted for resection in bitemporal lobe epilepsy

Velasco 2011

Methods	Prospective case series from a Brazilian centre
Participants	163 patients, over 18 years of age, with refractory mesial temporal lobe epilepsy and hippocampal sclerosis
Interventions	Temporal lobectomies
Outcomes	Seizure outcome measured at least 14 months after surgery using Engel's classification
Notes	-

Vogt 2018

Methods	Randomised controlled trial conducted at the University Hospital of Bonn, Germany from August 2019 to December 2012
Participants	All participants who recommended for selective amygdalohippocampectomy (SAH) were invited to join the study Participants had to be at least 16 years old with drug resistant mesial temporal lobe epilepsy as determined by long-term EEG, MRI and semiology
Interventions	Selective amygdalohippocampectomy (SAH) with participants randomised to a subtemporal (n = 26 randomised, n = 22 analysed) or transsylvian approach (n = 28 randomised, n = 25 analysed)
Outcomes	Primary outcome: Neuropsychological assessments at 12 months; memory, attention and executive functions, language functions (not relevant to this review) Freedom from seizures according to the ILAE scale at 12 months
Notes	

Walz 2003

Methods	Not stated whether prospective or retrospective
Participants	100 adults from a Brazilian centre with mesial temporal lobe epilepsy related to hippocampal sclerosis
Interventions	Anterior or mesial temporal lobectomy
Outcomes	Seizure outcome measured at least 12 months postoperatively using Engel's scale
Notes	-

Weinand 1992

Methods	Retrospective case series
Participants	89 participants (age not stated) from 1 American centre with intractable temporal lobe epilepsy

Weinand 1992 (*Continued*)

Interventions	For participants with medial temporal lobe onset, a standardised 4.5-cm lateral resection with the posterior resection line of the parahippocampal gyrus and hippocampus extending to at least the level of the cerebral peduncle; for lateral onset, a more extensive and tailored ECoG-guided resection; for regional temporal lobe onset, more extensive removal of the parahippocampal gyrus, hippocampus, and lateral cortex
Outcomes	Seizure outcome assessed by seizure freedom at least 12 months post surgery
Notes	-

Wellmer 2012

Methods	Retrospective case series from a German centre
Participants	197 participants, between 0 and 70 years of age, with pharmacoresistant epilepsy, who had undergone invasive monitoring before surgery
Interventions	Not stated
Outcomes	Seizure outcome measured at 3, 6, 12, and 24 months after surgery using Engel's classification
Notes	-

Widdess-Walsh 2007

Methods	Retrospective case series from a US centre
Participants	48 participants (30 were over 16 years of age) undergoing surgery for focal cortical dysplasia guided by subdual electrode recordings
Interventions	Temporal and extratemporal resections
Outcomes	Measurement of seizure freedom at follow-up at least 12 months from the time of surgery
Notes	-

Wiebe 2001

Methods	Randomised controlled trial conducted at 3 centres in 1 Canadian city
Participants	Participants had to be at least 16 years old and must have had seizures with strong temporal lobe semiology for longer than 1 year
Interventions	Randomisation (40 in each group) to resection of a maximum of 6.0 to 6.5 cm of the anterior lateral non-dominant temporal lobe, or 4.0 to 4.5 cm of the dominant temporal lobe. Mesial resection included the amygdala and, at a minimum, the anterior 1.0 to 3.0 cm of the hippocampus (most commonly, 4.0 cm) OR continued antiepileptic drugs

Wiebe 2001 (*Continued*)

Outcomes	Primary outcome was freedom from seizures that impair awareness of self and surroundings at 1 year
Notes	-

Wieshmann 2008

Methods	Retrospective case series from a UK centre
Participants	76 adults with refractory temporal lobe epilepsy
Interventions	Anterior temporal lobe resections
Outcomes	Seizure outcome assessed 2 years post surgery using Engel's classification
Notes	-

Wray 2012

Methods	Retrospective case series from a US centre
Participants	52 children from 1 American centre; all participants had the primary motor or somatosensory cortex localised via 2 or more of the following tests: SSEP, fMRI, or high gamma electrocorticography (hgECoG)
Interventions	Resection of epileptogenic zone: temporal and extratemporal
Outcomes	Assessed as Engel class at least 12 months post surgery
Notes	-

Wyler 1995

Methods	Prospective case series
Participants	70 adults from 1 American centre with intractable temporal lobe epilepsy
Interventions	The same procedure for either hemisphere and all participants: anterior lateral 4.5 cm of temporal neocortex was removed, including superior through inferior temporal gyri, leaving hippocampus, parahippocampus, and fusiform gyri. Fusiform gyrus was then dissected piecemeal, leaving only hippocampal and parahippocampal gyri. The hippocampus was removed en bloc to the anterior margin of the cerebral peduncle (partial hippocampectomy (P)) or to the level of the colliculi (total hippocampectomy (T))
Outcomes	Seizure outcome assessed by seizure freedom at least 12 months post surgery
Notes	-

Wyllie 1998

Methods	Case series (whether prospective or retrospective not stated)
Participants	136 children from 1 American centre with intractable extratemporal or temporal lobe epilepsy
Interventions	Participants with hippocampal sclerosis had anteromesial temporal resection. For other temporal lesions, resection of the lesion, surrounding cortex, and usually also the mesial temporal structures was performed. 46% of extratemporal resections were frontal, and the rest were parietal, occipital, perirolandic, or multi-lobar (frontal and temporal, temporal and occipital, or temporo-parietal-occipital). Functional hemispherectomies were performed as described by Rasmussen, with resection of central regions and hemispheric disconnection by transection of white matter tracts and corpus callosotomy
Outcomes	Seizure outcome assessed by Engel class at least 12 months post surgery
Notes	-

Yang 2011

Methods	Retrospective case series
Participants	99 children and adults from 1 Chinese centre followed for at least 1 year
Interventions	Lesion resection defined by clinical, neuroimaging, and electrophysiological results
Outcomes	Seizure outcome assessed at least 12 months post surgery using modified ILAE classification
Notes	-

Yeon 2009

Methods	Retrospective case series from a Korean centre
Participants	60 adults with an infratentorial cavernous haemangioma and seizures
Interventions	Temporal and extratemporal
Outcomes	Seizure outcome measured at least 12 months postoperatively and classified using Engel's scale
Notes	-

Yu 2009

Methods	Retrospective case series from a Chinese centre
Participants	43 adults and children with posterior cortex epilepsy
Interventions	Extratemporal resections

Yu 2009 (*Continued*)

Outcomes	Seizure outcome measured at least 12 months postoperatively and classified using Engel's scale
Notes	-

Yu 2012a

Methods	Prospective case series
Participants	100 adults from 1 Chinese centre with resective epilepsy surgery between 2001 and 2009
Interventions	Classic anterior temporal lobotomies were performed for temporal lobe epilepsy. Tailored resection was completed for patients with extratemporal lobe epilepsy. Resective microsurgeries were conducted with the guidance of presurgical localisation results and aimed to remove epileptogenic zones. Anatomical or functional hemispherectomy was performed on some participants with hemispheric lesions. 62 with temporal lobe epilepsy had anterior temporal lobectomies, 37 had tailored focal or lobar resections with extra temporal lobe epilepsy (6 with tumours), and 1 had anatomical hemispherectomy
Outcomes	Seizure outcome assessed at least 12 months post surgery using Engel classification
Notes	Yu 2012a and Yu 2012b were treated as 2 studies in a single publication. One quality assessment was performed for the single publication

Yu 2012b

Methods	Prospective case series
Participants	222 children from 1 Chinese centre with resective epilepsy surgery between 2001 and 2009
Interventions	Classic anterior temporal lobotomies were performed for temporal lobe epilepsy. Tailored resection was completed for participants with extratemporal lobe epilepsy. Resective microsurgeries were conducted with the guidance of presurgical localisation results and aimed to remove epileptogenic zones. Anatomical or functional hemispherectomy was performed on some participants with hemispheric lesions. 62 with temporal lobe epilepsy had anterior temporal lobectomies, 37 had tailored focal or lobar resections with extra temporal lobe epilepsy (6 with tumours), and 1 had anatomical hemispherectomy
Outcomes	Seizure outcome assessed at least 12 months post surgery using Engel classification
Notes	Yu 2012a and Yu 2012b were treated as 2 studies in a single publication. One quality assessment was performed for the single publication

Zangaladze 2008

Methods	Both retrospective and prospective case series from a US centre
Participants	99 participants 12 years of age and older with localisation-related epilepsy, who had obtained intracranial EEG recordings before surgery
Interventions	Temporal and extratemporal lobe resections
Outcomes	Seizure freedom at follow-up, which was no less than 2 years after surgery
Notes	-

Zentner 1995

Methods	Retrospective case series
Participants	178 children and adults from a single German centre with intractable temporal lobe epilepsy
Interventions	Procedures performed: anterior temporal lobectomy (standard or "keyhole") with hippocampectomy, anterior temporal lobectomy without hippocampectomy, extended lesionectomy with hippocampectomy, extended lesionectomy without hippocampectomy, and selective amygdalohippocampectomy
Outcomes	Seizure outcome assessed by Engel class at least 12 months post surgery
Notes	-

Zentner 1996

Methods	Prospective case series
Participants	60 children and adults from a single German centre with intractable extratemporal lobe epilepsy
Interventions	The following surgical procedures were performed: frontal lobectomy (n = 16), frontal topectomy (n = 24), parietal topectomy (n = 7), and occipital topectomy
Outcomes	Seizure outcome assessed by Engel class at least 20 months post surgery
Notes	-

ATL: anterior temporal lobectomy. |
BMI: body mass index.
CCT: corpus callosotomy.
CD: cortical dysplasia.
CMRglc: cerebral metabolic rate of glucose.
ECoG: electrocorticography.
EEG: electroencephalography.
EZ: epileptogenic zone.

FDG: fluorodeoxyglucose.
fMRI: functional magnetic resonance imaging.
HS: hippocampal sclerosis.
ICEEG: intracranial electroencephalography.
ILAE: International League Against Epilepsy.
MEG: magnetoencephalography.
MR: magnetic resonance.
MRI: magnetic resonance imaging.
MTLE: mesial temporal lobe epilepsy.
PET: positron emission tomography.
PO: postoperative.
QOL: quality of life.
SD: standard deviation.
SEEG: stereoelectroencephalography.
SISCOM: subtraction ictal SPECT co-registered with MRI.
SPECT: single-photon emission computed tomography.
SSEP: somatosensory evoked potential.
TLE: temporal lobe epilepsy.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Acar 2008	Only 17 participants followed up for longer than 12 months
Alemany-Rosales 2011	No seizure outcome data reported
Alpherts 2008	Only 6 months of follow-up reported
Andersson-Roswall 2010	No seizure outcome data reported
Asadi-Pooya 2008	Study of postoperative antiepileptic drug treatment rather than seizure outcome of surgery
Bauer 2007	Fewer than 30 participants included
Baxendale 2005	No seizure outcome data reported
Bell 2010	No seizure outcome data reported
Binder 2009	Minimum 4 months of follow-up reported; unknown number followed up for 1 year
Bindu 2018	Fewer than 30 surgical participants included
Boesebeck 2002	Subset of participants reported in Boesebeck 2007
Boshuisen 2012	Only those with 12 postoperative months seizure-free reported

(*Continued*)

Bourgeois 2007	Fewer than 30 participants included
Buckingham 2010	Only participants with postoperative seizures included in the study
Busch 2011	Only 5 to 7 months of postoperative follow-up reported
Caicoya 2007	Fewer than 30 participants included
Carne 2004	No seizure outcome data reported
Cascino 1996	Same participants reported as in Cascino 1995; more relevant information provided in Cascino 1995
Chang 2007	Unknown proportion in the study followed up for less than 1 year
Choi 2004b	No follow-up period defined for the study
Cohen-Gadol 2003	Unknown proportion in the study followed up for less than 1 year
Colonnelli 2012	No follow-up period defined for the study
Coutin-Churchman 2012	No follow-up period defined for the study
CTRI/2018/07/015007	Does not randomise surgical interventions; randomises stereoencephalography or no stereoencephalography as part of pre-surgical evaluation
Cukiert 2009	Fewer than 30 participants included
D'Angelo 2006	Unknown proportion in the study followed up for less than 1 year
D'Argenzio 2011	No seizure outcome data reported
da Costa-Neves 2012	Study follow-up 6 months
Danielsson 2009	Fewer than 30 participants included
Datta 2009	Fewer than 30 participants included
Dulay 2006	Follow-up period less than 12 months reported
Dulay 2009	Postoperative follow-up period less than 12 months reported for most participants
Elsharkawy 2008b	Subset of participants from Elsharkawy 2009a reported
Elsharkawy 2009b	Questionnaire follow-up study with no seizure outcome data
Elsharkawy 2011b	Only children not seizure-free 6 months postoperatively reported

(*Continued*)

Engel Jr 2012	Fewer than 30 surgical participants included
Fauser 2008	No seizure outcome data reported
Ferrari-Marinho 2012	No postoperative follow-up period defined for the study
Ferroli 2006	Unknown proportion of participants followed up for less than 12 months
Freitag 2005	Study follow-up defined as 6 to 12 months
Ghacibeh 2009	Study follow-up period not defined
Griffin 2007	No seizure outcome data reported
Grunert 2003	No duration of outcome; surgery not performed for epilepsy (surgery for tumours)
Haegelen 2013	Fewer than 30 participants in the study with 12-month follow-up
Harvey 2008	Study follow-up 6 months
Hellwig 2012	Follow-up less than 12 months
Helmstaedter 2004	Reported 3 months of follow-up
Helmstaedter 2011	Subset of participants from Schramm 2011 (results from a single centre of Schramm 2011) reported
Hervas-Navidad 2002	Some participants followed up for only 6 months; no seizure outcome data reported for some participants
Hildebrandt 2005	No seizure outcome data reported
Hu 2012	Unknown proportion of participants followed up for less than 12 months
Jehi 2010	Only those who experienced postoperative seizures included
Junna 2013	Seizure outcome not measured at 1 year for all participants; not possible to separate analyses
Kuzniecky 1996	Same participants reported as in Kuzniecky 1993; more relevant information provided in Kuzniecky 1993
Lach 2010	Case control design (participants selected based on seizure outcome) inappropriate for this review
Lachhwani 2003	Commentary on Wiebe 2001 provided
Lee 2010	Fewer than 30 participants included
Limbrick 2009	Unknown proportion of participants followed up for less than 12 months

(*Continued*)

Lodenkemper 2007	Seizure outcome data reported for fewer than 30 participants
Lutz 2004	No seizure outcome data reported
Malla 1998	Same participants reported as in Cascino 1995; more relevant information provided in Cascino 1995
McClelland 2007	No seizure outcome data reported
McClelland 2011	No seizure outcome data reported
Mikati 2004	Fewer than 30 participants included
Mohammed 2012	MRI scans obtained for less than 90%
Moien-Afshari 2009	Fewer than 30 participants included
NCT03643016	Does not randomise surgical interventions; randomises Virtual Epilepsy Patient software or no Virtual Epilepsy Patient software as part of pre-surgical evaluation
NCT03790280	Does not randomise surgical interventions; randomises Intra-operative electrocorticography or no Intra-operative electrocorticography as part of pre-surgical evaluation
Negishi 2011	Fewer than 30 participants included
Nikase 2007	Fewer than 30 participants included
Oertel 2004	No seizure outcome data reported
Ogiwara 2010	Unknown proportion of participants followed up for less than 12 months
Park 2010	Seizure outcome rather than outcome after surgery measured following antiepileptic drug reduction
Placantonakis 2010	Fewer than 30 participants included
Rocamora 2009	Fewer than 30 participants included
Roth 2011	Unknown proportion of participants followed up for less than 12 months
Sakuta 2005	Fewer than 30 participants included
Schatlo 2015	No seizure outcome data reported
Schwartz 2006	Data reported only for participants who were seizure-free at 12 months
Smyth 2007	Unknown proportion of participants followed up for less than 12 months
Soeder 2009	Fewer than 30 participants included

(*Continued*)

Stavem 2005	No seizure outcome data reported
Stavem 2008	No seizure outcome data reported
Stefan 2004	Unknown proportion of participants followed up for less than 12 months
Stefan 2008	Case-control design (participants selected based on seizure outcome) inappropriate for this review
Teutonico 2008	Fewer than 30 participants included
Tong 2015	No seizure outcome data reported
Upchurch 2010	Fewer than 30 participants included
Vachrajani 2012	Unknown proportion of participants followed up for less than 12 months
Vadera 2012	Unknown proportion of participants followed up for less than 12 months
Vadlamudi 2004	Only seizure-free participants included in the study
Vogt 2016	No seizure outcome data reported
Wang 2016	No seizure outcome data reported
Weinand 2001	Same participants reported as in Weinand 1992; more relevant information given in Weinand 1992
Wetjen 2006	No seizure outcome data reported
Wetjen 2009	Fewer than 30 participants included
Wieser 2003a	MRI scan obtained for less than 90%
Wieser 2003b	MRI scan obtained for less than 90%
Yasuda 2010a	No seizure outcome data reported
Yasuda 2010b	Fewer than 30 participants included
Zupanc 2010	Unknown proportion of participants followed up for less than 12 months

MRI: magnetic resonance imaging.

DATA AND ANALYSES

Comparison 1. Surgery versus medical treatment (randomised evidence)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Proportion free from seizures at 1 year	2	196	Risk Ratio (M-H, Fixed, 95% CI)	9.78 [4.73, 20.21]
1.1 Free from seizures impairing awareness at 1 year	1	80	Risk Ratio (M-H, Fixed, 95% CI)	7.67 [2.50, 23.51]
1.2 Free from seizures (ILAE Class 1) at 1 year	1	116	Risk Ratio (M-H, Fixed, 95% CI)	11.39 [4.37, 29.64]
2 Proportion free from all seizures (including auras) at 1 year	1	80	Risk Ratio (M-H, Fixed, 95% CI)	15.0 [2.08, 108.23]

Comparison 2. Comparison of surgical techniques (randomised evidence)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Parahippocampectomy (PHC) or anterior temporal lobectomy (ATL): Proportion free from seizures (Engel Class Scale)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1 Engel Class 1 at 1 year	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Engel Class 1A at 1 year	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.3 Engel Class 1 at 5 years	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.4 Engel Class 1A at 5 years	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Parahippocampectomy (PHC) or Selective Amygdalohippocampectomy (SAH): Proportion free from seizures (Engel Class Scale)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2.1 Engel Class 1 at 1 year	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 Engel Class 1A at 1 year	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.3 Engel Class 1 at 5 years	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.4 Engel Class 1A at 5 years	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Selective Amygdalohippocampectomy (SAH) or Anterior Temporal Lobectomy (ATL): Proportion free from seizures (Engel Class Scale)	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
3.1 Engel Class 1 at 1 year	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 Engel Class 1A at 1 year	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.3 Engel Class 1 at 5 years	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

3.4 Engel Class 1A at 5 years	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Stereotactic radiosurgery (SRS) or anterior temporal lobectomy (ATL): proportion with remission of seizures (at least Engel Class IB) between 25 and 36 months	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
5 Resection with or without corpus callosotomy (CCT): Proportion free from seizures (Engel Class 1)	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 Engel Class 1 at 1 year	1	43	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [0.76, 1.70]
5.2 Engel Class 1 at 3 years	1	43	Risk Ratio (M-H, Fixed, 95% CI)	1.19 [0.72, 1.95]
5.3 Engel Class 1 at 5 years	1	43	Risk Ratio (M-H, Fixed, 95% CI)	1.09 [0.53, 2.21]
6 Anterior temporal lobectomy (ATL) with or without corpus callosotomy (CCT): Proportion free from seizures (Engel Class 1) at 2 years	1	60	Risk Ratio (M-H, Fixed, 95% CI)	1.22 [0.85, 1.76]
7 Subtemporal or transsylvian selective amygdalohippocampectomy (SAH): Proportion free from all seizures (including auras, ILAE 1a) at 1 year	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
8 Total or partial hippocampectomy: Proportion free from all seizures (including auras) at 1 year	1	70	Risk Ratio (M-H, Fixed, 95% CI)	1.82 [1.12, 2.93]
9 Length of resection (2.5 or 3.5 cm): Proportion free from seizures (Engel Class 1) at 1 year	1	207	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.86, 1.20]

Comparison 3. Surgery for epilepsy (randomised and non-randomised evidence)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Proportion with a good outcome of surgery	178		Proportion (good outcome) (Fixed, 95% CI)	Totals not selected
1.1 > 1 year seizure-free	42		Proportion (good outcome) (Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Engel Class Scale	116		Proportion (good outcome) (Fixed, 95% CI)	0.0 [0.0, 0.0]
1.3 'Other' scale	20		Proportion (good outcome) (Fixed, 95% CI)	0.0 [0.0, 0.0]

Comparison 4. Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Good outcome by MRI results	43	3999	Risk Ratio (M-H, Fixed, 95% CI)	0.78 [0.73, 0.83]
1.1 > 1 year seizure-free	17	1691	Risk Ratio (M-H, Fixed, 95% CI)	0.82 [0.74, 0.90]
1.2 Engel Class Scale	22	2097	Risk Ratio (M-H, Fixed, 95% CI)	0.75 [0.69, 0.81]
1.3 'Other' scale	4	211	Risk Ratio (M-H, Fixed, 95% CI)	0.84 [0.53, 1.32]
2 Good outcome by use of intracranial monitoring (IM)	21	1547	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.78, 0.93]
2.1 > 1 year seizure-free	6	634	Risk Ratio (M-H, Fixed, 95% CI)	0.88 [0.76, 1.02]
2.2 Engel Class Scale	14	863	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.77, 0.94]
2.3 'Other' scale	1	50	Risk Ratio (M-H, Fixed, 95% CI)	0.53 [0.28, 0.98]
3 Good outcome by presence of mesial temporal sclerosis (MTS)	46	4430	Risk Ratio (M-H, Fixed, 95% CI)	1.17 [1.12, 1.23]
3.1 > 1 year seizure-free	9	958	Risk Ratio (M-H, Fixed, 95% CI)	1.25 [1.13, 1.39]
3.2 Engel Class Scale	31	2949	Risk Ratio (M-H, Fixed, 95% CI)	1.13 [1.07, 1.20]
3.3 'Other' scale	6	523	Risk Ratio (M-H, Fixed, 95% CI)	1.31 [1.14, 1.51]
4 Good outcome by concordance of pre-op MRI and EEG	23	1778	Risk Ratio (M-H, Fixed, 95% CI)	1.25 [1.15, 1.37]
4.1 > 1 year seizure-free	8	744	Risk Ratio (M-H, Fixed, 95% CI)	1.21 [1.07, 1.37]
4.2 Engel Class Scale	12	770	Risk Ratio (M-H, Fixed, 95% CI)	1.27 [1.11, 1.46]
4.3 'Other' scale	3	264	Risk Ratio (M-H, Fixed, 95% CI)	1.40 [1.02, 1.93]
5 Good outcome by history of febrile seizures (FS)	15	1368	Risk Ratio (M-H, Fixed, 95% CI)	1.09 [1.01, 1.17]
5.1 > 1 year seizure-free	5	644	Risk Ratio (M-H, Fixed, 95% CI)	1.18 [1.05, 1.32]
5.2 Engel Class Scale	9	631	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.92, 1.11]
5.3 'Other' scale	1	93	Risk Ratio (M-H, Fixed, 95% CI)	1.11 [0.90, 1.37]
6 Good outcome by history of head injury (HI)	7	551	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.86, 1.13]
6.1 > 1 year seizure-free	2	152	Risk Ratio (M-H, Fixed, 95% CI)	0.87 [0.72, 1.05]
6.2 Engel Class Scale	3	174	Risk Ratio (M-H, Fixed, 95% CI)	1.17 [0.99, 1.37]
6.3 'Other' scale	2	225	Risk Ratio (M-H, Fixed, 95% CI)	0.83 [0.51, 1.33]
7 Good outcome by presence of encephalomalacia	5	317	Risk Ratio (M-H, Fixed, 95% CI)	0.78 [0.52, 1.17]
7.1 Engel Class Scale	4	218	Risk Ratio (M-H, Fixed, 95% CI)	0.89 [0.60, 1.33]
7.2 'Other' scale	1	99	Risk Ratio (M-H, Fixed, 95% CI)	0.28 [0.04, 1.87]
8 Good outcome by presence of focal cortical dysplasia (FCD)/malformation of cortical development (MCD)	46	3572	Risk Ratio (M-H, Fixed, 95% CI)	0.90 [0.85, 0.95]
8.1 > 1 year seizure-free	8	784	Risk Ratio (M-H, Fixed, 95% CI)	0.92 [0.84, 1.02]
8.2 Engel Class Scale	33	2386	Risk Ratio (M-H, Fixed, 95% CI)	0.89 [0.82, 0.96]
8.3 'Other' scale	5	402	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.73, 1.13]
9 Good outcome by presence of tumour	41	3357	Risk Ratio (M-H, Random, 95% CI)	1.23 [1.14, 1.32]
9.1 > 1 year seizure-free	7	656	Risk Ratio (M-H, Random, 95% CI)	1.17 [0.97, 1.41]
9.2 Engel Class Scale	28	2199	Risk Ratio (M-H, Random, 95% CI)	1.23 [1.13, 1.33]
9.3 'Other' scale	6	502	Risk Ratio (M-H, Random, 95% CI)	1.35 [1.07, 1.70]

10 Good outcome by presence of vascular malformation	19	1488	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.94, 1.21]
10.1 > 1 year seizure-free	1	46	Risk Ratio (M-H, Fixed, 95% CI)	1.06 [0.62, 1.79]
10.2 Engel Class Scale	13	973	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [0.98, 1.34]
10.3 'Other' scale	5	469	Risk Ratio (M-H, Fixed, 95% CI)	0.94 [0.74, 1.20]
11 Good outcome by unilateral or bilateral interictal spikes	18	1414	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [1.05, 1.24]
11.1 > 1 year seizure-free	7	521	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.94, 1.24]
11.2 Engel Class Scale	6	502	Risk Ratio (M-H, Fixed, 95% CI)	1.19 [1.04, 1.36]
11.3 'Other' scale	5	391	Risk Ratio (M-H, Fixed, 95% CI)	1.16 [0.97, 1.39]
12 Good outcome by extent of resection	40	3013	Risk Ratio (M-H, Fixed, 95% CI)	1.41 [1.32, 1.50]
12.1 > 1 year seizure free	9	640	Risk Ratio (M-H, Fixed, 95% CI)	2.00 [1.66, 2.41]
12.2 Engel Class Scale	28	2189	Risk Ratio (M-H, Fixed, 95% CI)	1.29 [1.21, 1.39]
12.3 'Other' scale	3	184	Risk Ratio (M-H, Fixed, 95% CI)	1.59 [1.15, 2.20]
13 Good outcome by extent of resection	39	2930	Risk Ratio (M-H, Fixed, 95% CI)	1.46 [1.37, 1.56]
13.1 Site of surgery: extratemporal only	1	30	Risk Ratio (M-H, Fixed, 95% CI)	2.0 [0.76, 5.29]
13.2 Site of surgery: temporal only	13	1266	Risk Ratio (M-H, Fixed, 95% CI)	1.11 [1.03, 1.20]
13.3 Site of surgery: temporal and extratemporal	25	1634	Risk Ratio (M-H, Fixed, 95% CI)	1.92 [1.72, 2.15]
14 Good outcome by side of surgical resection	37	2976	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.91, 1.01]
14.1 > 1 year seizure-free	5	290	Risk Ratio (M-H, Random, 95% CI)	1.01 [0.91, 1.13]
14.2 Engel Class Scale	27	2407	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.89, 1.02]
14.3 'Other' scale	5	279	Risk Ratio (M-H, Random, 95% CI)	0.94 [0.82, 1.07]
15 Good outcome by side of surgical resection	36	2933	Risk Ratio (M-H, Fixed, 95% CI)	0.94 [0.90, 0.98]
15.1 Site of surgery: extratemporal only	2	123	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.76, 1.39]
15.2 Site of surgery: temporal only	30	2592	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.89, 0.98]
15.3 Site of surgery: temporal and extratemporal	4	218	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.84, 1.14]
16 Good outcome by presence of postoperative discharges	6	542	Risk Ratio (M-H, Random, 95% CI)	0.91 [0.68, 1.22]
16.1 > 1 year seizure-free	2	109	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.24, 3.93]
16.2 Engel Class Scale	4	433	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.70, 1.03]
17 Good outcome by presence of postoperative discharges	6	542	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.79, 1.04]
17.1 Site of surgery: temporal only	3	381	Risk Ratio (M-H, Fixed, 95% CI)	0.81 [0.70, 0.94]
17.2 Site of surgery: temporal and extratemporal	3	161	Risk Ratio (M-H, Fixed, 95% CI)	1.20 [0.89, 1.61]

Analysis 1.1. Comparison 1 Surgery versus medical treatment (randomised evidence), Outcome 1 Proportion free from seizures at 1 year.

Review: Surgery for epilepsy

Comparison: 1 Surgery versus medical treatment (randomised evidence)

Outcome: 1 Proportion free from seizures at 1 year

Study or subgroup	Surgery n/N	Medical treatment n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Free from seizures impairing awareness at 1 year					
Wiebe 2001	23/40	3/40		43.3 %	7.67 [2.50, 23.51]
Subtotal (95% CI)	**40**	**40**		**43.3 %**	**7.67 [2.50, 23.51]**
Total events: 23 (Surgery), 3 (Medical treatment)					
Heterogeneity: not applicable					
Test for overall effect: Z = 3.56 (P = 0.00037)					
2 Free from seizures (ILAE Class 1) at 1 year					
Dwivedi 2017	44/57	4/59		56.7 %	11.39 [4.37, 29.64]
Subtotal (95% CI)	**57**	**59**		**56.7 %**	**11.39 [4.37, 29.64]**
Total events: 44 (Surgery), 4 (Medical treatment)					
Heterogeneity: not applicable					
Test for overall effect: Z = 4.98 (P < 0.00001)					
Total (95% CI)	**97**	**99**		**100.0 %**	**9.78 [4.73, 20.21]**
Total events: 67 (Surgery), 7 (Medical treatment)					
Heterogeneity: Chi^2 = 0.28, df = 1 (P = 0.60); I^2 =0.0%					
Test for overall effect: Z = 6.15 (P < 0.00001)					
Test for subgroup differences: Chi^2 = 0.28, df = 1 (P = 0.60), I^2 =0.0%					

Analysis 1.2. Comparison 1 Surgery versus medical treatment (randomised evidence), Outcome 2 Proportion free from all seizures (including auras) at 1 year.

Review: Surgery for epilepsy

Comparison: 1 Surgery versus medical treatment (randomised evidence)

Outcome: 2 Proportion free from all seizures (including auras) at 1 year

Study or subgroup	Surgery n/N	Medical treatment n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Wiebe 2001	15/40	1/40		100.0 %	15.00 [2.08, 108.23]
Total (95% CI)	**40**	**40**		**100.0 %**	**15.00 [2.08, 108.23]**
Total events: 15 (Surgery), 1 (Medical treatment)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.69 (P = 0.0072)					
Test for subgroup differences: Not applicable					

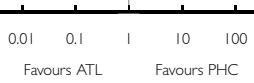
Analysis 2.1. Comparison 2 Comparison of surgical techniques (randomised evidence), Outcome 1 Parahippocampectomy (PHC) or anterior temporal lobectomy (ATL): Proportion free from seizures (Engel Class Scale).

Review: Surgery for epilepsy

Comparison: 2 Comparison of surgical techniques (randomised evidence)

Outcome: 1 Parahippocampectomy (PHC) or anterior temporal lobectomy (ATL): Proportion free from seizures (Engel Class Scale)

Study or subgroup	Parahippocampectomy (PHC) n/N	Anterior Temporal Lobectomy (ATL) n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Engel Class 1 at 1 year				
Alonso-Vanegas 2018	11/14	13/14		0.85 [0.62, 1.15]
2 Engel Class 1A at 1 year				
Alonso-Vanegas 2018	6/14	10/14		0.60 [0.30, 1.20]
3 Engel Class 1 at 5 years				
Alonso-Vanegas 2018	7/14	9/14		0.78 [0.40, 1.49]
4 Engel Class 1A at 5 years				
Alonso-Vanegas 2018	4/14	7/14		0.57 [0.21, 1.52]



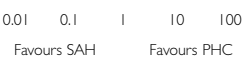
Analysis 2.2. Comparison 2 Comparison of surgical techniques (randomised evidence), Outcome 2 Parahippocampectomy (PHC) or Selective Amygdalohippocampectomy (SAH): Proportion free from seizures (Engel Class Scale).

Review: Surgery for epilepsy

Comparison: 2 Comparison of surgical techniques (randomised evidence)

Outcome: 2 Parahippocampectomy (PHC) or Selective Amygdalohippocampectomy (SAH): Proportion free from seizures (Engel Class Scale)

Study or subgroup	Parahippocampectomy (PHC) n/N	Selective Amygdalo-hippocampectomy (SAH) n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Engel Class I at 1 year				
Alonso-Vanegas 2018	11/14	14/15		0.84 [0.62, 1.14]
2 Engel Class IA at 1 year				
Alonso-Vanegas 2018	6/14	9/15		0.71 [0.34, 1.49]
3 Engel Class I at 5 years				
Alonso-Vanegas 2018	7/14	10/15		0.75 [0.40, 1.41]
4 Engel Class IA at 5 years				
Alonso-Vanegas 2018	4/14	8/15		0.54 [0.21, 1.39]



Analysis 2.3. Comparison 2 Comparison of surgical techniques (randomised evidence), Outcome 3 Selective Amygdalohippocampectomy (SAH) or Anterior Temporal Lobectomy (ATL): Proportion free from seizures (Engel Class Scale).

Review: Surgery for epilepsy

Comparison: 2 Comparison of surgical techniques (randomised evidence)

Outcome: 3 Selective Amygdalohippocampectomy (SAH) or Anterior Temporal Lobectomy (ATL): Proportion free from seizures (Engel Class Scale)

Study or subgroup	Selective Amygdalo-hippocampectomy (SAH) n/N	Anterior Temporal Lobectomy (ATL) n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Engel Class I at 1 year				
Alonso-Vanegas 2018	14/15	13/14		1.01 [0.82, 1.23]
2 Engel Class IA at 1 year				
Alonso-Vanegas 2018	9/15	10/14		0.84 [0.49, 1.43]
3 Engel Class I at 5 years				
Alonso-Vanegas 2018	10/15	9/14		1.04 [0.61, 1.76]
4 Engel Class IA at 5 years				
Alonso-Vanegas 2018	8/15	7/14		1.07 [0.53, 2.16]

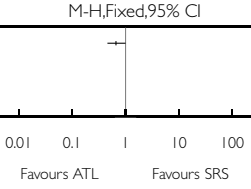
Analysis 2.4. Comparison 2 Comparison of surgical techniques (randomised evidence), Outcome 4 Stereotactic radiosurgery (SRS) or anterior temporal lobectomy (ATL): proportion with remission of seizures (at least Engel Class IB) between 25 and 36 months.

Review: Surgery for epilepsy

Comparison: 2 Comparison of surgical techniques (randomised evidence)

Outcome: 4 Stereotactic radiosurgery (SRS) or anterior temporal lobectomy (ATL): proportion with remission of seizures (at least Engel Class IB) between 25 and 36 months

Study or subgroup	Stereotactic radiosurgery (SRS) n/N	Anterior temporal lobectomy (ATL) n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Barbaro 2018	16/31	21/27		0.66 [0.45, 0.99]

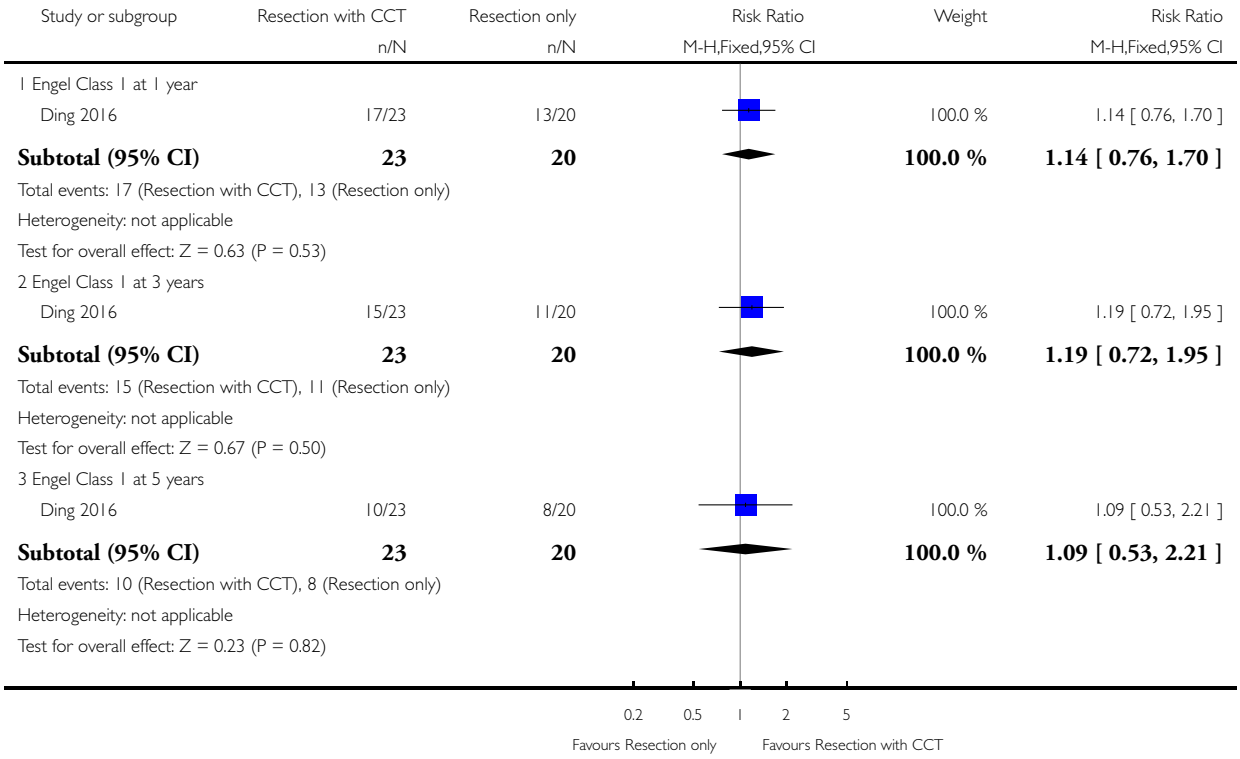


Analysis 2.5. Comparison 2 Comparison of surgical techniques (randomised evidence), Outcome 5 Resection with or without corpus callosotomy (CCT): Proportion free from seizures (Engel Class 1).

Review: Surgery for epilepsy

Comparison: 2 Comparison of surgical techniques (randomised evidence)

Outcome: 5 Resection with or without corpus callosotomy (CCT): Proportion free from seizures (Engel Class 1)

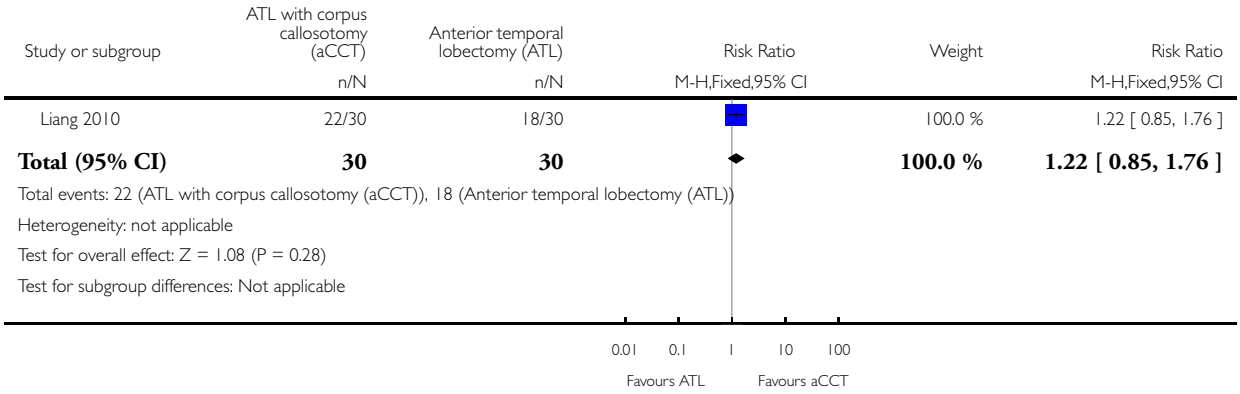


Analysis 2.6. Comparison 2 Comparison of surgical techniques (randomised evidence), Outcome 6 Anterior temporal lobectomy (ATL) with or without corpus callosotomy (CCT): Proportion free from seizures (Engel Class 1) at 2 years.

Review: Surgery for epilepsy

Comparison: 2 Comparison of surgical techniques (randomised evidence)

Outcome: 6 Anterior temporal lobectomy (ATL) with or without corpus callosotomy (CCT): Proportion free from seizures (Engel Class 1) at 2 years

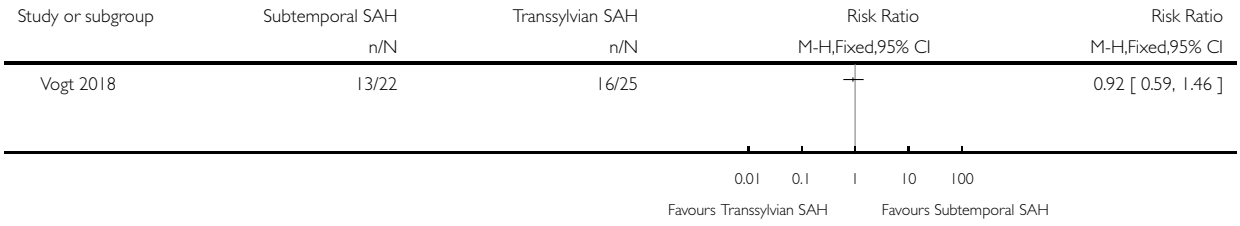


Analysis 2.7. Comparison 2 Comparison of surgical techniques (randomised evidence), Outcome 7 Subtemporal or transsylvian selective amygdalohippocampectomy (SAH): Proportion free from all seizures (including auras, ILAE 1a) at 1 year.

Review: Surgery for epilepsy

Comparison: 2 Comparison of surgical techniques (randomised evidence)

Outcome: 7 Subtemporal or transsylvian selective amygdalohippocampectomy (SAH): Proportion free from all seizures (including auras, ILAE 1a) at 1 year



Analysis 2.8. Comparison 2 Comparison of surgical techniques (randomised evidence), Outcome 8 Total or partial hippocampectomy: Proportion free from all seizures (including auras) at 1 year.

Review: Surgery for epilepsy

Comparison: 2 Comparison of surgical techniques (randomised evidence)

Outcome: 8 Total or partial hippocampectomy: Proportion free from all seizures (including auras) at 1 year

Study or subgroup	Total hippocampectomy n/N	Partial hippocampectomy n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Wyler 1995	25/36	13/34		100.0 %	1.82 [1.12, 2.93]
Total (95% CI)	**36**	**34**		**100.0 %**	**1.82 [1.12, 2.93]**
Total events: 25 (Total hippocampectomy), 13 (Partial hippocampectomy)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.44 (P = 0.015)					
Test for subgroup differences: Not applicable					

Analysis 2.9. Comparison 2 Comparison of surgical techniques (randomised evidence), Outcome 9 Length of resection (2.5 or 3.5 cm): Proportion free from seizures (Engel Class 1) at 1 year.

Review: Surgery for epilepsy

Comparison: 2 Comparison of surgical techniques (randomised evidence)

Outcome: 9 Length of resection (2.5 or 3.5 cm): Proportion free from seizures (Engel Class 1) at 1 year

Study or subgroup	2.5 cm resection n/N	3.5 cm resection n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Schramm 2011	77/104	75/103		100.0 %	1.02 [0.86, 1.20]
Total (95% CI)	**104**	**103**		**100.0 %**	**1.02 [0.86, 1.20]**
Total events: 77 (2.5 cm resection), 75 (3.5 cm resection)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.20 (P = 0.84)					
Test for subgroup differences: Not applicable					

Analysis 3.1. Comparison 3 Surgery for epilepsy (randomised and non-randomised evidence), Outcome 1 Proportion with a good outcome of surgery.

Review: Surgery for epilepsy

Comparison: 3 Surgery for epilepsy (randomised and non-randomised evidence)

Outcome: 1 Proportion with a good outcome of surgery

Study or subgroup	Poor outcome N	Good outcome N	Proportion (good outcome) (SE)	Proportion (good outcome) IV,Fixed,95% CI	Proportion (good outcome) IV,Fixed,95% CI
1 > 1 year seizure-free					
Adelson 1992	10	23	69.7 (8.00006)		69.70 [54.02, 85.38]
Althausen 2013	16	45	73.77 (5.63211)		73.77 [62.73, 84.81]
Awad 1991	20	27	57.45 (7.21191)		57.45 [43.31, 71.59]
Bautista 2003	15	28	65.12 (7.26812)		65.12 [50.87, 79.37]
Chee 1993	10	28	73.68 (7.14338)		73.68 [59.68, 87.68]
Dagar 2011	23	89	79.46 (3.81709)		79.46 [71.98, 86.94]
Duchowny 1998	15	16	51.61 (8.97559)		51.61 [34.02, 69.20]
Erba 1992	9	37	80.43 (5.84905)		80.43 [68.97, 91.89]
Fujiwara 2012	21	23	52.27 (7.52999)		52.27 [37.51, 67.03]
Garcia 1991	20	35	63.64 (6.48642)		63.64 [50.93, 76.35]
Garcia 1994	15	36	70.59 (6.38031)		70.59 [58.08, 83.10]
Gilliam 1997a	25	53	67.95 (5.28404)		67.95 [57.59, 78.31]
Gilliam 1997b	11	22	66.67 (8.2061)		66.67 [50.59, 82.75]
Greiner 2011	12	42	77.78 (5.6575)		77.78 [66.69, 88.87]
Hallbook 2010	22	88	80 (3.81385)		80.00 [72.52, 87.48]
Hemb 2010	102	223	68.62 (2.57411)		68.62 [63.57, 73.67]
Holmes 1997	22	22	50 (7.53778)		50.00 [35.23, 64.77]
Jack 1992	16	34	68 (6.59697)		68.00 [55.07, 80.93]
Jeha 2006	140	231	62.26 (2.51657)		62.26 [57.33, 67.19]
Jehi 2012	147	165	52.88 (2.82598)		52.88 [47.34, 58.42]
Jennum 1993	22	42	65.63 (5.93699)		65.63 [53.99, 77.27]
Kim 2009	72	94	56.63 (3.84652)		56.63 [49.09, 64.17]

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Study or subgroup	Poor outcome N	Good outcome N	Proportion (good outcome) (SE)	Proportion (good outcome) IV,Fixed,95% CI	Proportion (good outcome) IV,Fixed,95% CI
Kim 2010b	26	14	35 (7.54155)		35.00 [20.22, 49.78]
Lei 2008	16	180	91.84 (1.95574)		91.84 [88.01, 95.67]
Lopez-Gonzalez 2012	21	65	75.58 (4.63253)		75.58 [66.50, 84.66]
Morino 2009	7	55	88.71 (4.01923)		88.71 [80.83, 96.59]
O'Brien 1996	10	36	78.26 (6.08155)		78.26 [66.34, 90.18]
Oertel 2005	15	20	57.14 (8.36486)		57.14 [40.75, 73.53]
Paolicchi 2000	31	44	58.67 (5.68611)		58.67 [47.53, 69.81]
Rausch 2003	21	21	50 (7.71517)		50.00 [34.88, 65.12]
Spencer 2005	91	264	74.37 (2.31729)		74.37 [69.83, 78.91]
Swartz 1992	7	27	79.41 (6.93446)		79.41 [65.82, 93.00]
Tatum 2008	17	22	56.41 (7.94034)		56.41 [40.85, 71.97]
Theodore 2012	15	26	63.41 (7.5224)		63.41 [48.67, 78.15]
Walz 2003	13	85	86.73 (3.42643)		86.73 [80.01, 93.45]
Weinand 1992	32	57	64.04 (5.0866)		64.04 [54.07, 74.01]
Widdess-Walsh 2007	26	22	45.83 (7.19178)		45.83 [31.73, 59.93]
Wiebe 2001	13	23	63.89 (8.00538)		63.89 [48.20, 79.58]
Wyler 1995	32	38	54.29 (5.95415)		54.29 [42.62, 65.96]
Yu 2012a	39	61	61 (4.8775)		61.00 [51.44, 70.56]
Yu 2012b	74	148	66.67 (3.16386)		66.67 [60.47, 72.87]
Zangaladze 2008	33	66	66.67 (4.73779)		66.67 [57.38, 75.96]
2 Engel Class Scale					
Aaberg 2012	24	30	55.56 (6.76201)		55.56 [42.31, 68.81]
Adam 1996	4	26	86.67 (6.20633)		86.67 [74.51, 98.83]
Alfstad 2011	23	25	52.08 (7.21061)		52.08 [37.95, 66.21]
Alonso-Vanegas 2018	5	38	88.37 (4.88848)		88.37 [78.79, 97.95]
Arruda 1996	21	53	71.62 (5.24083)		71.62 [61.35, 81.89]
Babini 2013	4	26	86.67 (6.20633)		86.67 [74.51, 98.83]
Battaglia 2006	13	32	71.11 (6.7566)		71.11 [57.87, 84.35]
Baumann 2007	50	118	70.24 (3.52746)		70.24 [63.33, 77.15]
Bell 2009	16	24	60 (7.74597)		60.00 [44.82, 75.18]
Benifla 2006	28	78	73.58 (4.28221)		73.58 [65.19, 81.97]

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Study or subgroup	Poor outcome N	Good outcome N	Proportion (good outcome) (SE)	Proportion (good outcome) IV,Fixed,95% CI	Proportion (good outcome) IV,Fixed,95% CI
Berkovic 1995	61	74	54.81 (4.28332)		54.81 [46.41, 63.21]
Blount 2004	18	12	40 (8.94427)		40.00 [22.47, 57.53]
Blume 2004	44	26	37.14 (5.77519)		37.14 [25.82, 48.46]
Brainer-Lima 1996	3	29	90.63 (5.1527)		90.63 [80.53, 100.73]
Britton 1994	17	34	66.67 (6.60098)		66.67 [53.73, 79.61]
Caraballo 2011	12	33	73.33 (6.59218)		73.33 [60.41, 86.25]
Cascino 1995	52	113	68.48 (3.61672)		68.48 [61.39, 75.57]
Chabardes 2005	7	47	87.04 (4.57096)		87.04 [78.08, 96.00]
Chang 2009	12	45	78.95 (5.39989)		78.95 [68.37, 89.53]
Chkhenkeli 2007	55	12	17.91 (4.68446)		17.91 [8.73, 27.09]
Choi 2004a	8	27	77.14 (7.09782)		77.14 [63.23, 91.05]
Chung 2005	70	58	45.31 (4.39995)		45.31 [36.69, 53.93]
Cossu 2005	72	93	56.36 (3.86084)		56.36 [48.79, 63.93]
Cossu 2008	36	77	68.14 (4.38308)		68.14 [59.55, 76.73]
Costello 2009	10	32	76.19 (6.57205)		76.19 [63.31, 89.07]
Cukiert 2002	11	89	89 (3.1289)		89.00 [82.87, 95.13]
Dalmagro 2005	15	28	65.12 (7.26812)		65.12 [50.87, 79.37]
Delbeke 1996	15	23	60.53 (7.92929)		60.53 [44.99, 76.07]
Dellabadia 2002	15	20	57.14 (8.36486)		57.14 [40.75, 73.53]
Devlin 2003	16	17	51.52 (8.69989)		51.52 [34.47, 68.57]
Ding 2016	13	30	69.77 (7.00373)		69.77 [56.04, 83.50]
Donadio 2011	24	60	71.43 (4.92904)		71.43 [61.77, 81.09]
Dorward 2011	15	18	54.55 (8.66784)		54.55 [37.56, 71.54]
Dunkley 2011	22	20	47.62 (7.70642)		47.62 [32.52, 62.72]
Dunlea 2010	80	119	59.8 (3.47567)		59.80 [52.99, 66.61]
Elsharkawy 2008a	97	121	55.5 (3.36584)		55.50 [48.90, 62.10]
Elsharkawy 2009a	119	311	72.33 (2.1575)		72.33 [68.10, 76.56]
Elsharkawy 2011a	9	38	80.85 (5.7394)		80.85 [69.60, 92.10]
Erickson 2005	25	46	64.79 (5.66841)		64.79 [53.68, 75.90]
Fauser 2004	24	35	59.32 (6.39531)		59.32 [46.79, 71.85]
Gelinas 2011	15	52	77.61 (5.09255)		77.61 [67.63, 87.59]

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Study or subgroup	Poor outcome N	Good outcome N	Proportion (good outcome) (SE)	Proportion (good outcome) IV,Fixed,95% CI	Proportion (good outcome) IV,Fixed,95% CI
Georgakoulias 2008	8	42	84 (5.18459)		84.00 [73.84, 94.16]
Grivas 2006	15	37	71.15 (6.28263)		71.15 [58.84, 83.46]
Hader 2004	18	21	53.85 (7.98269)		53.85 [38.20, 69.50]
Hajek 2009	10	25	71.43 (7.63604)		71.43 [56.46, 86.40]
Hamiwka 2005	21	17	44.74 (8.06601)		44.74 [28.93, 60.55]
Hartley 2002	15	20	57.14 (8.36486)		57.14 [40.75, 73.53]
Hartzfield 2008	32	24	42.86 (6.613)		42.86 [29.90, 55.82]
Janszky 2003a	24	60	71.43 (4.92904)		71.43 [61.77, 81.09]
Janszky 2003b	24	123	83.67 (3.04847)		83.67 [77.70, 89.64]
Jaramillo-Betancur 2009	24	43	64.18 (5.85771)		64.18 [52.70, 75.66]
Jayakar 2008	57	44	43.56 (4.9338)		43.56 [33.89, 53.23]
Jayalakshmi 2011	28	50	64.1 (5.43153)		64.10 [53.45, 74.75]
Kan 2008	15	43	74.14 (5.7496)		74.14 [62.87, 85.41]
Kang 2009	50	194	79.51 (2.58405)		79.51 [74.45, 84.57]
Kanner 2009	14	86	86 (3.46987)		86.00 [79.20, 92.80]
Kilpatrick 1997	11	39	78 (5.85833)		78.00 [66.52, 89.48]
Kim 2010a	102	75	42.37 (3.71425)		42.37 [35.09, 49.65]
Kloss 2002	34	34	50 (6.06339)		50.00 [38.12, 61.88]
Knowlton 2008	25	37	59.68 (6.22993)		59.68 [47.47, 71.89]
Lee 2008	33	38	53.52 (5.91918)		53.52 [41.92, 65.12]
Lee 2010a	16	36	69.23 (6.40039)		69.23 [56.69, 81.77]
Lee 2011	3	37	92.5 (4.16458)		92.50 [84.34, 100.66]
Li 1997	12	39	76.47 (5.93974)		76.47 [64.83, 88.11]
Li 1999	22	16	42.11 (8.00933)		42.11 [26.41, 57.81]
Liang 2010	20	40	66.67 (6.08581)		66.67 [54.74, 78.60]
Liang 2012	33	173	83.98 (2.55552)		83.98 [78.97, 88.99]
Liava 2012	13	39	75 (6.00481)		75.00 [63.23, 86.77]
Lorenzo 1995	31	17	35.42 (6.90309)		35.42 [21.89, 48.95]
Madhavan 2007	33	37	52.86 (5.96638)		52.86 [41.17, 64.55]
Mani 2006	36	86	70.49 (4.12915)		70.49 [62.40, 78.58]
Mihara 2004	88	269	75.35 (2.28095)		75.35 [70.88, 79.82]

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Poor outcome Good outcome

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Study or subgroup	Poor outcome N	Good outcome N	Proportion (good outcome) (SE)	Proportion (good outcome) IV,Fixed,95% CI	Proportion (good outcome) IV,Fixed,95% CI
Miserocchi 2013	10	58	85.29 (4.29488)		85.29 [76.87, 93.71]
Morris 1998	10	26	72.22 (7.46505)		72.22 [57.59, 86.85]
O'Brien 2000	22	14	38.89 (8.12497)		38.89 [22.97, 54.81]
Paglioli 2006	17	143	89.38 (2.4362)		89.38 [84.61, 94.15]
Park 2002	40	108	72.97 (3.65047)		72.97 [65.82, 80.12]
Park 2006	10	20	66.67 (8.60663)		66.67 [49.80, 83.54]
Perego 2009	8	29	78.38 (6.7677)		78.38 [65.12, 91.64]
Perry 2010	49	34	40.96 (5.39784)		40.96 [30.38, 51.54]
Phi 2009	7	80	91.95 (2.91619)		91.95 [86.23, 97.67]
Pinheiro-Martins 2012	37	33	47.14 (5.96638)		47.14 [35.45, 58.83]
Prevedello 2000	31	53	63.1 (5.26502)		63.10 [52.78, 73.42]
Raabe 2012	19	57	75 (4.967)		75.00 [65.26, 84.74]
Radhakrishnan 1998	41	134	76.57 (3.20175)		76.57 [70.29, 82.85]
Remi 2011	16	138	89.61 (2.45877)		89.61 [84.79, 94.43]
Roberti 2007	15	27	64.29 (7.39356)		64.29 [49.80, 78.78]
Russo 2003	37	64	63.37 (4.79412)		63.37 [53.97, 72.77]
Sagher 2012	11	85	88.54 (3.25087)		88.54 [82.17, 94.91]
Salanova 1994	36	53	59.55 (5.2024)		59.55 [49.35, 69.75]
Sarkis 2012	24	38	61.29 (6.186)		61.29 [49.17, 73.41]
Schramm 2011	55	152	73.43 (3.07007)		73.43 [67.41, 79.45]
Seymour 2012	138	153	52.58 (2.92716)		52.58 [46.84, 58.32]
Sinclair 2003	20	57	74.03 (4.99708)		74.03 [64.24, 83.82]
Sindou 2006	15	85	85 (3.57071)		85.00 [78.00, 92.00]
Sola 2005	63	74	54.01 (4.258)		54.01 [45.66, 62.36]
Sperling 1992	10	41	80.39 (5.55951)		80.39 [69.49, 91.29]
Stavrou 2008	8	45	84.91 (4.91742)		84.91 [75.27, 94.55]
Suppiah 2009	80	94	54.02 (3.7782)		54.02 [46.61, 61.43]
Tanriverdi 2010	96	160	62.5 (3.02577)		62.50 [56.57, 68.43]
Terra-Bustamante 2005a	45	62	57.94 (4.77229)		57.94 [48.59, 67.29]
Terra-Bustamante 2005b	8	27	77.14 (7.09782)		77.14 [63.23, 91.05]
Tezer 2008	19	90	82.57 (3.63378)		82.57 [75.45, 89.69]

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Study or subgroup	Poor outcome N	Good outcome N	Proportion (good outcome) (SE)	Proportion (good outcome) IV,Fixed,95% CI	Proportion (good outcome) IV,Fixed,95% CI
Tigaran 2003	33	32	49.23 (6.201)		49.23 [37.08, 61.38]
Tripathi 2008	26	29	52.73 (6.73196)		52.73 [39.54, 65.92]
Trottier 2008	23	73	76.04 (4.35631)		76.04 [67.50, 84.58]
Urbach 2007	17	25	59.52 (7.57392)		59.52 [44.68, 74.36]
Velasco 2011	70	93	57.06 (3.87712)		57.06 [49.46, 64.66]
Wellmer 2012	59	106	64.24 (3.73124)		64.24 [56.93, 71.55]
Wieshmann 2008	30	46	60.53 (5.60685)		60.53 [49.54, 71.52]
Wray 2012	16	36	69.23 (6.40039)		69.23 [56.69, 81.77]
Wyllie 1998	44	92	67.65 (4.01155)		67.65 [59.79, 75.51]
Yeon 2009	10	50	83.33 (4.81125)		83.33 [73.90, 92.76]
Yu 2009	17	26	60.47 (7.45604)		60.47 [45.86, 75.08]
Zentner 1995	64	103	61.68 (3.76213)		61.68 [54.31, 69.05]
Zentner 1996	26	30	53.57 (6.66446)		53.57 [40.51, 66.63]
3 'Other' scale					
Barbaro 2018	21	37	63.79 (7.32906)		63.79 [49.43, 78.15]
Boesebeck 2007	48	33	66.67 (4.73779)		66.67 [57.38, 75.96]
Boshuisen 2010	10	33	76.74 (6.4425)		76.74 [64.11, 89.37]
de Tisi 2011	370	245	39.84 (1.97411)		39.84 [35.97, 43.71]
Dwivedi 2017	13	44	77.19 (5.55758)		77.19 [66.30, 88.08]
Engman 2004	19	35	64.81 (6.49861)		64.81 [52.07, 77.55]
Goldstein 1996	18	15	45.45 (8.66784)		45.45 [28.46, 62.44]
Gyimesi 2007	26	74	74 (4.38634)		74.00 [65.40, 82.60]
Holmes 2000	72	54	42.86 (4.40867)		42.86 [34.22, 51.50]
Jeong 1999	15	78	83.87 (3.81389)		83.87 [76.39, 91.35]
Kral 2007	13	27	67.5 (7.40566)		67.50 [52.99, 82.01]
Lackmayer 2013	13	32	71.11 (6.7566)		71.11 [57.87, 84.35]
Lee 2006	14	37	72.55 (6.24899)		72.55 [60.30, 84.80]
Mathern 1999	120	78	39.39 (3.47248)		39.39 [32.58, 46.20]
McIntosh 2012	70	11	13.58 (3.80643)		13.58 [6.12, 21.04]
Phi 2010	21	20	48.78 (7.80637)		48.78 [33.48, 64.08]
Rossi 1994	52	86	62.32 (4.12508)		62.32 [54.23, 70.41]

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Poor outcome Good outcome

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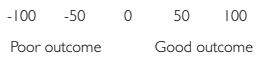
Study or subgroup	Poor outcome N	Good outcome N	Proportion (good outcome) (SE)	Proportion (good outcome) IV,Fixed,95% CI	Proportion (good outcome) IV,Fixed,95% CI
Sakamoto 2009	17	19	52.78 (8.32046)		52.78 [36.47, 69.09]
Vogt 2018	18	29	61.7 (7.41316)		61.70 [47.17, 76.23]
Yang 2011	72	27	27.27 (4.47605)		27.27 [18.50, 36.04]



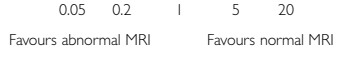
Analysis 4.1. Comparison 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence), Outcome 1 Good outcome by MRI results.

Review: Surgery for epilepsy

Comparison: 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence)

Outcome: 1 Good outcome by MRI results

Study or subgroup	Normal MRI n/N	Abnormal MRI n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 > 1 year seizure-free					
Duchowny 1998	4/5	15/24		0.5 %	1.28 [0.75, 2.19]
Erba 1992	6/10	31/36		1.4 %	0.70 [0.41, 1.18]
Fujiwara 2012	6/15	16/26		1.2 %	0.65 [0.33, 1.30]
Garcia 1994	10/20	26/31		2.1 %	0.60 [0.37, 0.95]
Gilliam 1997a	11/19	42/59		2.1 %	0.81 [0.54, 1.23]
Gilliam 1997b	2/3	20/30		0.4 %	1.00 [0.43, 2.31]
Hallbook 2010	24/29	64/81		3.4 %	1.05 [0.86, 1.28]
Jehi 2012	10/33	137/279		2.9 %	0.62 [0.36, 1.05]
Kim 2009	49/96	45/70		5.2 %	0.79 [0.61, 1.03]
Kim 2010b	7/24	7/16		0.8 %	0.67 [0.29, 1.54]
Paolicchi 2000	18/35	26/40		2.4 %	0.79 [0.53, 1.17]



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Study or subgroup	Normal MRI n/N	Abnormal MRI n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Spencer 2005	22/40	157/225		4.8 %	0.79 [0.59, 1.06]
Swartz 1992	5/5	22/29		0.8 %	1.22 [0.89, 1.68]
Theodore 2012	8/15	18/26		1.3 %	0.77 [0.45, 1.32]
Widdess-Walsh 2007	12/25	10/23		1.0 %	1.10 [0.59, 2.05]
Yu 2012a	12/21	49/79		2.1 %	0.92 [0.61, 1.39]
Yu 2012b	36/62	112/160		6.3 %	0.83 [0.66, 1.05]
Subtotal (95% CI)	**457**	**1234**		**38.6 %**	**0.82 [0.74, 0.90]**
Total events: 242 (Normal MRI), 797 (Abnormal MRI)					
Heterogeneity: Chi^2 = 20.10, df = 16 (P = 0.22); I^2 =20%					
Test for overall effect: Z = 4.02 (P = 0.000058)					
2 Engel Class Scale					
Adam 1996	0/1	26/29		0.3 %	0.28 [0.03, 3.13]
Alfstad 2011	5/8	20/40		0.7 %	1.25 [0.67, 2.32]
Berkovic 1995	8/24	66/111		2.4 %	0.56 [0.31, 1.01]
Chabardes 2005	7/8	34/40		1.1 %	1.03 [0.77, 1.38]
Cossu 2005	16/42	77/123		3.9 %	0.61 [0.40, 0.92]
Ding 2016	13/19	17/24		1.5 %	0.97 [0.65, 1.44]
Erickson 2005	8/16	49/63		2.0 %	0.64 [0.39, 1.07]
Hartley 2002	2/4	18/31		0.4 %	0.86 [0.31, 2.40]
Hartzfield 2008	5/15	19/41		1.0 %	0.72 [0.33, 1.58]
Kim 2010a	34/111	41/66		5.2 %	0.49 [0.35, 0.69]
Liang 2012	67/88	106/118		9.1 %	0.85 [0.74, 0.97]
Liava 2012	5/10	34/42		1.3 %	0.62 [0.33, 1.17]
Lorenzo 1995	7/26	10/22		1.1 %	0.59 [0.27, 1.29]
Mihara 2004	150/195	71/87		9.9 %	0.94 [0.83, 1.07]
O'Brien 2000	7/17	7/19		0.7 %	1.12 [0.49, 2.53]
Perego 2009	2/6	27/31		0.9 %	0.38 [0.12, 1.20]
Perry 2010	5/18	29/65		1.3 %	0.62 [0.28, 1.38]
Radhakrishnan 1998	45/71	89/104		7.3 %	0.74 [0.61, 0.90]
Sinclair 2003	5/12	52/65		1.6 %	0.52 [0.26, 1.03]
Sindou 2006	8/13	77/87		2.0 %	0.70 [0.45, 1.08]
Sola 2005	21/34	75/99		3.9 %	0.82 [0.61, 1.09]
Wray 2012	2/6	34/46		0.8 %	0.45 [0.14, 1.42]

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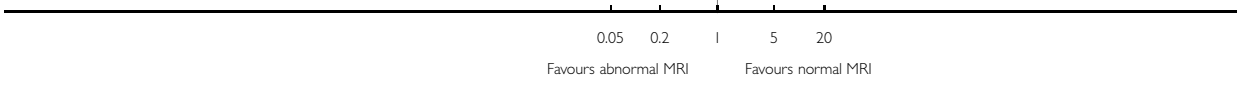
Study or subgroup	Normal MRI n/N	Abnormal MRI n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Subtotal (95% CI)	**744**	**1353**		**58.3 %**	**0.75 [0.69, 0.81]**
Total events: 422 (Normal MRI), 978 (Abnormal MRI)					
Heterogeneity: Chi^2 = 39.20, df = 21 (P = 0.01); I^2 =46%					
Test for overall effect: Z = 7.32 (P < 0.00001)					
3 'Other' scale					
Boshuisen 2010	28/32	5/11		0.7 %	1.93 [0.99, 3.73]
Goldstein 1996	5/14	10/19		0.9 %	0.68 [0.30, 1.54]
Sakamoto 2009	0/4	19/32		0.5 %	0.17 [0.01, 2.38]
Yang 2011	3/20	24/79		1.0 %	0.49 [0.17, 1.48]
Subtotal (95% CI)	**70**	**141**		**3.1 %**	**0.84 [0.53, 1.32]**
Total events: 36 (Normal MRI), 58 (Abnormal MRI)					
Heterogeneity: Chi^2 = 8.65, df = 3 (P = 0.03); I^2 =65%					
Test for overall effect: Z = 0.76 (P = 0.45)					
Total (95% CI)	**1271**	**2728**		**100.0 %**	**0.78 [0.73, 0.83]**
Total events: 700 (Normal MRI), 1833 (Abnormal MRI)					
Heterogeneity: Chi^2 = 68.37, df = 42 (P = 0.01); I^2 =39%					
Test for overall effect: Z = 8.10 (P < 0.00001)					
Test for subgroup differences: Chi^2 = 2.07, df = 2 (P = 0.35), I^2 =4%					



Analysis 4.2. Comparison 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence), Outcome 2 Good outcome by use of intracranial monitoring (IM).

Review: Surgery for epilepsy

Comparison: 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence)

Outcome: 2 Good outcome by use of intracranial monitoring (IM)

Study or subgroup	IM used n/N	IM not used n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 > 1 year seizure-free					
Garcia 1994	8/14	28/37		3.7 %	0.76 [0.46, 1.23]
Kim 2009	87/146	7/20		3.0 %	1.70 [0.92, 3.14]
Kim 2010b	10/33	4/7		1.6 %	0.53 [0.23, 1.21]
Spencer 2005	73/116	129/181		24.3 %	0.88 [0.75, 1.04]
Tatum 2008	4/8	18/31		1.8 %	0.86 [0.40, 1.83]
Theodore 2012	7/17	19/24		3.8 %	0.52 [0.28, 0.95]
Subtotal (95% CI)	**334**	**300**		**38.1 %**	**0.88 [0.76, 1.02]**
Total events: 189 (IM used), 205 (IM not used)					
Heterogeneity: Chi^2 = 9.23, df = 5 (P = 0.10); I^2 =46%					
Test for overall effect: Z = 1.66 (P = 0.097)					
2 Engel Class Scale					
Adam 1996	5/8	21/22		2.7 %	0.65 [0.38, 1.13]
Alfstad 2011	7/13	18/35		2.3 %	1.05 [0.58, 1.90]
Chang 2009	8/13	24/31		3.4 %	0.79 [0.50, 1.27]
Cossu 2008	62/96	15/17		6.1 %	0.73 [0.58, 0.92]
Gelinas 2011	27/34	25/33		6.1 %	1.05 [0.81, 1.36]
Grivas 2006	11/11	36/41		3.9 %	1.10 [0.93, 1.30]
Lee 2008	34/65	4/6		1.8 %	0.78 [0.43, 1.45]
Liava 2012	23/33	16/19		4.9 %	0.83 [0.61, 1.11]
Morris 1998	14/21	12/15		3.4 %	0.83 [0.56, 1.24]
O'Brien 2000	6/20	8/16		2.1 %	0.60 [0.26, 1.38]
Perry 2010	16/34	18/49		3.6 %	1.28 [0.77, 2.14]
Raabe 2012	15/25	42/51		6.7 %	0.73 [0.52, 1.03]
Terra-Bustamante 2005a	11/15	16/20		3.3 %	0.92 [0.63, 1.33]
Wyllie 1998	15/30	66/90		7.9 %	0.68 [0.47, 1.00]
Subtotal (95% CI)	**418**	**445**		**58.2 %**	**0.85 [0.77, 0.94]**

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Study or subgroup	IM used n/N	IM not used n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Total events: 254 (IM used), 321 (IM not used)					
Heterogeneity: Chi^2 = 20.47, df = 13 (P = 0.08); I^2 =37%					
Test for overall effect: Z = 3.03 (P = 0.0024)					
3 'Other' scale					
Kan 2008	5/10	38/40		3.7 %	0.53 [0.28, 0.98]
Subtotal (95% CI)	**10**	**40**		**3.7 %**	**0.53 [0.28, 0.98]**
Total events: 5 (IM used), 38 (IM not used)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.02 (P = 0.044)					
Total (95% CI)	**762**	**785**		**100.0 %**	**0.85 [0.78, 0.93]**
Total events: 448 (IM used), 564 (IM not used)					
Heterogeneity: Chi^2 = 31.89, df = 20 (P = 0.04); I^2 =37%					
Test for overall effect: Z = 3.70 (P = 0.00021)					
Test for subgroup differences: Chi^2 = 2.51, df = 2 (P = 0.29), I^2 =20%					

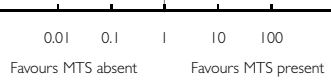
Analysis 4.3. Comparison 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence), Outcome 3 Good outcome by presence of mesial temporal sclerosis (MTS).

Review: Surgery for epilepsy

Comparison: 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence)

Outcome: 3 Good outcome by presence of mesial temporal sclerosis (MTS)

Study or subgroup	MTS present n/N	MTS absent n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 > 1 year seizure-free					
Dagar 2011	23/26	66/86		3.0 %	1.15 [0.96, 1.38]
Erba 1992	8/9	29/37		1.1 %	1.13 [0.85, 1.51]
Gilliam 1997b	1/2	21/31		0.3 %	0.74 [0.18, 3.01]
Hemb 2010	24/27	199/298		3.3 %	1.33 [1.14, 1.56]
Jennum 1993	4/7	38/57		0.8 %	0.86 [0.44, 1.67]
O'Brien 1996	27/31	9/15		1.2 %	1.45 [0.94, 2.24]
Spencer 2005	128/171	47/86		6.2 %	1.37 [1.11, 1.69]
Swartz 1992	12/15	15/19		1.3 %	1.01 [0.72, 1.43]
Theodore 2012	16/23	10/18		1.1 %	1.25 [0.76, 2.05]
Subtotal (95% CI)	**311**	**647**		**18.3 %**	**1.25 [1.13, 1.39]**
Total events: 243 (MTS present), 434 (MTS absent)					
Heterogeneity: Chi^2 = 6.24, df = 8 (P = 0.62); I^2 =0.0%					
Test for overall effect: Z = 4.29 (P = 0.000018)					
2 Engel Class Scale					
Aaberg 2012	5/7	25/48		0.6 %	1.37 [0.80, 2.36]
Alfstad 2011	12/18	13/30		1.0 %	1.54 [0.91, 2.60]
Bell 2009	4/7	20/33		0.7 %	0.94 [0.47, 1.89]
Berkovic 1995	49/85	25/50		3.1 %	1.15 [0.83, 1.61]
Chabardes 2005	23/28	18/20		2.1 %	0.91 [0.73, 1.14]
Cossu 2005	18/27	13/22		1.4 %	1.13 [0.73, 1.75]
Cossu 2008	7/11	70/102		1.3 %	0.93 [0.58, 1.48]
Delbeke 1996	16/27	7/11		1.0 %	0.93 [0.54, 1.61]
Donadio 2011	25/32	35/52		2.6 %	1.16 [0.89, 1.51]
Erickson 2005	19/22	35/55		2.0 %	1.36 [1.05, 1.76]
Georgakoulias 2008	15/21	21/23		2.0 %	0.78 [0.58, 1.05]
Grivas 2006	22/31	15/21		1.8 %	0.99 [0.70, 1.41]



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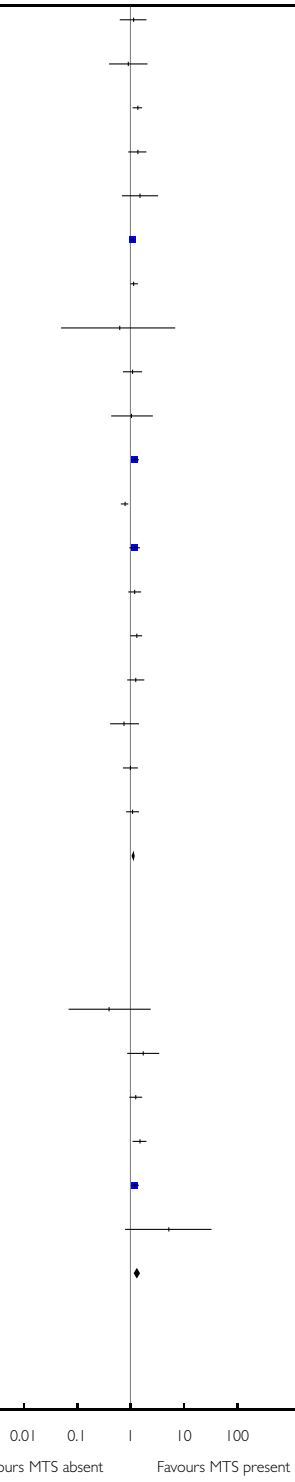
Study or subgroup	MTS present n/N	MTS absent n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Hartley 2002	8/13	12/22		0.9 %	1.13 [0.64, 2.00]
Hartzfield 2008	4/10	20/46		0.7 %	0.92 [0.40, 2.10]
Kanner 2009	60/63	26/37		3.2 %	1.36 [1.09, 1.68]
Kilpatrick 1997	29/34	10/16		1.3 %	1.36 [0.91, 2.04]
Li 1999	10/20	6/18		0.6 %	1.50 [0.68, 3.29]
Mihara 2004	138/172	131/185		12.5 %	1.13 [1.01, 1.28]
Miserocchi 2013	19/20	39/48		2.3 %	1.17 [0.99, 1.38]
O'Brien 2000	0/1	14/35		0.2 %	0.62 [0.05, 7.07]
Perego 2009	21/26	8/11		1.1 %	1.11 [0.74, 1.67]
Perry 2010	3/7	31/76		0.5 %	1.05 [0.43, 2.58]
Radhakrishnan 1998	63/74	71/101		5.9 %	1.21 [1.03, 1.42]
Schramm 2011	133/186	19/21		3.4 %	0.79 [0.67, 0.93]
Seymour 2012	85/158	63/143		6.5 %	1.22 [0.97, 1.54]
Sinclair 2003	12/14	45/63		1.6 %	1.20 [0.92, 1.56]
Sindou 2006	63/69	22/31		3.0 %	1.29 [1.02, 1.63]
Terra-Bustamante 2005a	12/17	50/90		1.6 %	1.27 [0.89, 1.82]
Wray 2012	5/9	31/43		1.1 %	0.77 [0.42, 1.42]
Wyllie 1998	14/21	67/99		2.3 %	0.99 [0.71, 1.37]
Zentner 1995	26/39	77/128		3.6 %	1.11 [0.85, 1.44]
Subtotal (95% CI)	**1269**	**1680**		**72.0 %**	**1.13 [1.07, 1.20]**
Total events: 920 (MTS present), 1039 (MTS absent)					
Heterogeneity: Chi² = 42.81, df = 30 (P = 0.06); I² =30%					
Test for overall effect: Z = 4.49 (P < 0.00001)					
3 'Other' scale					
Goldstein 1996	1/5	14/28		0.4 %	0.40 [0.07, 2.40]
Jeong 1999	74/85	4/8		0.7 %	1.74 [0.87, 3.50]
Kan 2008	14/16	29/42		1.6 %	1.27 [0.96, 1.67]
Mathern 1999	7/8	71/120		0.9 %	1.48 [1.09, 2.00]
Sakamoto 2009	63/74	71/101		5.9 %	1.21 [1.03, 1.42]
Yang 2011	18/28	1/8		0.2 %	5.14 [0.81, 32.84]
Subtotal (95% CI)	**216**	**307**		**9.7 %**	**1.31 [1.14, 1.51]**
Total events: 177 (MTS present), 190 (MTS absent)					
Heterogeneity: Chi² = 6.05, df = 5 (P = 0.30); I² =17%					
Test for overall effect: Z = 3.73 (P = 0.00019)					



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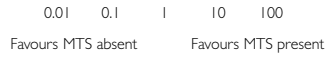
Study or subgroup	MTS present n/N	MTS absent n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Total (95% CI)	**1796**	**2634**		**100.0 %**	**1.17 [1.12, 1.23]**
Total events: 1340 (MTS present), 1663 (MTS absent)					
Heterogeneity: Chi^2 = 62.32, df = 45 (P = 0.04); I^2 =28%					
Test for overall effect: Z = 6.83 (P < 0.00001)					
Test for subgroup differences: Chi^2 = 5.49, df = 2 (P = 0.06), I^2 =64%					



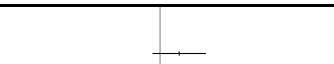
Analysis 4.4. Comparison 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence), Outcome 4 Good outcome by concordance of pre-op MRI and EEG.

Review: Surgery for epilepsy

Comparison: 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence)

Outcome: 4 Good outcome by concordance of pre-op MRI and EEG

Study or subgroup	Concordant n/N	Discordant n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 > 1 year seizure-free					
Garcia 1994	34/45	2/6		1.0 %	2.27 [0.72, 7.11]
Gilliam 1997a	37/48	16/30		5.5 %	1.45 [1.00, 2.09]
Gilliam 1997b	15/20	7/13		2.4 %	1.39 [0.79, 2.45]
Kim 2009	68/127	26/39		11.1 %	0.80 [0.61, 1.06]
Kim 2010b	12/29	2/11		0.8 %	2.28 [0.60, 8.57]
Spencer 2005	111/153	90/143		25.9 %	1.15 [0.98, 1.35]
Tatum 2008	20/27	2/12		0.8 %	4.44 [1.23, 16.06]
Theodore 2012	16/24	10/17		3.3 %	1.13 [0.70, 1.85]
Subtotal (95% CI)	**473**	**271**		**50.7 %**	**1.21 [1.07, 1.37]**
Total events: 313 (Concordant), 155 (Discordant)					
Heterogeneity: Chi^2 = 16.01, df = 7 (P = 0.03); I^2 =56%					
Test for overall effect: Z = 2.97 (P = 0.0030)					



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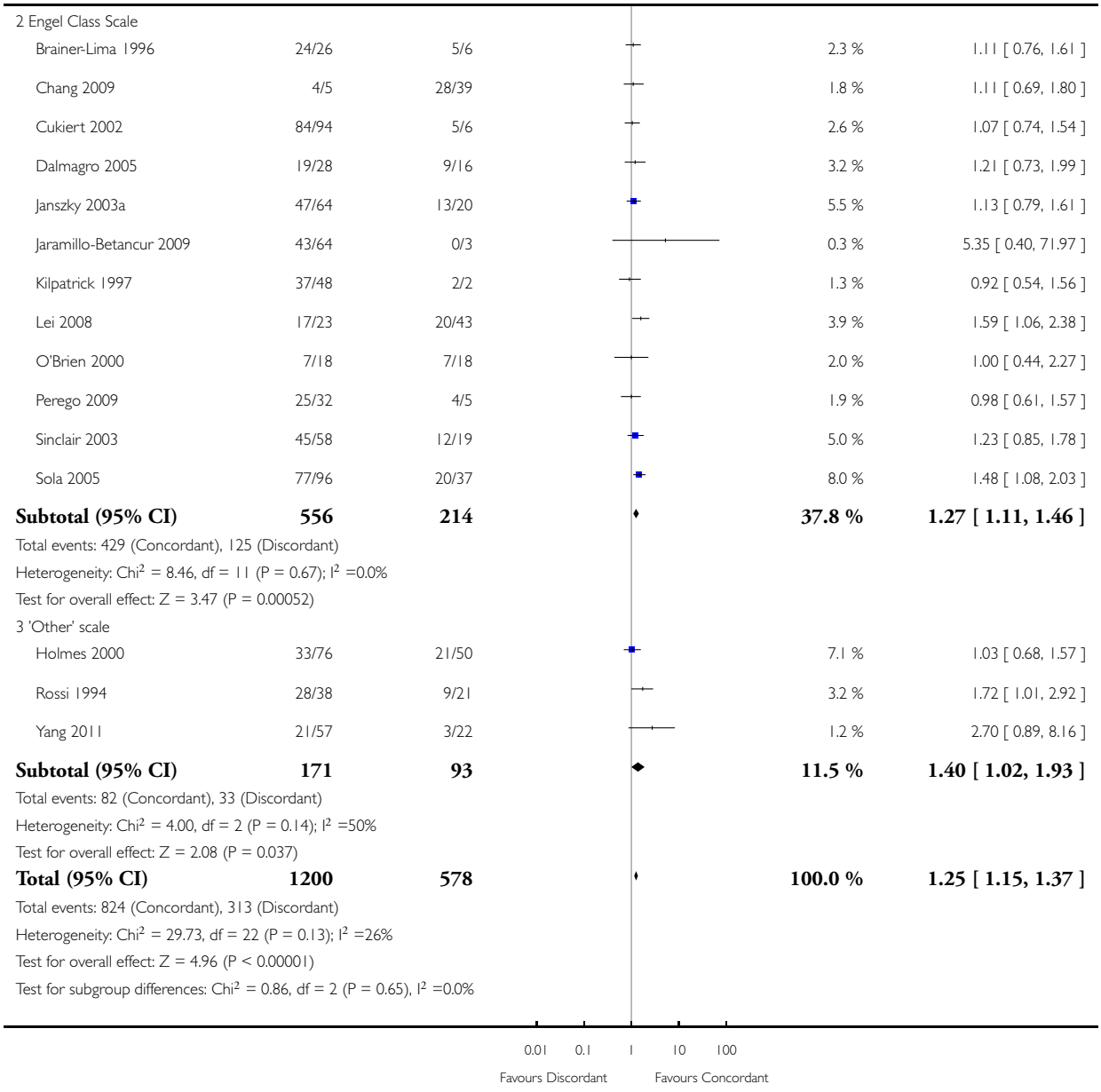
Study or subgroup	Concordant n/N	Discordant n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
2 Engel Class Scale					
Brainer-Lima 1996	24/26	5/6		2.3 %	1.11 [0.76, 1.61]
Chang 2009	4/5	28/39		1.8 %	1.11 [0.69, 1.80]
Cukiert 2002	84/94	5/6		2.6 %	1.07 [0.74, 1.54]
Dalmagro 2005	19/28	9/16		3.2 %	1.21 [0.73, 1.99]
Janszky 2003a	47/64	13/20		5.5 %	1.13 [0.79, 1.61]
Jaramillo-Betancur 2009	43/64	0/3		0.3 %	5.35 [0.40, 71.97]
Kilpatrick 1997	37/48	2/2		1.3 %	0.92 [0.54, 1.56]
Lei 2008	17/23	20/43		3.9 %	1.59 [1.06, 2.38]
O'Brien 2000	7/18	7/18		2.0 %	1.00 [0.44, 2.27]
Perego 2009	25/32	4/5		1.9 %	0.98 [0.61, 1.57]
Sinclair 2003	45/58	12/19		5.0 %	1.23 [0.85, 1.78]
Sola 2005	77/96	20/37		8.0 %	1.48 [1.08, 2.03]
Subtotal (95% CI)	**556**	**214**		**37.8 %**	**1.27 [1.11, 1.46]**
Total events: 429 (Concordant), 125 (Discordant)					
Heterogeneity: Chi^2 = 8.46, df = 11 (P = 0.67); I^2 =0.0%					
Test for overall effect: Z = 3.47 (P = 0.00052)					
3 'Other' scale					
Holmes 2000	33/76	21/50		7.1 %	1.03 [0.68, 1.57]
Rossi 1994	28/38	9/21		3.2 %	1.72 [1.01, 2.92]
Yang 2011	21/57	3/22		1.2 %	2.70 [0.89, 8.16]
Subtotal (95% CI)	**171**	**93**		**11.5 %**	**1.40 [1.02, 1.93]**
Total events: 82 (Concordant), 33 (Discordant)					
Heterogeneity: Chi^2 = 4.00, df = 2 (P = 0.14); I^2 =50%					
Test for overall effect: Z = 2.08 (P = 0.037)					
Total (95% CI)	**1200**	**578**		**100.0 %**	**1.25 [1.15, 1.37]**
Total events: 824 (Concordant), 313 (Discordant)					
Heterogeneity: Chi^2 = 29.73, df = 22 (P = 0.13); I^2 =26%					
Test for overall effect: Z = 4.96 (P < 0.00001)					
Test for subgroup differences: Chi^2 = 0.86, df = 2 (P = 0.65), I^2 =0.0%					



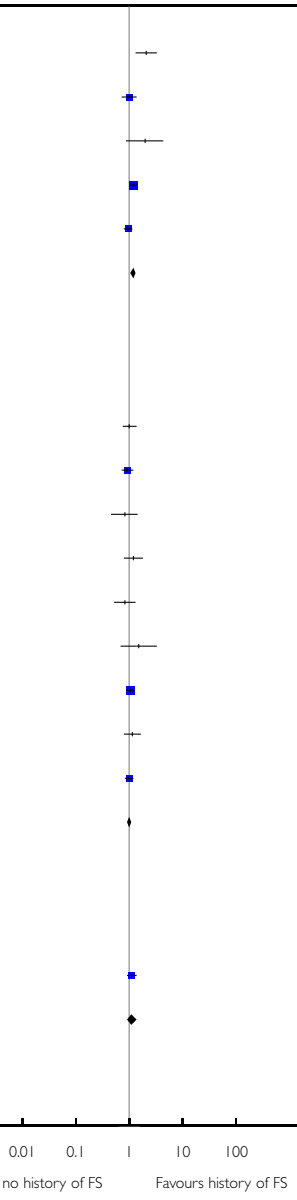
Analysis 4.5. Comparison 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence), Outcome 5 Good outcome by history of febrile seizures (FS).

Review: Surgery for epilepsy

Comparison: 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence)

Outcome: 5 Good outcome by history of febrile seizures (FS)

Study or subgroup	History of FS n/N	No history of FS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 > 1 year seizure-free					
Holmes 1997	7/8	15/36		1.5 %	2.10 [1.32, 3.35]
Kim 2009	17/30	77/136		7.7 %	1.00 [0.71, 1.41]
Kim 2010b	6/11	8/29		1.2 %	1.98 [0.89, 4.40]
Spencer 2005	67/86	134/210		21.6 %	1.22 [1.05, 1.42]
Walz 2003	20/24	65/74		8.8 %	0.95 [0.78, 1.16]
Subtotal (95% CI)	**159**	**485**		**40.9 %**	**1.18 [1.05, 1.32]**
Total events: 117 (History of FS), 299 (No history of FS)					
Heterogeneity: Chi^2 = 13.13, df = 4 (P = 0.01); I^2 =70%					
Test for overall effect: Z = 2.75 (P = 0.0059)					
2 Engel Class Scale					
Adam 1996	14/16	12/14		3.6 %	1.02 [0.77, 1.35]
Chabardes 2005	18/22	23/26		5.9 %	0.92 [0.73, 1.18]
Grivas 2006	3/4	41/45		1.9 %	0.82 [0.46, 1.46]
Hajek 2009	14/18	11/17		3.1 %	1.20 [0.78, 1.85]
Jaramillo-Betancur 2009	10/18	33/49		4.9 %	0.82 [0.52, 1.30]
Perry 2010	3/5	31/78		1.0 %	1.51 [0.70, 3.25]
Radhakrishnan 1998	45/57	89/118		16.1 %	1.05 [0.88, 1.24]
Terra-Bustamante 2005a	6/7	21/28		2.3 %	1.14 [0.79, 1.66]
Tezer 2008	60/73	30/36		11.2 %	0.99 [0.82, 1.18]
Subtotal (95% CI)	**220**	**411**		**50.0 %**	**1.01 [0.92, 1.11]**
Total events: 173 (History of FS), 291 (No history of FS)					
Heterogeneity: Chi^2 = 4.12, df = 8 (P = 0.85); I^2 =0.0%					
Test for overall effect: Z = 0.22 (P = 0.83)					
3 'Other' scale					
Jeong 1999	53/61	25/32		9.1 %	1.11 [0.90, 1.37]
Subtotal (95% CI)	**61**	**32**		**9.1 %**	**1.11 [0.90, 1.37]**
Total events: 53 (History of FS), 25 (No history of FS)					
Heterogeneity: not applicable					



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Study or subgroup	History of FS n/N	No history of FS n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Test for overall effect: Z = 1.00 (P = 0.32)					
Total (95% CI)	**440**	**928**		**100.0 %**	**1.09 [1.01, 1.17]**
Total events: 343 (History of FS), 615 (No history of FS)					
Heterogeneity: Chi^2 = 20.64, df = 14 (P = 0.11); I^2 =32%					
Test for overall effect: Z = 2.34 (P = 0.019)					
Test for subgroup differences: Chi^2 = 3.95, df = 2 (P = 0.14), I^2 =49%					

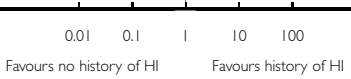
Analysis 4.6. Comparison 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence), Outcome 6 Good outcome by history of head injury (HI).

Review: Surgery for epilepsy

Comparison: 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence)

Outcome: 6 Good outcome by history of head injury (HI)

Study or subgroup	History of HI n/N	No history of HI n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 > 1 year seizure-free					
Greiner 2011	0/1	42/53		2.3 %	0.32 [0.03, 3.52]
Walz 2003	31/38	54/60		32.1 %	0.91 [0.76, 1.08]
Subtotal (95% CI)	**39**	**113**		**34.4 %**	**0.87 [0.72, 1.05]**
Total events: 31 (History of HI), 96 (No history of HI)					
Heterogeneity: Chi^2 = 0.93, df = 1 (P = 0.34); I^2 =0.0%					
Test for overall effect: Z = 1.46 (P = 0.14)					
2 Engel Class Scale					
Adam 1996	5/5	21/25		6.2 %	1.11 [0.82, 1.49]
Terra-Bustamante 2005a	13/14	14/21		8.6 %	1.39 [1.00, 1.95]
Tezer 2008	34/43	47/66		28.4 %	1.11 [0.89, 1.38]
Subtotal (95% CI)	**62**	**112**		**43.2 %**	**1.17 [0.99, 1.37]**
Total events: 52 (History of HI), 82 (No history of HI)					
Heterogeneity: Chi^2 = 1.38, df = 2 (P = 0.50); I^2 =0.0%					



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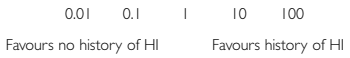
Study or subgroup	History of HI n/N	No history of HI n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Test for overall effect: Z = 1.85 (P = 0.064)					
3 'Other' scale					
Holmes 2000	6/24	48/102		14.0 %	0.53 [0.26, 1.09]
Yang 2011	11/34	16/65		8.4 %	1.31 [0.69, 2.51]
Subtotal (95% CI)	**58**	**167**		**22.4 %**	**0.83 [0.51, 1.33]**
Total events: 17 (History of HI), 64 (No history of HI)					
Heterogeneity: Chi^2 = 3.42, df = 1 (P = 0.06); I^2 =71%					
Test for overall effect: Z = 0.79 (P = 0.43)					
Total (95% CI)	**159**	**392**		**100.0 %**	**0.99 [0.86, 1.13]**
Total events: 100 (History of HI), 242 (No history of HI)					
Heterogeneity: Chi^2 = 11.13, df = 6 (P = 0.08); I^2 =46%					
Test for overall effect: Z = 0.19 (P = 0.85)					
Test for subgroup differences: Chi^2 = 6.13, df = 2 (P = 0.05), I^2 =67%					

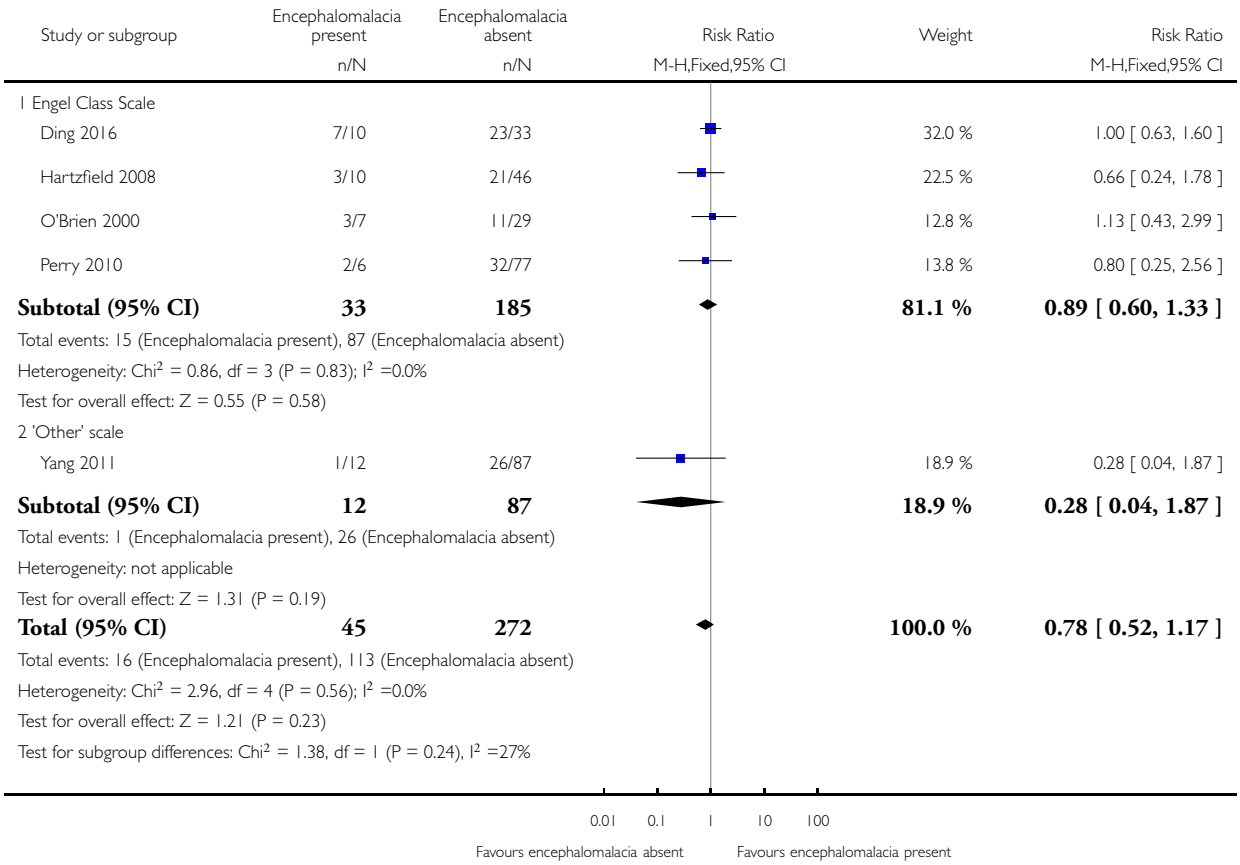


Analysis 4.7. Comparison 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence), Outcome 7 Good outcome by presence of encephalomalacia.

Review: Surgery for epilepsy

Comparison: 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence)

Outcome: 7 Good outcome by presence of encephalomalacia



Analysis 4.8. Comparison 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence), Outcome 8 Good outcome by presence of focal cortical dysplasia (FCD)/malformation of cortical development (MCD).

Review: Surgery for epilepsy

Comparison: 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence)

Outcome: 8 Good outcome by presence of focal cortical dysplasia (FCD)/malformation of cortical development (MCD)

Study or subgroup	FCD/MCD present n/N	FCD/MCD absent n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 > 1 year seizure-free					
Dagar 2011	13/18	76/94		2.8 %	0.89 [0.66, 1.21]
Duchowny 1998	9/21	7/10		1.1 %	0.61 [0.32, 1.16]
Fujiwara 2012	16/34	7/10		1.3 %	0.67 [0.39, 1.15]
Gilliam 1997b	5/12	17/21		1.4 %	0.51 [0.26, 1.04]
Greiner 2011	17/21	25/33		2.3 %	1.07 [0.80, 1.42]
Hallbook 2010	31/43	57/67		5.2 %	0.85 [0.69, 1.05]
Hemb 2010	86/120	137/205		11.7 %	1.07 [0.92, 1.24]
Paolicchi 2000	22/42	22/33		2.9 %	0.79 [0.54, 1.14]
Subtotal (95% CI)	**311**	**473**		**28.7 %**	**0.92 [0.84, 1.02]**
Total events: 199 (FCD/MCD present), 348 (FCD/MCD absent)					
Heterogeneity: Chi^2 = 11.93, df = 7 (P = 0.10); I^2 =41%					
Test for overall effect: Z = 1.61 (P = 0.11)					
2 Engel Class Scale					
Aaberg 2012	10/21	20/33		1.8 %	0.79 [0.46, 1.33]
Battaglia 2006	7/16	25/29		2.1 %	0.51 [0.29, 0.90]
Blount 2004	2/6	10/24		0.5 %	0.80 [0.23, 2.73]
Cossu 2005	41/72	52/93		5.3 %	1.02 [0.78, 1.33]
Cossu 2008	54/88	23/25		4.2 %	0.67 [0.54, 0.82]
Cukiert 2002	5/6	84/94		1.2 %	0.93 [0.65, 1.34]
Dalmagro 2005	15/22	13/21		1.5 %	1.10 [0.71, 1.71]
Ding 2016	15/22	15/21		1.8 %	0.95 [0.64, 1.41]
Donadio 2011	11/15	49/69		2.0 %	1.03 [0.73, 1.45]
Elsharkawy 2008a	28/68	93/150		6.7 %	0.66 [0.49, 0.91]
Erickson 2005	3/5	51/72		0.8 %	0.85 [0.41, 1.76]
Georgakoulias 2008	3/3	33/41		0.7 %	1.10 [0.73, 1.64]

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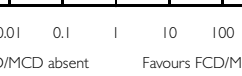
Study or subgroup	FCD/MCD present n/N	FCD/MCD absent n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Hajek 2009	9/14	16/21		1.5 %	0.84 [0.53, 1.33]
Hamiwka 2005	12/31	5/7		0.9 %	0.54 [0.28, 1.03]
Kilpatrick 1997	1/2	38/48		0.4 %	0.63 [0.16, 2.54]
Kim 2010a	43/103	32/74		4.3 %	0.97 [0.68, 1.37]
Lee 2011	8/9	29/31		1.5 %	0.95 [0.74, 1.22]
Li 1997	5/7	31/44		1.0 %	1.01 [0.61, 1.68]
Li 1999	4/9	12/29		0.7 %	1.07 [0.46, 2.51]
Liava 2012	22/28	17/24		2.1 %	1.11 [0.80, 1.53]
Miserocchi 2013	30/32	28/36		3.1 %	1.21 [0.99, 1.47]
Morris 1998	9/13	17/23		1.4 %	0.94 [0.61, 1.45]
O'Brien 2000	2/3	12/33		0.2 %	1.83 [0.73, 4.59]
Perego 2009	2/3	27/34		0.5 %	0.84 [0.37, 1.90]
Perry 2010	16/40	18/43		2.0 %	0.96 [0.57, 1.60]
Raabe 2012	2/3	55/73		0.5 %	0.88 [0.39, 1.99]
Sinclair 2003	7/12	50/65		1.8 %	0.76 [0.46, 1.25]
Sindou 2006	3/5	82/95		1.0 %	0.70 [0.34, 1.43]
Terra-Bustamante 2005a	14/27	48/80		2.8 %	0.86 [0.58, 1.30]
Tripathi 2008	16/26	13/29		1.4 %	1.37 [0.83, 2.28]
Urbach 2007	11/16	14/26		1.2 %	1.28 [0.79, 2.07]
Wray 2012	2/5	34/47		0.8 %	0.55 [0.19, 1.64]
Wyllie 1998	16/31	65/89		3.9 %	0.71 [0.49, 1.02]
Subtotal (95% CI)	**763**	**1623**		**61.5 %**	**0.89 [0.82, 0.96]**
Total events: 428 (FCD/MCD present), 1111 (FCD/MCD absent)					
Heterogeneity: Chi² = 44.27, df = 32 (P = 0.07); I² =28%					
Test for overall effect: Z = 3.02 (P = 0.0025)					
3 'Other' scale					
Boesebeck 2007	10/26	23/55		1.7 %	0.92 [0.52, 1.64]
Kan 2008	8/13	35/45		1.8 %	0.79 [0.50, 1.25]
Mathern 1999	35/54	43/74		4.2 %	1.12 [0.85, 1.47]
Sakamoto 2009	1/1	18/35		0.2 %	1.46 [0.62, 3.45]
Yang 2011	6/37	21/62		1.8 %	0.48 [0.21, 1.08]
Subtotal (95% CI)	**131**	**271**		**9.8 %**	**0.91 [0.73, 1.13]**
Total events: 60 (FCD/MCD present), 140 (FCD/MCD absent)					
Heterogeneity: Chi² = 6.01, df = 4 (P = 0.20); I² =33%					



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Study or subgroup	FCD/MCD present n/N	FCD/MCD absent n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Test for overall effect: Z = 0.85 (P = 0.39)					
Total (95% CI)	**1205**	**2367**		**100.0 %**	**0.90 [0.85, 0.95]**
Total events: 687 (FCD/MCD present), 1599 (FCD/MCD absent)					
Heterogeneity: Chi^2 = 62.49, df = 45 (P = 0.04); I^2 =28%					
Test for overall effect: Z = 3.50 (P = 0.00047)					
Test for subgroup differences: Chi^2 = 0.38, df = 2 (P = 0.83), I^2 =0.0%					

Analysis 4.9. Comparison 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence), Outcome 9 Good outcome by presence of tumour.

Review: Surgery for epilepsy

Comparison: 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence)

Outcome: 9 Good outcome by presence of tumour

Study or subgroup	Tumour present n/N	Tumour absent n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 > 1 year seizure-free					
Dagar 2011	14/18	75/94		3.5 %	0.97 [0.75, 1.27]
Duchowny 1998	7/7	9/24		1.4 %	2.47 [1.45, 4.20]
Erba 1992	20/26	17/20		3.4 %	0.90 [0.68, 1.20]
Gilliam 1997b	10/13	12/20		1.8 %	1.28 [0.80, 2.04]
Hemb 2010	18/22	205/303		4.3 %	1.21 [0.98, 1.49]
Paolicchi 2000	17/25	27/50		2.4 %	1.26 [0.87, 1.83]
Swartz 1992	5/6	22/28		2.1 %	1.06 [0.71, 1.59]
Subtotal (95% CI)	**117**	**539**		**18.9 %**	**1.17 [0.97, 1.41]**
Total events: 91 (Tumour present), 367 (Tumour absent)					
Heterogeneity: Tau^2 = 0.03; Chi^2 = 13.11, df = 6 (P = 0.04); I^2 =54%					
Test for overall effect: Z = 1.66 (P = 0.097)					

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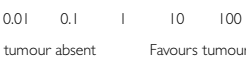
Study or subgroup	Tumour present n/N	Tumour absent n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
2 Engel Class Scale					
Aaberg 2012	1/5	29/49		0.2 %	0.34 [0.06, 1.98]
Battaglia 2006	3/12	29/33		0.5 %	0.28 [0.11, 0.76]
Cossu 2005	17/30	76/135		2.6 %	1.01 [0.71, 1.42]
Cossu 2008	31/35	46/78		4.2 %	1.50 [1.21, 1.87]
Dalmagro 2005	5/6	23/37		1.9 %	1.34 [0.87, 2.08]
Elsharkawy 2008a	50/79	71/139		4.0 %	1.24 [0.98, 1.57]
Erickson 2005	10/16	44/61		2.1 %	0.87 [0.57, 1.31]
Grivas 2006	6/7	31/45		2.5 %	1.24 [0.87, 1.78]
Hamiwka 2005	5/7	12/31		1.0 %	1.85 [0.97, 3.52]
Kilpatrick 1997	6/10	33/40		1.5 %	0.73 [0.43, 1.23]
Kim 2010a	6/10	69/167		1.4 %	1.45 [0.85, 2.49]
Lee 2011	28/30	9/10		4.1 %	1.04 [0.83, 1.30]
Li 1997	24/32	12/19		2.2 %	1.19 [0.80, 1.77]
Li 1999	5/10	11/18		0.9 %	0.82 [0.40, 1.68]
Liava 2012	10/12	29/40		2.9 %	1.15 [0.84, 1.58]
Miserocchi 2013	32/35	26/33		4.4 %	1.16 [0.95, 1.42]
O'Brien 2000	3/8	11/28		0.5 %	0.95 [0.35, 2.61]
Perego 2009	6/7	23/30		2.5 %	1.12 [0.78, 1.60]
Perry 2010	12/18	22/65		1.7 %	1.97 [1.23, 3.16]
Sinclair 2003	18/21	39/56		3.8 %	1.23 [0.96, 1.57]
Sindou 2006	9/10	76/90		4.1 %	1.07 [0.85, 1.33]
Sperling 1992	15/16	26/35		4.0 %	1.26 [1.00, 1.59]
Terra-Bustamante 2005a	15/18	47/89		3.3 %	1.58 [1.19, 2.10]
Urbach 2007	8/13	17/29		1.5 %	1.05 [0.62, 1.78]
Wray 2012	20/22	16/30		2.5 %	1.70 [1.19, 2.44]
Wyllie 1998	36/44	45/76		4.0 %	1.38 [1.09, 1.74]
Zentner 1995	50/73	53/94		3.9 %	1.21 [0.96, 1.54]
Zentner 1996	12/15	18/41		2.0 %	1.82 [1.19, 2.80]
Subtotal (95% CI)	**601**	**1598**		**70.1 %**	**1.23 [1.13, 1.33]**
Total events: 443 (Tumour present), 943 (Tumour absent)					
Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 44.62$, df = 27 (P = 0.02); $I^2 = 39\%$					



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Study or subgroup	Tumour present n/N	Tumour absent n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Test for overall effect: Z = 4.76 (P < 0.00001)					
3 'Other' scale					
Boesebeck 2007	11/18	22/63		1.6 %	1.75 [1.06, 2.88]
Goldstein 1996	8/11	7/22		0.9 %	2.29 [1.12, 4.65]
Kan 2008	13/16	30/42		3.1 %	1.14 [0.84, 1.54]
Mathern 1999	6/12	72/116		1.2 %	0.81 [0.45, 1.44]
Rossi 1994	20/24	47/79		3.7 %	1.40 [1.09, 1.81]
Yang 2011	3/7	24/92		0.6 %	1.64 [0.65, 4.13]
Subtotal (95% CI)	**88**	**414**		**11.0 %**	**1.35 [1.07, 1.70]**
Total events: 61 (Tumour present), 202 (Tumour absent)					
Heterogeneity: Tau^2 = 0.03; Chi^2 = 7.62, df = 5 (P = 0.18); I^2 =34%					
Test for overall effect: Z = 2.55 (P = 0.011)					
Total (95% CI)	**806**	**2551**		**100.0 %**	**1.23 [1.14, 1.32]**
Total events: 595 (Tumour present), 1512 (Tumour absent)					
Heterogeneity: Tau^2 = 0.02; Chi^2 = 67.33, df = 40 (P = 0.004); I^2 =41%					
Test for overall effect: Z = 5.56 (P < 0.00001)					
Test for subgroup differences: Chi^2 = 0.88, df = 2 (P = 0.64), I^2 =0.0%					

Analysis 4.10. Comparison 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence), Outcome 10 Good outcome by presence of vascular malformation.

Review: Surgery for epilepsy

Comparison: 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence)

Outcome: 10 Good outcome by presence of vascular malformation

Study or subgroup	Malformation present n/N	Malformation absent n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 > 1 year seizure-free					
Erba 1992	2/2	35/44		2.9 %	1.06 [0.62, 1.79]
Subtotal (95% CI)	**2**	**44**		**2.9 %**	**1.06 [0.62, 1.79]**
Total events: 2 (Malformation present), 35 (Malformation absent)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.20 (P = 0.84)					
2 Engel Class Scale					
Aaberg 2012	8/9	22/45		4.9 %	1.82 [1.25, 2.65]
Battaglia 2006	3/4	29/41		3.4 %	1.06 [0.58, 1.93]
Cossu 2008	3/3	74/110		3.4 %	1.30 [0.88, 1.93]
Dalmagro 2005	2/2	26/41		2.3 %	1.32 [0.76, 2.30]
Elsharkawy 2008a	15/24	106/194		15.5 %	1.14 [0.82, 1.60]
Erickson 2005	6/8	47/69		6.5 %	1.10 [0.72, 1.70]
Kilpatrick 1997	3/4	36/46		3.8 %	0.96 [0.53, 1.72]
Li 1997	5/8	31/43		6.5 %	0.87 [0.49, 1.53]
Li 1999	2/5	14/33		2.4 %	0.94 [0.30, 2.96]
Perry 2010	0/3	34/80		2.2 %	0.29 [0.02, 3.97]
Terra-Bustamante 2005a	3/4	59/103		2.9 %	1.31 [0.73, 2.36]
Urbach 2007	3/4	22/38		2.8 %	1.30 [0.69, 2.43]
Wray 2012	2/2	34/50		2.5 %	1.23 [0.72, 2.11]
Subtotal (95% CI)	**80**	**893**		**59.2 %**	**1.14 [0.98, 1.34]**
Total events: 55 (Malformation present), 534 (Malformation absent)					
Heterogeneity: Chi^2 = 9.41, df = 12 (P = 0.67); I^2 =0.0%					
Test for overall effect: Z = 1.68 (P = 0.092)					
3 'Other' scale					
Boesebeck 2007	2/8	31/73		4.1 %	0.59 [0.17, 2.01]
Kan 2008	4/5	39/53		4.5 %	1.09 [0.68, 1.73]
Mathern 1999	12/21	66/107		14.4 %	0.93 [0.62, 1.38]

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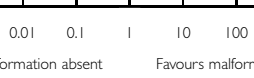
Study or subgroup	Malformation present n/N	Malformation absent n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Rossi 1994	13/20	54/83		13.9 %	1.00 [0.70, 1.43]
Yang 2011	1/3	26/96		1.0 %	1.23 [0.24, 6.30]
Subtotal (95% CI)	**57**	**412**		**37.9 %**	**0.94 [0.74, 1.20]**
Total events: 32 (Malformation present), 216 (Malformation absent)					
Heterogeneity: Chi^2 = 1.12, df = 4 (P = 0.89); I^2 =0.0%					
Test for overall effect: Z = 0.47 (P = 0.64)					
Total (95% CI)	**139**	**1349**		**100.0 %**	**1.07 [0.94, 1.21]**
Total events: 89 (Malformation present), 785 (Malformation absent)					
Heterogeneity: Chi^2 = 13.73, df = 18 (P = 0.75); I^2 =0.0%					
Test for overall effect: Z = 0.96 (P = 0.34)					
Test for subgroup differences: Chi^2 = 1.72, df = 2 (P = 0.42), I^2 =0.0%					



Analysis 4.11. Comparison 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence), Outcome 11 Good outcome by unilateral or bilateral interictal spikes.

Review: Surgery for epilepsy

Comparison: 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence)

Outcome: 11 Good outcome by unilateral or bilateral interictal spikes

Study or subgroup	Unilateral spikes n/N	Bilateral Spikes n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 > 1 year seizure-free					
Chee 1993	30/33	2/5		1.0 %	2.27 [0.77, 6.69]
Greiner 2011	29/38	13/16		5.3 %	0.94 [0.70, 1.26]
Kim 2009	41/71	53/95		13.2 %	1.04 [0.79, 1.35]
Kim 2010b	10/28	4/12		1.6 %	1.07 [0.42, 2.75]
Tatum 2008	16/27	6/12		2.4 %	1.19 [0.62, 2.26]
Walz 2003	39/42	44/53		11.3 %	1.12 [0.96, 1.30]
Weinand 1992	52/82	5/7		2.7 %	0.89 [0.54, 1.46]
Subtotal (95% CI)	**321**	**200**		**37.6 %**	**1.08 [0.94, 1.24]**
Total events: 217 (Unilateral spikes), 127 (Bilateral Spikes)					
Heterogeneity: Chi^2 = 3.68, df = 6 (P = 0.72); I^2 =0.0%					
Test for overall effect: Z = 1.12 (P = 0.26)					
2 Engel Class Scale					
Dalmagro 2005	15/23	13/19		4.1 %	0.95 [0.62, 1.46]
Erickson 2005	45/60	6/13		2.9 %	1.63 [0.89, 2.98]
Jayakar 2008	45/75	7/26		3.0 %	2.23 [1.15, 4.31]
Lee 2008	10/16	27/50		3.8 %	1.16 [0.73, 1.83]
Madhavan 2007	24/35	11/31		3.4 %	1.93 [1.14, 3.27]
Remi 2011	67/78	71/76		20.9 %	0.92 [0.83, 1.02]
Subtotal (95% CI)	**287**	**215**		**38.2 %**	**1.19 [1.04, 1.36]**
Total events: 206 (Unilateral spikes), 135 (Bilateral Spikes)					
Heterogeneity: Chi^2 = 31.24, df = 5 (P<0.00001); I^2 =84%					
Test for overall effect: Z = 2.60 (P = 0.0094)					
3 'Other' scale					
Boshuisen 2010	16/19	17/24		4.4 %	1.19 [0.86, 1.64]
Goldstein 1996	9/21	6/12		2.2 %	0.86 [0.40, 1.82]
Holmes 2000	20/26	34/100		4.1 %	2.26 [1.60, 3.19]
Lee 2006	23/29	14/22		4.6 %	1.25 [0.86, 1.80]

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Study or subgroup	Unilateral spikes n/N	Bilateral Spikes n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Rossi 1994	13/29	73/109		8.9 %	0.67 [0.44, 1.02]
Subtotal (95% CI)	**124**	**267**		**24.2 %**	**1.16 [0.97, 1.39]**
Total events: 81 (Unilateral spikes), 144 (Bilateral Spikes)					
Heterogeneity: Chi^2 = 21.67, df = 4 (P = 0.00023); I^2 =82%					
Test for overall effect: Z = 1.59 (P = 0.11)					
Total (95% CI)	**732**	**682**		**100.0 %**	**1.14 [1.05, 1.24]**
Total events: 504 (Unilateral spikes), 406 (Bilateral Spikes)					
Heterogeneity: Chi^2 = 52.27, df = 17 (P = 0.00002); I^2 =67%					
Test for overall effect: Z = 3.10 (P = 0.0020)					
Test for subgroup differences: Chi^2 = 1.08, df = 2 (P = 0.58), I^2 =0.0%					

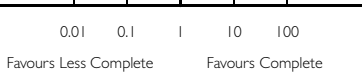
Analysis 4.12. Comparison 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence), Outcome 12 Good outcome by extent of resection.

Review: Surgery for epilepsy

Comparison: 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence)

Outcome: 12 Good outcome by extent of resection

Study or subgroup	Complete n/N	Less Complete n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 > 1 year seizure free					
Awad 1991	17/18	10/29		1.1 %	2.74 [1.64, 4.58]
Fujiwara 2012	15/26	8/18		1.4 %	1.30 [0.70, 2.39]
Jennum 1993	36/50	6/14		1.4 %	1.68 [0.90, 3.15]
Kim 2009	77/111	17/55		3.4 %	2.24 [1.48, 3.40]
Kim 2010b	12/24	2/16		0.4 %	4.00 [1.03, 15.53]
Paolicchi 2000	37/49	7/26		1.4 %	2.80 [1.46, 5.39]
Walz 2003	72/82	9/11		2.4 %	1.07 [0.80, 1.43]



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Study or subgroup	Complete n/N	Less Complete n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Widdess-Walsh 2007	15/22	5/19		0.8 %	2.59 [1.16, 5.79]
Wyler 1995	25/36	13/34		2.0 %	1.82 [1.12, 2.93]
Subtotal (95% CI)	**418**	**222**		**14.2 %**	**2.00 [1.66, 2.41]**
Total events: 306 (Complete), 77 (Less Complete)					
Heterogeneity: Chi^2 = 24.17, df = 8 (P = 0.002); I^2 =67%					
Test for overall effect: Z = 7.27 (P < 0.00001)					
2 Engel Class Scale					
Arruda 1996	25/37	28/37		4.2 %	0.89 [0.67, 1.19]
Babini 2013	10/10	16/30		1.3 %	1.79 [1.26, 2.56]
Blount 2004	12/26	0/4		0.1 %	4.63 [0.32, 66.24]
Brainer-Lima 1996	25/25	4/7		1.0 %	1.74 [0.94, 3.22]
Chang 2009	32/42	0/2		0.1 %	4.53 [0.36, 57.27]
Choi 2004a	20/22	7/13		1.3 %	1.69 [1.00, 2.84]
Cossu 2005	70/115	23/50		4.8 %	1.32 [0.95, 1.85]
Cossu 2008	57/72	20/41		3.8 %	1.62 [1.16, 2.27]
Dalmagro 2005	11/18	17/25		2.1 %	0.90 [0.57, 1.42]
Hamiwka 2005	24/29	1/9		0.2 %	7.45 [1.16, 47.62]
Jayakar 2008	35/63	9/38		1.7 %	2.35 [1.27, 4.33]
Kanner 2009	23/25	63/75		4.7 %	1.10 [0.94, 1.28]
Kloss 2002	21/26	5/30		0.7 %	4.85 [2.13, 11.02]
Lee 2011	32/32	5/8		1.3 %	1.61 [0.96, 2.72]
Li 1997	35/41	4/10		1.0 %	2.13 [0.99, 4.61]
Madhavan 2007	26/39	11/31		1.8 %	1.88 [1.11, 3.17]
Miserocchi 2013	54/63	4/5		1.1 %	1.07 [0.68, 1.68]
Morris 1998	20/28	6/8		1.4 %	0.95 [0.60, 1.51]
O'Brien 2000	4/4	6/11		0.6 %	1.66 [0.91, 3.02]
Paglioli 2006	58/80	58/81		8.6 %	1.01 [0.84, 1.23]
Raabe 2012	10/26	47/50		4.8 %	0.41 [0.25, 0.67]
Sagher 2012	43/51	38/45		6.0 %	1.00 [0.84, 1.19]
Schramm 2011	62/74	84/125		9.3 %	1.25 [1.06, 1.46]
Stavrou 2008	14/18	23/35		2.3 %	1.18 [0.84, 1.67]
Tanriverdi 2010	81/123	79/133		11.3 %	1.11 [0.92, 1.34]
Terra-Bustamante 2005a	69/79	3/28		0.7 %	8.15 [2.79, 23.83]

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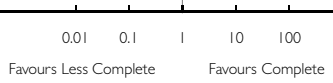
Study or subgroup	Complete n/N	Less Complete n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Yeon 2009	21/27	29/33		3.9 %	0.89 [0.70, 1.12]
Zentner 1996	14/21	3/9		0.6 %	2.00 [0.76, 5.29]
Subtotal (95% CI)	**1216**	**973**		**80.6 %**	**1.29 [1.21, 1.39]**
Total events: 908 (Complete), 593 (Less Complete)					
Heterogeneity: Chi^2 = 107.28, df = 27 (P<0.00001); I^2 =75%					
Test for overall effect: Z = 7.17 (P < 0.00001)					
3 'Other' scale					
Lackmayer 2013	5/9	27/36		1.6 %	0.74 [0.40, 1.37]
Rossi 1994	54/63	13/40		2.4 %	2.64 [1.67, 4.17]
Sakamoto 2009	4/10	15/26		1.2 %	0.69 [0.30, 1.59]
Subtotal (95% CI)	**82**	**102**		**5.2 %**	**1.59 [1.15, 2.20]**
Total events: 63 (Complete), 55 (Less Complete)					
Heterogeneity: Chi^2 = 14.50, df = 2 (P = 0.00071); I^2 =86%					
Test for overall effect: Z = 2.80 (P = 0.0051)					
Total (95% CI)	**1716**	**1297**		**100.0 %**	**1.41 [1.32, 1.50]**
Total events: 1277 (Complete), 725 (Less Complete)					
Heterogeneity: Chi^2 = 175.37, df = 39 (P<0.00001); I^2 =78%					
Test for overall effect: Z = 10.29 (P < 0.00001)					
Test for subgroup differences: Chi^2 = 19.07, df = 2 (P = 0.00), I^2 =90%					

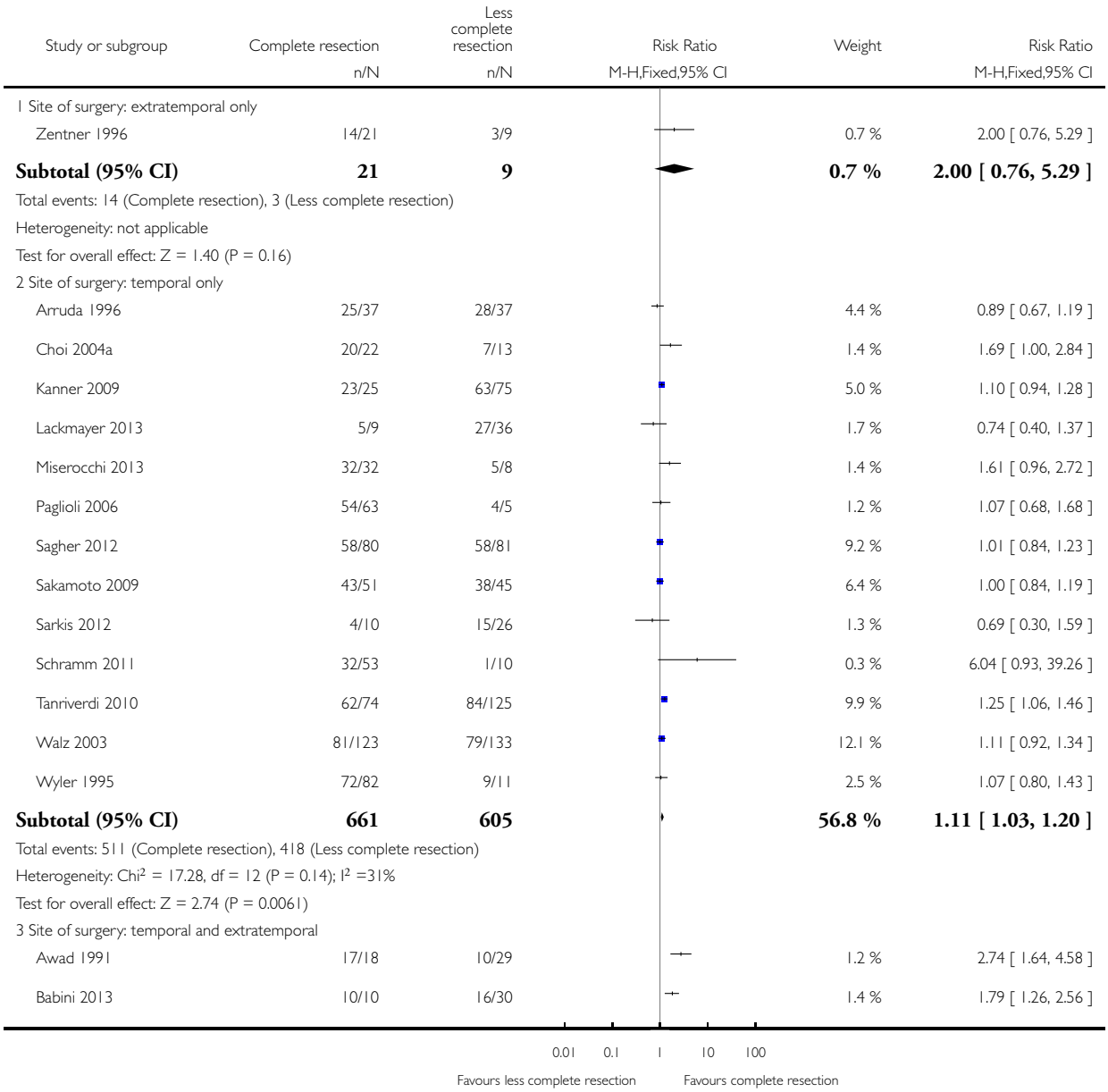


Analysis 4.13. Comparison 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence), Outcome 13 Good outcome by extent of resection.

Review: Surgery for epilepsy

Comparison: 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence)

Outcome: 13 Good outcome by extent of resection



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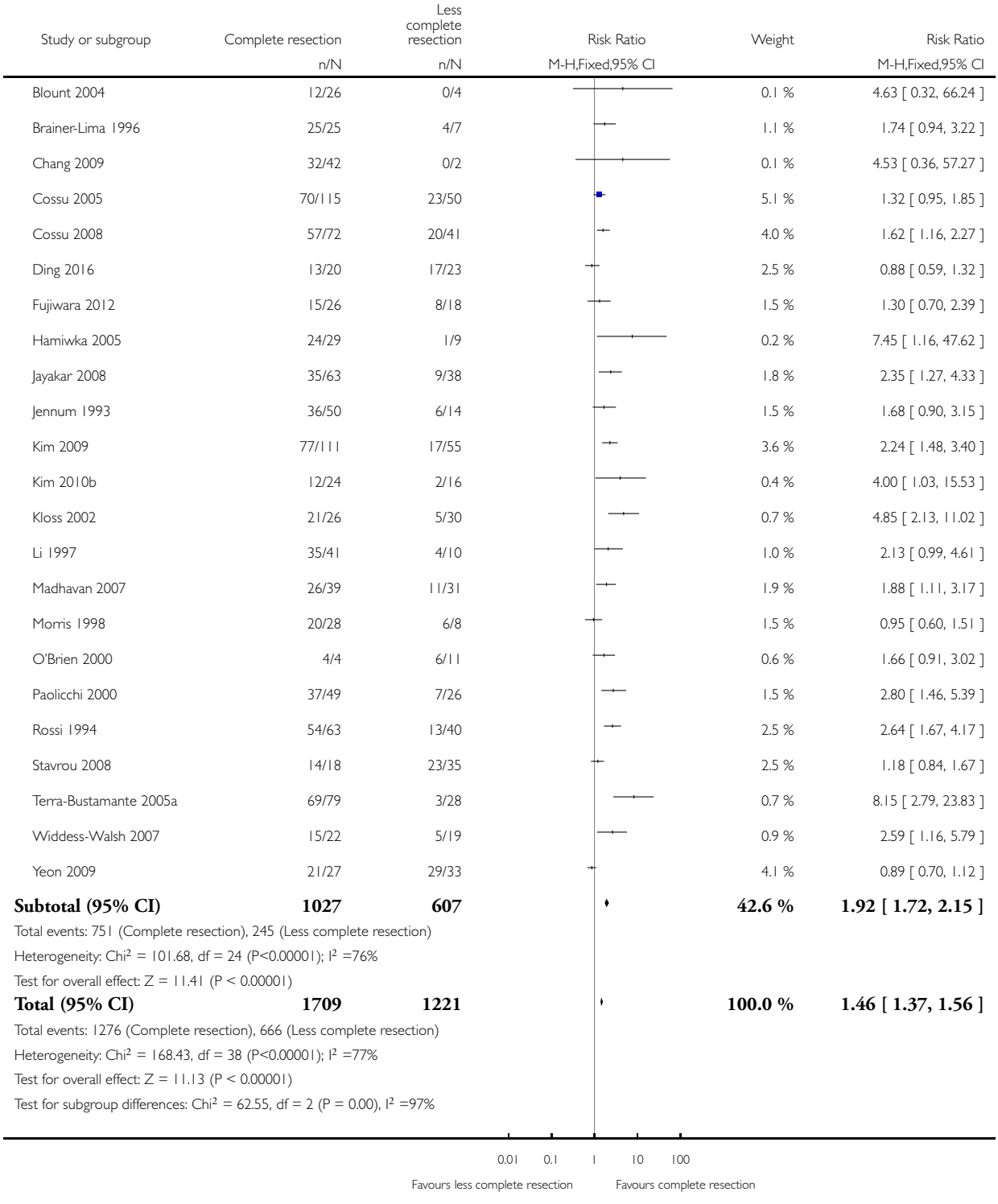

Analysis 4.14. Comparison 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence), Outcome 14 Good outcome by side of surgical resection.

Review: Surgery for epilepsy

Comparison: 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence)

Outcome: 14 Good outcome by side of surgical resection

Study or subgroup	Left side resection n/N	Right side resection n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 > 1 year seizure-free					
Jack 1992	22/27	18/23		2.6 %	1.04 [0.79, 1.38]
Morino 2009	27/31	28/31		4.8 %	0.96 [0.81, 1.15]
Tatum 2008	12/23	10/16		0.9 %	0.83 [0.48, 1.44]
Theodore 2012	15/23	11/18		1.1 %	1.07 [0.66, 1.71]
Walz 2003	54/61	31/37		5.1 %	1.06 [0.89, 1.25]
Subtotal (95% CI)	**165**	**125**		**14.4 %**	**1.01 [0.91, 1.13]**
Total events: 130 (Left side resection), 98 (Right side resection)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.11$, df = 4 (P = 0.89); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.21 (P = 0.84)					
2 Engel Class Scale					
Adam 1996	13/15	13/15		2.6 %	1.00 [0.76, 1.32]
Babini 2013	12/13	14/17		2.8 %	1.12 [0.86, 1.47]
Battaglia 2006	17/26	15/19		1.8 %	0.83 [0.58, 1.19]
Brainer-Lima 1996	14/15	15/17		3.7 %	1.06 [0.85, 1.32]
Cascino 1995	63/92	50/73		4.0 %	1.00 [0.81, 1.23]
Chabardes 2005	14/20	27/28		2.4 %	0.73 [0.54, 0.98]
Chang 2009	14/20	18/23		1.8 %	0.89 [0.62, 1.28]
Choi 2004a	17/22	10/13		1.7 %	1.00 [0.69, 1.46]
Cossu 2008	37/56	40/57		3.1 %	0.94 [0.73, 1.21]
Dalmagro 2005	13/21	15/22		1.3 %	0.91 [0.58, 1.41]
Georgakoulias 2008	20/23	21/26		3.2 %	1.08 [0.84, 1.38]
Grivas 2006	22/23	25/29		5.0 %	1.11 [0.94, 1.31]
Hartzfield 2008	12/23	12/27		0.8 %	1.17 [0.66, 2.09]

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Study or subgroup	Left side resection n/N	Right side resection n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Janszky 2003a	23/33	20/34		1.8 %	1.18 [0.83, 1.70]
Jaramillo-Betancur 2009	28/46	32/38		2.8 %	0.72 [0.55, 0.95]
Kilpatrick 1997	19/27	20/23		2.5 %	0.81 [0.60, 1.08]
Lee 2008	22/34	16/37		1.2 %	1.50 [0.96, 2.33]
Liava 2012	11/19	28/33		1.4 %	0.68 [0.45, 1.03]
Miserocchi 2013	31/34	27/34		4.2 %	1.15 [0.94, 1.40]
Perego 2009	11/13	18/24		2.1 %	1.13 [0.81, 1.56]
Prevedello 2000	24/41	29/43		2.0 %	0.87 [0.62, 1.21]
Schramm 2011	84/110	68/97		5.1 %	1.09 [0.92, 1.29]
Seymour 2012	68/155	80/128		3.6 %	0.70 [0.56, 0.88]
Sola 2005	35/74	39/63		2.3 %	0.76 [0.56, 1.04]
Tanriverdi 2010	75/132	84/124		4.4 %	0.84 [0.69, 1.02]
Tezer 2008	40/51	50/58		4.8 %	0.91 [0.76, 1.09]
Zentner 1995	44/68	59/99		3.3 %	1.09 [0.85, 1.38]
Subtotal (95% CI)	**1206**	**1201**		**75.6 %**	**0.96 [0.89, 1.02]**
Total events: 783 (Left side resection), 845 (Right side resection)					
Heterogeneity: Tau^2 = 0.01; Chi^2 = 45.40, df = 26 (P = 0.01); I^2 =43%					
Test for overall effect: Z = 1.30 (P = 0.19)					
3 'Other' scale					
Engman 2004	16/25	19/29		1.5 %	0.98 [0.66, 1.45]
Jeong 1999	35/42	43/51		4.7 %	0.99 [0.83, 1.18]
Lackmayer 2013	14/22	18/23		1.6 %	0.81 [0.55, 1.19]
Lee 2006	12/20	25/31		1.5 %	0.74 [0.50, 1.11]
Sakamoto 2009	11/20	8/16		0.7 %	1.10 [0.59, 2.07]
Subtotal (95% CI)	**129**	**150**		**10.0 %**	**0.94 [0.82, 1.07]**
Total events: 88 (Left side resection), 113 (Right side resection)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 2.51, df = 4 (P = 0.64); I^2 =0.0%					
Test for overall effect: Z = 0.96 (P = 0.34)					
Total (95% CI)	**1500**	**1476**		**100.0 %**	**0.96 [0.91, 1.01]**
Total events: 1001 (Left side resection), 1056 (Right side resection)					
Heterogeneity: Tau^2 = 0.01; Chi^2 = 50.15, df = 36 (P = 0.06); I^2 =28%					
Test for overall effect: Z = 1.46 (P = 0.14)					
Test for subgroup differences: Chi^2 = 1.02, df = 2 (P = 0.60), I^2 =0.0%					

Analysis 4.15. Comparison 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence), Outcome 15 Good outcome by side of surgical resection.

Review: Surgery for epilepsy

Comparison: 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence)

Outcome: 15 Good outcome by side of surgical resection

Study or subgroup	Left side n/N	Right side n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Site of surgery: extratemporal only					
Lee 2008	22/34	16/37		1.5 %	1.50 [0.96, 2.33]
Liava 2012	11/19	28/33		2.0 %	0.68 [0.45, 1.03]
Subtotal (95% CI)	**53**	**70**		**3.5 %**	**1.03 [0.76, 1.39]**
Total events: 33 (Left side), 44 (Right side)					
Heterogeneity: Chi^2 = 6.59, df = 1 (P = 0.01); I^2 =85%					
Test for overall effect: Z = 0.20 (P = 0.84)					
2 Site of surgery: temporal only					
Adam 1996	13/15	13/15		1.3 %	1.00 [0.76, 1.32]
Battaglia 2006	17/26	15/19		1.7 %	0.83 [0.58, 1.19]
Cascino 1995	63/92	50/73		5.4 %	1.00 [0.81, 1.23]
Chabardes 2005	14/20	27/28		2.2 %	0.73 [0.54, 0.98]
Choi 2004a	17/22	10/13		1.2 %	1.00 [0.69, 1.46]
Engman 2004	16/25	19/29		1.7 %	0.98 [0.66, 1.45]
Georgakoulias 2008	20/23	21/26		1.9 %	1.08 [0.84, 1.38]
Grivas 2006	22/23	25/29		2.1 %	1.11 [0.94, 1.31]
Hartzfield 2008	12/23	12/27		1.1 %	1.17 [0.66, 2.09]
Jack 1992	22/27	18/23		1.9 %	1.04 [0.79, 1.38]
Janszky 2003a	28/46	32/38		3.4 %	0.72 [0.55, 0.95]
Jaramillo-Betancur 2009	23/33	20/34		1.9 %	1.18 [0.83, 1.70]
Jeong 1999	35/42	43/51		3.8 %	0.99 [0.83, 1.18]
Kilpatrick 1997	19/27	20/23		2.1 %	0.81 [0.60, 1.08]
Lackmayer 2013	14/22	18/23		1.7 %	0.81 [0.55, 1.19]
Lee 2006	12/20	25/31		1.9 %	0.74 [0.50, 1.11]
Miserocchi 2013	31/34	27/34		2.6 %	1.15 [0.94, 1.40]

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Study or subgroup	Left side n/N	Right side n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Morino 2009	27/31	28/31		2.7 %	0.96 [0.81, 1.15]
Perego 2009	11/13	18/24		1.2 %	1.13 [0.81, 1.56]
Prevedello 2000	24/41	29/43		2.7 %	0.87 [0.62, 1.21]
Sakamoto 2009	11/20	8/16		0.9 %	1.10 [0.59, 2.07]
Schramm 2011	84/110	68/97		7.0 %	1.09 [0.92, 1.29]
Seymour 2012	68/155	80/128		8.5 %	0.70 [0.56, 0.88]
Sola 2005	35/74	39/63		4.1 %	0.76 [0.56, 1.04]
Tanriverdi 2010	75/132	84/124		8.4 %	0.84 [0.69, 1.02]
Tatum 2008	12/23	10/16		1.1 %	0.83 [0.48, 1.44]
Tezer 2008	40/51	50/58		4.5 %	0.91 [0.76, 1.09]
Theodore 2012	15/23	11/18		1.2 %	1.07 [0.66, 1.71]
Walz 2003	54/61	31/37		3.7 %	1.06 [0.89, 1.25]
Zentner 1995	44/68	59/99		4.7 %	1.09 [0.85, 1.38]
Subtotal (95% CI)	**1322**	**1270**		**88.5 %**	**0.93 [0.89, 0.98]**
Total events: 878 (Left side), 910 (Right side)					
Heterogeneity: Chi^2 = 41.49, df = 29 (P = 0.06); I^2 =30%					
Test for overall effect: Z = 2.76 (P = 0.0058)					
3 Site of surgery: temporal and extratemporal					
Babini 2013	12/13	14/17		1.2 %	1.12 [0.86, 1.47]
Brainer-Lima 1996	14/15	15/17		1.4 %	1.06 [0.85, 1.32]
Chang 2009	14/20	18/23		1.6 %	0.89 [0.62, 1.28]
Cossu 2008	37/56	40/57		3.8 %	0.94 [0.73, 1.21]
Subtotal (95% CI)	**104**	**114**		**8.0 %**	**0.98 [0.84, 1.14]**
Total events: 77 (Left side), 87 (Right side)					
Heterogeneity: Chi^2 = 1.79, df = 3 (P = 0.62); I^2 =0.0%					
Test for overall effect: Z = 0.29 (P = 0.77)					
Total (95% CI)	**1479**	**1454**		**100.0 %**	**0.94 [0.90, 0.98]**
Total events: 988 (Left side), 1041 (Right side)					
Heterogeneity: Chi^2 = 50.07, df = 35 (P = 0.05); I^2 =30%					
Test for overall effect: Z = 2.62 (P = 0.0089)					
Test for subgroup differences: Chi^2 = 0.76, df = 2 (P = 0.68), I^2 =0.0%					

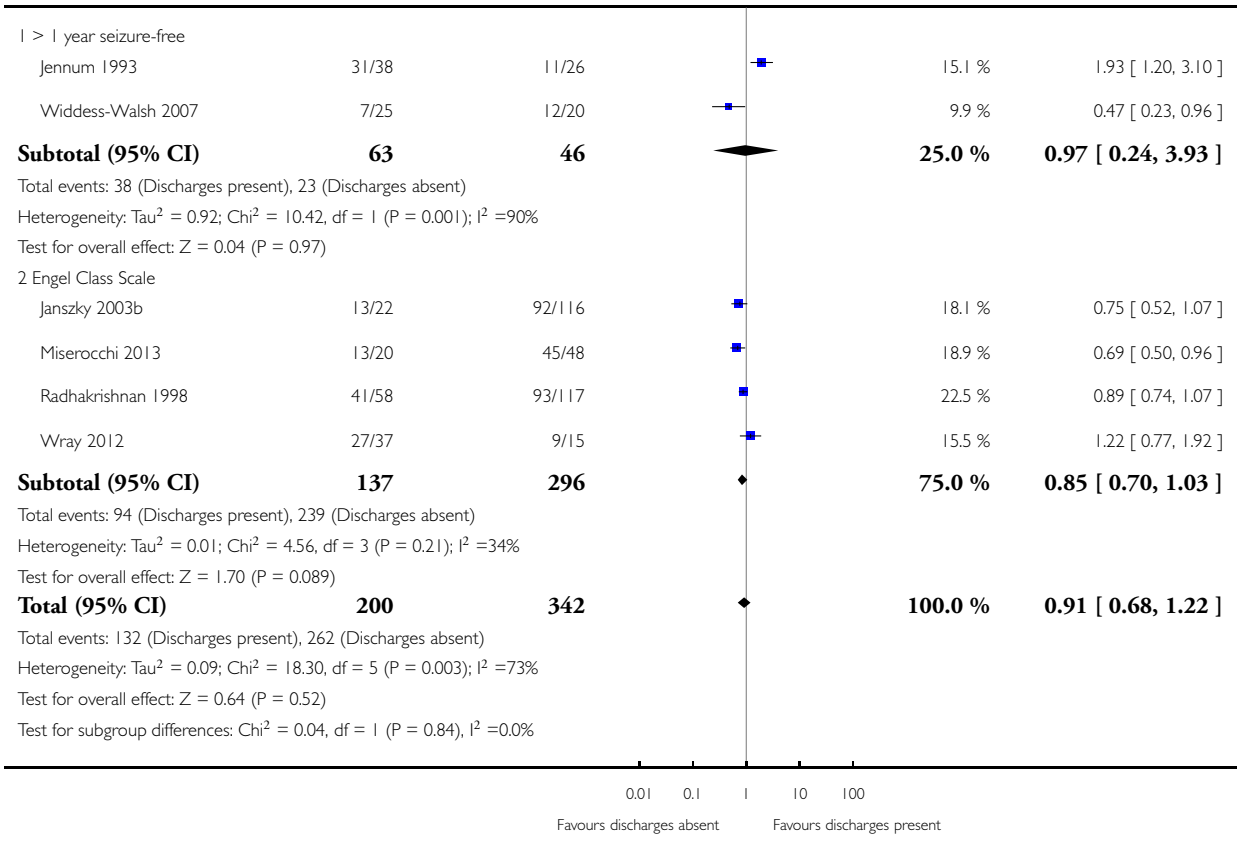
Analysis 4.16. Comparison 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence), Outcome 16 Good outcome by presence of postoperative discharges.

Review: Surgery for epilepsy

Comparison: 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence)

Outcome: 16 Good outcome by presence of postoperative discharges

Study or subgroup	Discharges present n/N	Discharges absent n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 > 1 year seizure-free					
Jennum 1993	31/38	11/26		15.1 %	1.93 [1.20, 3.10]
Widdess-Walsh 2007	7/25	12/20		9.9 %	0.47 [0.23, 0.96]
Subtotal (95% CI)	**63**	**46**		**25.0 %**	**0.97 [0.24, 3.93]**
Total events: 38 (Discharges present), 23 (Discharges absent)					
Heterogeneity: Tau^2 = 0.92; Chi^2 = 10.42, df = 1 (P = 0.001); I^2 =90%					
Test for overall effect: Z = 0.04 (P = 0.97)					
2 Engel Class Scale					
Janszky 2003b	13/22	92/116		18.1 %	0.75 [0.52, 1.07]
Miserocchi 2013	13/20	45/48		18.9 %	0.69 [0.50, 0.96]
Radhakrishnan 1998	41/58	93/117		22.5 %	0.89 [0.74, 1.07]
Wray 2012	27/37	9/15		15.5 %	1.22 [0.77, 1.92]
Subtotal (95% CI)	**137**	**296**		**75.0 %**	**0.85 [0.70, 1.03]**
Total events: 94 (Discharges present), 239 (Discharges absent)					
Heterogeneity: Tau^2 = 0.01; Chi^2 = 4.56, df = 3 (P = 0.21); I^2 =34%					
Test for overall effect: Z = 1.70 (P = 0.089)					
Total (95% CI)	**200**	**342**		**100.0 %**	**0.91 [0.68, 1.22]**
Total events: 132 (Discharges present), 262 (Discharges absent)					
Heterogeneity: Tau^2 = 0.09; Chi^2 = 18.30, df = 5 (P = 0.003); I^2 =73%					
Test for overall effect: Z = 0.64 (P = 0.52)					
Test for subgroup differences: Chi^2 = 0.04, df = 1 (P = 0.84), I^2 =0.0%					

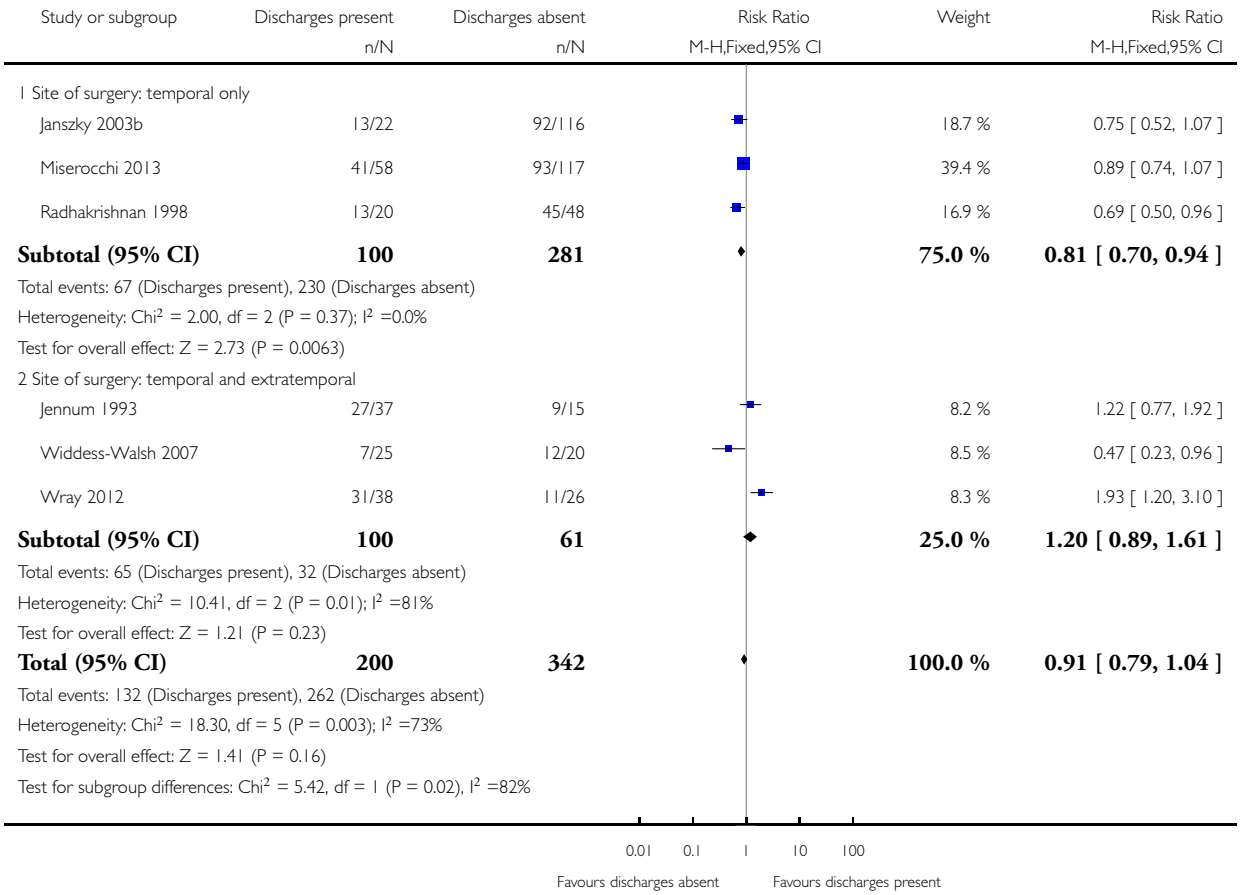


Analysis 4.17. Comparison 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence), Outcome 17 Good outcome by presence of postoperative discharges.

Review: Surgery for epilepsy

Comparison: 4 Prognostic factors of a good outcome of surgery (randomised and non-randomised evidence)

Outcome: 17 Good outcome by presence of postoperative discharges



ADDITIONAL TABLES

Table 1. Study characteristics and participant demographics for 182 included studies

Author (year)	Outcome scale used	Study design	Participants having surgery	Good outcome	Males	Site of surgery	Age at surgery (min to max), years [a]	Duration of epilepsy (min to max), years [a]	Follow-up (min to max), months [a]
Aaberg 2012	Engel Class Scale	Retrospective	54	30	32	Temporal and extratemporal	0.5 to 16	NA	> 24
Adam 1996	Engel Class Scale	Prospective	30	26	11	Temporal only	18 to 44	NA	12 to 44
Adelson 1992	> 1 year seizure-free	Retrospective	33	23	19	Temporal and extratemporal	0 to 17	NA	18 to 72
Alfstad 2011	Engel Class Scale	Retrospective	48	25	26	Temporal and extratemporal	24.6 (NA)	14.5 (NA)	> 24
Alonso-Vanegas 2018	Engel Class Scale	Prospective	43	38	15	Temporal	18 to 56	NA	12 to 60
Althausen 2013	> 1 year seizure-free	Retrospective	61	45	29	Extratemporal only	14.5 (12.0)	11.9 (10.8)	13 to 233
Arruda 1996	Engel Class Scale	Retrospective	74	53	34	Temporal only	32.1 (10.5)	NA	33.4 (13.1)
Awad 1991	> 1 year seizure-free	Not stated	47	27	38	Temporal and extratemporal	2 to 45	0 to 29	20 to 114
Babini 2013	Engel Class Scale	Retrospective	30	26	20	Temporal and extratemporal	3 to 18	0 to 16	12 to 204
Barbaro 2018	'Other' scale	Prospective	58	37	28	Temporal	40.2 (13.4)	28.6 (14.5)	12 to 36
Battaglia 2006	Engel Class Scale	Not stated	45	32	29	Temporal only	0 to 7	0 to 5	24 to 179
Baumann 2007	Engel Class Scale	Retrospective	168	118	90	Temporal and ex-	1 to 71	0 to 41	12 to 39

Table 1. Study characteristics and participant demographics for 182 included studies (*Continued*)

						tratemporal			
Bautista 2003	> 1 year seizure-free	Retrospective	43	28	29	Temporal and extratemporal	29.6 (10.9)	2 to 48	> 12
Bell 2009	Engel Class Scale	Retrospective	40	24	17	Temporal only	13 to 62	1 to 36	18 to 126
Benifla 2006	Engel Class Scale	Retrospective	106	78	65	Temporal only	13.5 (NA)	5.9 (NA)	24 to 162
Berkovic 1995	Engel Class Scale	Prospective	135	74	NA	Temporal only	11 to 58	NA	18 to 81
Blount 2004	Engel Class Scale	Retrospective	30	12	13	Temporal and extratemporal	11.7 (4.4)	NA	> 30
Blume 2004	Engel Class Scale	Retrospective	70	26	41	Temporal and extratemporal	6 to 65	1 to 41	24 to 144
Boesebeck 2007	'Other' scale	Retrospective	81	33	51	Extratemporal only	16 to 53	2 to 43	> 24
Boshuisen 2010	'Other' scale	Retrospective	43	33	18	Temporal and extratemporal	0 to 14	0 to 12	12 to 188
Brainer-Lima 1996	Engel Class Scale	Retrospective	32	29	24	Temporal and extratemporal	6 to 57	2 to 30	4 to 68
Britton 1994	Engel Class Scale	Retrospective	51	34	NA	Temporal and extratemporal	6 to 60	NA	24 to 96
Caraballo 2011	Engel Class Scale	Retrospective	45	33	27	Not stated	0 to 18	NA	12 to 192
Cascino 1995	Engel Class Scale	Retrospective	165	113	NA	Temporal only	32.1 (10.5)	NA	> 12
Chabardes 2005	Engel Class Scale	Retrospective	54	47	24	Temporal only	NA	2.5 to 41	48 to 100

Table 1. Study characteristics and participant demographics for 182 included studies (*Continued*)

Chang 2009	Engel Class Scale	Retrospective	57	45	NA	Temporal and extratemporal	NA	NA	> 12
Chee 1993	> 1 year seizure-free	Retrospective	38	28	25	Temporal only	18 to 53	3 to 36	> 12
Chkhenkeli 2007	Engel Class Scale	Retrospective	67	12	NA	Temporal only	NA	NA	>24
Choi 2004a	Engel Class Scale	Retrospective	35	27	19	Temporal only	16 to 61	4 to 22	16 to 105
Chung 2005	Engel Class Scale	Retrospective	128	58	85	Temporal and extratemporal	NA	NA	26.9 (12)
Cossu 2005	Engel Class Scale	Retrospective	165	93	NA	Temporal and extratemporal	NA	NA	> 12
Cossu 2008	Engel Class Scale	Retrospective	113	77	67	Temporal and extratemporal	1 to 15	0 to 14	24 to 115
Costello 2009	Engel Class Scale	Retrospective	42	32	21	Temporal and extratemporal	45 to 66	0.5 to 55.5	13 to 173
Cukiert 2002	Engel Class Scale	Prospective	100	89	43	Temporal only	28 (9)	NA	18 to 48
Dagar 2011	> 1 year seizure-free	Retrospective	112	89	67	Temporal and extratemporal	0 to 18	0 to 15	> 12
Dalmagro 2005	Engel Class Scale	Retrospective	43	28	23	Not stated	22.4 (NA)	14.7 (11.5)	> 12
de Tisi 2011	'Other' scale	Retrospective	615	245	287	Temporal and extratemporal	16 to 63	20.7 (median)	12 to 228
Delbeke 1996	Engel Class Scale	Retrospective	38	23	15	Temporal only	15 to 59	NA	18 to 58

Table 1. Study characteristics and participant demographics for 182 included studies (*Continued*)

Dellabadia 2002	Engel Class Scale	Retrospective	35	20	NA	Temporal and extratemporal	NA	NA	22 to 48
Devlin 2003	Engel Class Scale	Retrospective	33	17	21	Temporal and extratemporal	0 to 17	7.4 (median)	12 to 96
Ding 2016	Engel Class Scale	Prospective	43	30	24	Temporal and Extratemporal	4 to 18	NA	12 to 60
Donadio 2011	Engel Class Scale	Retrospective	84	60	45	Temporal and extratemporal	2 to 59	1 to 50	12 to 126
Dorward 2011	Engel Class Scale	Retrospective	33	18	18	Extratemporal only	3 to 19	0.5 to 16	49.4 (NA)
Duchowny 1998	> 1 year seizure-free	Retrospective	31	16	16	Temporal and extratemporal	0 to 3	NA	> 12
Dunkley 2011	Engel Class Scale	Retrospective	42	20	24	Temporal and extratemporal	0 to 3	0 to 3	27 to 158
Dunlea 2010	Engel Class Scale	Retrospective	199	119	95	Temporal and extratemporal	1 to 61	0.5 to 43	12 to 288
Dwivedi 2017	'Other' scale	Prospective	57	44	44	Temporal and Extratemporal	0.8 to 17.0	0.4-16.3	> 12
Elsharkawy 2008a	Engel Class Scale	Retrospective	218	121	129	Extratemporal only	16 to 69	1 to 65	12 to 60
Elsharkawy 2009a	Engel Class Scale	Retrospective	430	311	220	Temporal and extratemporal	16 to 61	1 to 57	> 24
Elsharkawy 2011a	Engel Class Scale	Retrospective	47	38	33	Temporal only	32 (12)	11.8 (8.8)	6 to 72
Engman 2004	'Other' scale	Retrospective	54	35	NA	Temporal only	34 (median)	NA	33.6 (median)

Table 1. Study characteristics and participant demographics for 182 included studies (*Continued*)

Erba 1992	> 1 year seizure-free	Retrospective	46	37	28	Temporal only	4 to 34	1 to 31	38 to 216
Erickson 2005	Engel Class Scale	Retrospective	71	46	27	Temporal only	5 to 64	0 to 46	> 12
Fauser 2004	Engel Class Scale	Retrospective	59	35	34	Temporal only	2 to 66	NA	6 to 48
Fujiwara 2012	> 1 year seizure-free	Retrospective	44	23	0	Temporal and extratemporal	NA	NA	12 to 26
Garcia 1991	> 1 year seizure-free	Retrospective	55	35	NA	Temporal only	9 to 47	NA	12 to 48
Garcia 1994	> 1 year seizure-free	Prospective	51	36	NA	Temporal only	NA	NA	12 to 48
Gelinas 2011	Engel Class Scale	Retrospective	67	52	39	Temporal and extratemporal	0 to 16	2.7 (NA)	75.6 (NA)
Georgakoulias 2008	Engel Class Scale	Retrospective	50	42	25	Temporal only	14 to 62	NA	60 to 120
Gilliam 1997a	> 1 year seizure-free	Retrospective	78	53	18	Temporal and extratemporal	1 to 12	1 to 11	7 to 72
Gilliam 1997b	> 1 year seizure-free	Retrospective	33	22	40	Temporal only	9 to 50	NA	> 12
Goldstein 1996	'Other' scale	Retrospective	33	15	17	Temporal only	0 to 15	0 to 12	24 to 120
Greiner 2011	> 1 year seizure-free	Retrospective	54	42	NA	Temporal and extratemporal	0.5 to 40	7.6 (median)	> 12
Grivas 2006	Engel Class Scale	Retrospective	52	37	22	Temporal only	50 to 71	1 to 62	12 to 84

Table 1. Study characteristics and participant demographics for 182 included studies (*Continued*)

Gyimesi 2007	'Other' scale	Retrospective	100	74	NA	Temporal only	NA	NA	> 24
Hader 2004	Engel Class Scale	Retrospective	39	21	16	Temporal and extratemporal	0 to 18.5	0.19	> 18
Hajek 2009	Engel Class Scale	Retrospective	35	25	15	Temporal only	10 to 58	5 to 47	24 to 91
Hallbook 2010	> 1 year seizure-free	Retrospective	110	88	71	Temporal and extratemporal	0 to 18	NA	12 to 84
Hamiwka 2005	Engel Class Scale	Retrospective	38	17	NA	Temporal and extratemporal	0.5 to 18	NA	> 24
Hartley 2002	Engel Class Scale	Retrospective	35	20	11	Temporal and extratemporal	1 to 18	1 to 17	36 to 72
Hartzfield 2008	Engel Class Scale	Retrospective	56	24	35	Temporal only	8 to 70	4.5 to 41	6 to 108
Hemb 2010	> 1 year seizure-free	Retrospective	325	223	229	Temporal and extratemporal	7.7(6.3)	4.9 (4.6)	> 24
Holmes 1997	> 1 year seizure-free	Retrospective	44	22	17	Temporal only	14 to 55	3 to 46	12 to 48
Holmes 2000	'Other' scale	Retrospective	126	54	71	Temporal and extratemporal	6 to 69	1 to 46	24 to 72
Jack 1992	> 1 year seizure-free	Retrospective	50	34	27	Temporal only	14 to 51	2 to 37	12 to 34
Janszky 2003a	Engel Class Scale	Retrospective	84	60	NA	Temporal only	NA	NA	> 24
Janszky 2003b	Engel Class Scale	Retrospective	147	123	NA	Temporal only	NA	NA	> 6

Table 1. Study characteristics and participant demographics for 182 included studies (*Continued*)

Jaramillo-Betancur 2009	Engel Class Scale	Retrospective	67	43	52	Temporal only	27 (11)	20 (10)	> 24
Jayakar 2008	Engel Class Scale	Retrospective	101	44	60	Temporal and extratemporal	1.5 to 21	NA	> 24
Jayalakshmi 2011	Engel Class Scale	Retrospective	78	50	44	Temporal and extratemporal	2 to 16	1 to 16	12 to 58
Jeha 2006	> 1 year seizure-free	Retrospective	371	231	NA	Temporal only	NA	NA	> 12
Jehi 2012	> 1 year seizure-free	Retrospective	312	165	149	Temporal only	2.5 to 74	1 to 64	42 (20.4)
Jennum 1993	> 1 year seizure-free	Retrospective	64	42	45	Temporal and extratemporal	8 to 52	1 to 38	> 12
Jeong 1999	'Other' scale	Not stated	93	78	54	Temporal only	9 to 51	NA	18 to 33
Kan 2008	Engel Class Scale	Retrospective	58	43	34	Temporal and extratemporal	2 to 21	0.5 to 15	12 to 96
Kang 2009	Engel Class Scale	Retrospective	244	194	108	Temporal only	18 to 68	NA	12 to 204
Kanner 2009	Engel Class Scale	Retrospective	100	86	60	Temporal only	31.2 (10.7)	12.7 (NA)	24 to 168
Kilpatrick 1997	Engel Class Scale	Prospective	50	39	28	Temporal only	16 to 57	NA	12 to 38
Kim 2009	> 1 year seizure-free	Retrospective	166	94	102	Temporal and extratemporal	3 to 51	0.5 to 37	95.3 (NA)
Kim 2010a	Engel Class Scale	Retrospective	177	75	121	Temporal and extratemporal	11 to 51	1 to 50	24 to 180

Table 1. Study characteristics and participant demographics for 182 included studies (*Continued*)

Kim 2010b	> 1 year seizure-free	Retrospective	40	14	26	Temporal and extratemporal	4 to 51	1 to 48	> 24
Kloss 2002	Engel Class Scale	Combination	68	34	30	Temporal and extratemporal	0 to 16	NA	12 to 108
Knowlton 2008	Engel Class Scale	Prospective	62	37	33	Temporal and extratemporal	1 to 60	NA	> 12
Kral 2007	'Other' scale	Retrospective	40	27	23	Temporal and extratemporal	5 to 47	1 to 45	97 (54)
Krsek 2013	Engel Class Scale	Retrospective	106	64	49	Not stated	0 to 30	NA	> 24
Kuzniecky 1993	'Other' scale	Prospective	34	23	14	Temporal only	7 to 38	> 2	12 to 30
Kwan 2010	Engel Class Scale	Retrospective	41	27	22	Extratemporal only	0 to 17.5	0 to 16	72 (NA)
Lackmayer 2013	'Other' scale	Retrospective	45	32	21	Temporal only	40.8 (10.2)	13.0 (10.1)	> 12
Lee 2006	'Other' scale	Retrospective	51	37	29	Temporal only	16 to 50	4 to 38	> 24
Lee 2008	Engel Class Scale	Not stated	71	38	44	Extratemporal only	12 to 57	3 to 34	> 24
Lee 2010	Engel Class Scale	Retrospective	52	36	31	Temporal only	9 to 54	1 to 33	14 to 42
Lee 2011	Engel Class Scale	Retrospective	40	37	23	Temporal only	1 to 15	0 to 14	11 to 151
Lei 2008	> 1 year seizure-free	Retrospective	196	180	210	Temporal and extratemporal	17 to 66	NA	> 48
Li 1997	Engel Class Scale	Retrospective	51	39	23	Temporal and extratemporal	8 to 73	NA	12 to 157

Table 1. Study characteristics and participant demographics for 182 included studies (*Continued*)

Li 1999	Engel Class Scale	Not stated	38	16	23	Temporal and extratemporal	14 to 63	NA	12 to 180
Liang 2010	Engel Class Scale	Prospective	60	40	34	Temporal and extratemporal	16.7 (NA)	NA	> 24
Liang 2012	Engel Class Scale	Retrospective	206	173	94	Temporal and extratemporal	6 to 14	2 to 14	> 12
Liava 2012	Engel Class Scale	Retrospective	52	39	NA	Extratemporal only	1 to 26	7.9 (NA)	18 to 162
Lopez-Gonzalez 2012	> 1 year seizure-free	Retrospective	86	65	63	Temporal only	1 to 18	1 to 17	> 12
Lorenzo 1995	Engel Class Scale	Retrospective	48	17	NA	Extratemporal only	NA	NA	> 12
Madhavan 2007	Engel Class Scale	Retrospective	70	37	39	Temporal and extratemporal	9.9 (10.2)	NA	
Mani 2006	Engel Class Scale	Retrospective	122	86	72	Temporal and extratemporal	8.2 (5.5)	5.2 (4.6)	> 6
Mathern 1999	'Other' scale	Retrospective	198	78	111	Temporal and extratemporal	0 to 37	0 to 31	6 to 120
McIntosh 2012	'Other' scale	Retrospective	81	11	38	Extratemporal only	4 to 60	16 (median)	12 to 212
Mihara 2004	Engel Class Scale	Retrospective	357	269	NA	Temporal and extratemporal	2 to 55	1 to 40	24 to 196
Miserocchi 2013	Engel Class Scale	Retrospective	68	58	43	Temporal only	1 to 15	0.5 to 14	> 12
Morino 2009	> 1 year seizure-free	Retrospective	62	55	24	Temporal only	34.4 (NA)	NA	> 12

Table 1. Study characteristics and participant demographics for 182 included studies (*Continued*)

Morris 1998	Engel Class Scale	Retrospective	36	26	22	Temporal and extratemporal	2 to 56	1 to 29	6 to 41
O'Brien 1996	> 1 year seizure-free	Retrospective	46	36	24	Temporal only	16 to 58	2 to 43	12 to 33
O'Brien 2000	Engel Class Scale	Retrospective	36	14	23	Temporal and extratemporal	1 to 56	NA	12 to 40
Oertel 2005	> 1 year seizure-free	Prospective	35	20	11	Temporal only	35.1 (NA)	NA	12 to 42
Paglioli 2006	Engel Class Scale	Prospective	160	143	88	Temporal only	8 to 62	3 to 60	24 to 132
Paolicchi 2000	> 1 year seizure-free	Retrospective	75	44	40	Temporal and extratemporal	0 to 12	NA	12 to 120
Park 2002	Engel Class Scale	Retrospective	148	108	76	Temporal and extratemporal	0.5 to 18	0 to 19	0 to 166
Park 2006	Engel Class Scale	Retrospective	30	20	19	Temporal and extratemporal	0 to 13	1 to 18	12 to 64
Perego 2009	Engel Class Scale	Retrospective	37	29	19	Temporal only	33 (10)	19 (NA)	> 36
Perry 2010	Engel Class Scale	Retrospective	83	34	50	Temporal and extratemporal	NA	0 to 17	> 24
Phi 2009	Engel Class Scale	Retrospective	87	80	49	Temporal only	1 to 62	0 to 48	12 to 128
Phi 2010	'Other' scale	Retrospective	41	20	20	Temporal and extratemporal	1 to 17	1 to 11	24 to 153
Pinheiro-Martins 2012	Engel Class Scale	Retrospective	70	33	27	Extratemporal only	1 to 52	1 to 36	59.1 (30.5)

Table 1. Study characteristics and participant demographics for 182 included studies (*Continued*)

Prevedello 2000	Engel Class Scale	Retrospective	84	53	48	Temporal only	19 to 43	10 to 33	15 to 44
Raabe 2012	Engel Class Scale	Retrospective	76	57	55	Not stated	6 to 67	0 to 53	24 to 200
Radhakrishnan 1998	Engel Class Scale	Combination	175	134	77	Temporal only	7 to 86	0 to 81	24 to 68
Rausch 2003	> 1 year seizure-free	Not stated	42	21	21	Temporal only	NA	NA	109 to 228
Remi 2011	Engel Class Scale	Retrospective	154	138	NA	Temporal and extratemporal	NA	NA	22 to 228
Roberti 2007	Engel Class Scale	Retrospective	42	27	17	Temporal only	10 to 52	3 to 51	44 to 121
Rossi 1994	'Other' scale	Retrospective	138	86	100	Temporal and extratemporal	1 to 46	> 3	> 36
Russo 2003	Engel Class Scale	Retrospective	101	64	67	Temporal and extratemporal	0 to 53	0 to 46	> 12
Sagher 2012	Engel Class Scale	Retrospective	96	85	46	Temporal only	17 to 59	1 to 57	> 12
Sakamoto 2009	'Other' scale	Retrospective	36	19	16	Temporal only	12 to 58	4 to 49	24 to 63
Salanova 1994	Engel Class Scale	Retrospective	89	53	46	Temporal only	8 to 53	1 to 43	12 to 96
Sarkis 2012	Engel Class Scale	Retrospective	62	38	34	Temporal only	1 to 56	NA	6 to 170
Schramm 2011	Engel Class Scale	Prospective	207	152	100	Temporal only	39.7 (13.2)	22 (median)	> 12
Seymour 2012	Engel Class Scale	Retrospective	291	153	159	Temporal only	3 to 59	NA	28 to 144

Table 1. Study characteristics and participant demographics for 182 included studies (*Continued*)

Sinclair 2003	Engel Class Scale	Retrospective	77	57	39	Temporal and extratemporal	0 to 16	0 to 15	12 to 144
Sindou 2006	Engel Class Scale	Not stated	100	85	42	Temporal only	18 to 58	NA	12 to 120
Sola 2005	Engel Class Scale	Retrospective	137	74	63	Temporal only	12 to 69	1 to 44	24 to 138
Spencer 2005	> 1 year seizure-free	Prospective	355	264	174	Temporal and extratemporal	NA	NA	> 12
Sperling 1992	Engel Class Scale	Prospective	51	41	31	Temporal only	17 to 59	NA	21 to 64
Stavrou 2008	Engel Class Scale	Retrospective	53	45	31	Temporal and extratemporal	NA	3.4 (0.8)	> 24
Suppiah 2009	Engel Class Scale	Retrospective	174	94	75	Temporal only	10 to 61	NA	57 (32)
Swartz 1992	> 1 year seizure-free	Prospective	34	27	NA	Temporal only	29 (NA)	NA	20 to 71
Tanriverdi 2010	Engel Class Scale	Retrospective	256	160	123	Temporal only	30.3 (10.5)	20.6 (10.7)	> 12
Tatum 2008	> 1 year seizure-free	Retrospective	39	22	15	Temporal only	33.8 (10.9)	14.5 (NA)	30.8
Terra-Bustamante 2005a	Engel Class Scale	Prospective	107	62	55	Temporal and extratemporal	10.2 (5.4)	6.4 (4.8)	12 to 108
Terra-Bustamante 2005b	Engel Class Scale	Prospective	35	27	11	Temporal only	1 to 18	0 to 15	12 to 84
Tezer 2008	Engel Class Scale	Retrospective	109	90	42	Temporal only	15 to 52	18.5 (7.8)	57.4 (30.6)

Table 1. Study characteristics and participant demographics for 182 included studies (*Continued*)

Theodore 2012	> 1 year seizure-free	Prospective	41	26	19	Temporal only	34.2 (9.5)	25 (12)	12 to 132
Tigaran 2003	Engel Class Scale	Retrospective	65	32	41	Extratemporal only	4 to 50	1 to 40	12 to 144
Tripathi 2008	Engel Class Scale	Retrospective	55	29	33	Temporal and extratemporal	1 to 45	NA	60 to 120
Trottier 2008	Engel Class Scale	Retrospective	96	73	69	Extratemporal only	0.5 to 52	16 (NA)	> 12
Urbach 2007	Engel Class Scale	Retrospective	42	25	20	Extratemporal only	7 to 50	2 to 42	> 12
Ure 2009	Engel Class Scale	Retrospective	74	28	0	Not stated	14 to 53	NA	12 to 336
Velasco 2011	Engel Class Scale	Prospective	163	93	NA	Not stated	NA	NA	14 to 73
Vogt 2018	'Other' scale	Prospective	47	29	22	Temporal	19 to 77	4 to 71	>12
Walz 2003	> 1 year seizure-free	Not stated	98	85	44	Temporal only	36.2 (10.7)	25.2 (10.5)	12 to 90
Weinand 1992	> 1 year seizure-free	Retrospective	89	57	NA	Temporal only	6 to 52	2 to 42	12 to 54
Wellmer 2012	Engel Class Scale	Retrospective	165	106	NA	Not stated	NA	NA	24 to 103
Widdess-Walsh 2007	> 1 year seizure-free	Retrospective	48	22	26	Temporal and extratemporal	2 to 56	0 to 27	32.4 (median)
Wiebe 2001	> 1 year seizure-free	Prospective	36	23	NA	Temporal only	NA	NA	> 12
Wiesh-mann 2008	Engel Class Scale	Retrospective	76	46	32	Not stated	NA	NA	> 12

Table 1. Study characteristics and participant demographics for 182 included studies (*Continued*)

Wray 2012	Engel Class Scale	Retrospective	52	36	24	Temporal and extratemporal	0 to 17	NA	> 12
Wyler 1995	> 1 year seizure-free	Prospective	70	38	33	Temporal only	NA	NA	> 12
Wyllie 1998	Engel Class Scale	Not stated	136	92	78	Temporal and extratemporal	13 to 20	NA	12 to 88
Yang 2011	'Other' scale	Retrospective	99	27	63	Not stated	8 to 59	NA	12 to 72
Yeon 2009	Engel Class Scale	Retrospective	60	50	37	Temporal and extratemporal	NA	1 to 26	34.9 (22.5)
Yu 2009	Engel Class Scale	Retrospective	43	26	28	Extratemporal only	4 to 43	1 to 30	33.6 (16.8)
Yu 2012a	> 1 year seizure-free	Retrospective	100	61	NA	Temporal and extratemporal	26.8 (7.6)	14.3 (8.3)	12 to 108
Yu 2012b	> 1 year seizure-free	Retrospective	222	148	NA	Temporal and extratemporal	12.5 (8.1)	6.6 (4.3)	12 to 108
Zangaladze 2008	> 1 year seizure-free	Combination	99	66	NA	Temporal and extratemporal	NA	NA	> 24
Zentner 1995	Engel Class Scale	Retrospective	167	103	82	Temporal only	3 to 64	2 to 52	12 to 72
Zentner 1996	Engel Class Scale	Prospective	56	30	39	Extratemporal only	1 to 49	2 to 35	20 to 85

[a] Age at surgery (years), duration of epilepsy (years), and duration of follow-up (months) expressed as minimum and maximum years or months when reported. If minimum and maximum not available, reported as mean (standard deviation (SD)) or median (noted in table). Follow-up expressed as minimum only (e.g. > 12 months) for 59 studies.

NA: not available.

Table 2. Quality assessment of 182 included studies according to EPHPP tool

Author	Design	Study design	Selection bias rating	Study design rating	Confounders rating	Blinding rating	Data collection rating	Withdrawals rating	Global rating
Aaberg 2012	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Adam 1996	Prospective	Cohort	Moderate	Moderate	Strong	Weak	Weak	Strong	Weak
Adelson 1992	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Weak	Not applicable	Weak
Alfstad 2011	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Alonso-Vanegas 2018	Prospective	Randomised controlled trial	Strong	Strong	Strong	Weak	Strong	Strong	Moderate
Althausen 2013	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Weak	Not applicable	Weak
Arruda 1996	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Awad 1991	Not stated	Cohort	Moderate	Moderate	Strong	Weak	Strong	Weak	Weak
Babini 2013	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Barbaro 2018	Prospective	Randomised controlled trial	Moderate	Strong	Strong	Strong	Strong	Strong	Strong
Battaglia 2006	Not stated	Cohort	Moderate	Moderate	Strong	Weak	Weak	Weak	Weak
Baumann 2007	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Weak	Not applicable	Weak

Table 2. Quality assessment of 182 included studies according to EPHPP tool *(Continued)*

Bautista 2003	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Bell 2009	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Benifla 2006	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Berkovic 1995	Prospective	Cohort	Moderate	Moderate	Strong	Weak	Weak	Strong	Weak
Blount 2004	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Blume 2004	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Boesebeck 2007	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Boshuisen 2010	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Brainer-Lima 1996	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Weak	Not applicable	Weak
Britton 1994	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Caraballo 2011	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Cascino 1995	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Weak	Not applicable	Weak
Chabardes 2005	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak

Table 2. Quality assessment of 182 included studies according to EPHPP tool *(Continued)*

Chang 2009	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Chee 1993	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Weak	Not applicable	Weak
Chkhenkeli 2007	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Choi 2004a	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Chung 2005	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Cossu 2005	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Cossu 2008	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Costello 2009	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Cukiert 2002	Prospective	Cohort	Moderate	Moderate	Strong	Weak	Weak	Strong	Weak
Dagar 2011	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Dalmagro 2005	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
de Tisi 2011	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Delbeke 1996	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate

Table 2. Quality assessment of 182 included studies according to EPHPP tool *(Continued)*

Dellabadia 2002	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Devlin 2003	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Ding 2016	Prospective	Randomised controlled trial	Moderate	Strong	Strong	Weak	Strong	Strong	Moderate
Donadio 2011	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Dorward 2011	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Duchowny 1998	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Weak	Not applicable	Weak
Dunkley 2011	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Dunlea 2010	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Dwivedi 2017	Prospective	Randomised controlled trial	Strong	Strong	Strong	Strong	Strong	Strong	Strong
Elsharkawy 2008a	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Elsharkawy 2009a	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Elsharkawy 2011a	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate

Table 2. Quality assessment of 182 included studies according to EPHPP tool *(Continued)*

Engman 2004	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Weak
Erba 1992	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Erickson 2005	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Fauser 2004	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Weak	Not applicable	Weak
Fujiwara 2012	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Garcia 1991	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Garcia 1994	Prospective	Cohort	Moderate	Moderate	Strong	Weak	Strong	Weak	Weak
Gelinas 2011	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Georgakoulias 2008	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Gilliam 1997a	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Gilliam 1997b	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Goldstein 1996	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Weak	Not applicable	Weak
Greiner 2011	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Strong	Not applicable	Moderate

Table 2. Quality assessment of 182 included studies according to EPHPP tool (*Continued*)

Grivas 2006	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Gyimesi 2007	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Hader 2004	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Hajek 2009	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Weak	Not applicable	Weak
Hallbook 2010	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Hamiwka 2005	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Hartley 2002	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Hartzfield 2008	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Hemb 2010	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Holmes 1997	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Weak	Not applicable	Weak
Holmes 2000	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Jack 1992	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate

Table 2. Quality assessment of 182 included studies according to EPHPP tool *(Continued)*

Janszky 2003a	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Weak	Not applicable	Weak
Janszky 2003b	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Jaramillo-Betancur 2009	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Jayakar 2008	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Jayalakshmi 2011	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Weak	Not applicable	Weak
Jeha 2006	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Jehi 2012	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Jennum 1993	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Jeong 1999	Not stated	Cohort	Moderate	Moderate	Strong	Weak	Strong	Weak	Weak
Kan 2008	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Kang 2009	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Kanner 2009	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Kilpatrick 1997	Prospective	Cohort	Moderate	Moderate	Strong	Weak	Weak	Weak	Weak

Table 2. Quality assessment of 182 included studies according to EPHPP tool (*Continued*)

Kim 2009	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Kim 2010a	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Kim 2010b	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Kloss 2002	Combination	Cohort	Moderate	Moderate	Strong	Weak	Weak	Weak	Weak
Knowlton 2008	Prospective	Cohort	Moderate	Moderate	Strong	Weak	Strong	Weak	Weak
Kral 2007	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Krsek 2013	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Kuzniecky 1993	Prospective	Cohort	Moderate	Moderate	Strong	Weak	Weak	Strong	Weak
Kwan 2010	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Lackmayer 2013	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Weak
Lee 2006	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Lee 2008	Not stated	Cohort	Moderate	Moderate	Strong	Weak	Weak	Weak	Weak
Lee 2010	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Lee 2011	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Weak	Not applicable	Weak

Table 2. Quality assessment of 182 included studies according to EPHPP tool (*Continued*)

Lei 2008	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Li 1997	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Li 1999	Not stated	Cohort	Moderate	Moderate	Strong	Weak	Weak	Weak	Weak
Liang 2010	Prospective	Randomised controlled trial	Moderate	Strong	Strong	Moderate	Strong	Strong	Strong
Liang 2012	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Liava 2012	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Lopez-Gonzalez 2012	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Lorenzo 1995	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Madhavan 2007	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Mani 2006	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Mathern 1999	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Strong	Not applicable	Moderate
McIntosh 2012	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Mihara 2004	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak

Table 2. Quality assessment of 182 included studies according to EPHPP tool (*Continued*)

Miserocchi 2013	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Morino 2009	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Weak	Not applicable	Weak
Morris 1998	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Strong	Not applicable	Moderate
O'Brien 1996	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Strong	Not applicable	Moderate
O'Brien 2000	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Oertel 2005	Prospective	Cohort analytic	Moderate	Strong	Moderate	Weak	Weak	Weak	Weak
Paglioli 2006	Prospective	Cohort	Moderate	Moderate	Strong	Weak	Strong	Strong	Moderate
Paolicchi 2000	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Park 2002	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Park 2006	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Perego 2009	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Perry 2010	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Phi 2009	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate

Table 2. Quality assessment of 182 included studies according to EPHPP tool (*Continued*)

Phi 2010	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Pinheiro-Martins 2012	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Prevedello 2000	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Weak	Not applicable	Weak
Raabe 2012	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Radhakrishnan 1998	Combination	Cohort	Moderate	Moderate	Strong	Weak	Strong	Weak	Weak
Rausch 2003	Not stated	Cohort	Moderate	Moderate	Strong	Weak	Strong	Weak	Weak
Remi 2011	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Roberti 2007	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Rossi 1994	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Russo 2003	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Sagher 2012	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Sakamoto 2009	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Salanova 1994	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Strong	Not applicable	Moderate

Table 2. Quality assessment of 182 included studies according to EPHPP tool *(Continued)*

Sarkis 2012	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Schramm 2011	Prospective	Randomised controlled trial	Moderate	Strong	Strong	Strong	Weak	Strong	Moderate
Seymour 2012	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Sinclair 2003	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Weak	Not applicable	Weak
Sindou 2006	Not stated	Cohort	Moderate	Moderate	Strong	Weak	Weak	Weak	Weak
Sola 2005	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Spencer 2005	Prospective	Cohort	Moderate	Moderate	Strong	Weak	Strong	Weak	Weak
Sperling 1992	Prospective	Cohort	Moderate	Moderate	Strong	Weak	Strong	Strong	Moderate
Stavrou 2008	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Suppiah 2009	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Swartz 1992	Prospective	Cohort	Moderate	Moderate	Strong	Weak	Weak	Weak	Weak
Tanriverdi 2010	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Tatum 2008	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak

Table 2. Quality assessment of 182 included studies according to EPHPP tool (*Continued*)

Terra-Bustamante 2005a	Prospective	Cohort	Moderate	Moderate	Strong	Weak	Strong	Weak	Weak
Terra-Bustamante 2005b	Prospective	Cohort	Moderate	Moderate	Strong	Weak	Strong	Weak	Weak
Tezer 2008	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Theodore 2012	Prospective	Cohort	Moderate	Moderate	Strong	Weak	Weak	Weak	Weak
Tigaran 2003	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Tripathi 2008	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Trottier 2008	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Urbach 2007	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Ure 2009	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Velasco 2011	Prospective	Cohort analytic	Strong	Strong	Strong	Weak	Weak	Strong	Weak
Vogt 2018	Prospective	Randomised controlled trial	Strong	Strong	Strong	Moderate	Strong	Strong	Strong
Walz 2003	Not stated	Cohort	Moderate	Moderate	Strong	Weak	Weak	Weak	Weak
Weinand 1992	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak

Table 2. Quality assessment of 182 included studies according to EPHPP tool (*Continued*)

Wellmer 2012	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Widdess-Walsh 2007	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Wiebe 2001	Prospective	Randomised controlled trial	Strong	Strong	Strong	Weak	Strong	Strong	Moderate
Wieshmann 2008	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Weak	Not applicable	Weak
Wray 2012	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Wyler 1995	Prospective	Randomised controlled trial	Moderate	Strong	Strong	Strong	Strong	Strong	Strong
Wyllie 1998	Not stated	Cohort	Strong	Moderate	Strong	Weak	Strong	Weak	Weak
Yang 2011	Retrospective	Retrospective case series	Moderate	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Yeon 2009	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Strong	Not applicable	Moderate
Yu 2009	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Yu 2012a	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Yu 2012b	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak

Table 2. Quality assessment of 182 included studies according to EPHPP tool (*Continued*)

Zangaladze 2008	Combination	Cohort	Moderate	Moderate	Strong	Weak	Weak	Weak	Weak
Zentner 1995	Retrospective	Retrospective case series	Strong	Moderate	Strong	Weak	Weak	Not applicable	Weak
Zentner 1996	Prospective	Cohort	Strong	Moderate	Strong	Weak	Weak	Strong	Weak

EPHPP: Effective Public Health Practice Project.

Table 3. Summary of EPHPP tool quality assessment component ratings

Quality assessment criteria	**Number and proportion of studies**	
Method of identifying participants	Retrospective	144 (79%)
	Prospective	26 (14%)
	Combination	3 (2%)
	Not stated	9 (5%)
A. Selection bias		
(Q1) Are the individuals selected to participate in the study likely to be representative of the target population?	Very likely	129 (71%)
	Somewhat likely	53 (29%)
(Q2) What percentage of selected individuals agreed to participate?	80% to 100%	9 (5%)
	less than 60%	1 (1%)
	Can't tell	28 (15%)
	Not applicable	144 (79%)
Selection bias rating	Moderate	64 (35%)
	Strong	118 (65%)
B. Study design	Retrospective case series	144 (79%)
	Cohort	27 (15%)

Table 3. Summary of EPHPP tool quality assessment component ratings (*Continued*)

	Cohort analytic	2 (1%)
	Randomised controlled trial	9 (5%)
Study design rating	Moderate	171 (94%)
	Strong	11 (6%)
C. Confounders		
(Q1) Were there important differences between groups before the intervention?	No	181 (99%)
	Unclear/Can't tell	1 (1%)
(Q2) If yes, indicate the percentage of relevant confounders that were controlled (either in the design (e.g. stratification, matching) or in the analysis)?	Unclear/Can't tell	1 (1%)
	Not applicable	181 (99%)
Confounders rating	Strong	181 (99%)
	Moderate	1 (1%)
D. Blinding		
(Q1) Was (were) the outcome assessor(s) aware of the intervention or exposure status of participants?	Yes	176 (97%)
	No	4 (2%)
	Can't tell	2 (1%)
(Q2) Were the study participants aware of the research question?	Yes	176 (97%)
	No	4 (1%)
	Can't tell	2 (1%)
Blinding rating	Strong	4 (2%)
	Moderate	2 (1%)
	Weak	176 (97%)
E. Data collection methods		
(Q1) Were data collection tools shown to be valid?	Yes	95 (52%)
	Unclear/Can't tell	87 (48%)

Table 3. Summary of EPHPP tool quality assessment component ratings (*Continued*)

(Q2) Were data collection tools shown to be reliable?	Yes	95 (52%)
	Unclear/Can't tell	87 (48%)
Data collection rating	Strong	95 (52%)
	Weak	87 (48%)
F. Withdrawals and dropouts		
(Q1) Were withdrawals and dropouts reported in terms of numbers and/or reasons per group?	Yes	17 (9%)
	No	21 (12%)
	Not applicable	144 (79%)
(Q2) Indicate the percentage of participants completing the study	80% to 100%	17 (9%)
	Can't tell	21 (12%)
	Not applicable	144 (79%)
Withdrawals rating	Strong	17 (9%)
	Weak	21 (12%)
	Not applicable	144 (79%)
G. Intervention integrity		
(Q1) What percentage of participants received the allocated intervention or exposure of interest?	80% to 100%	182 (100%)
(Q2) Was the consistency of the intervention measured?	Yes	164 (90%)
	No	18 (10%)
(Q3) Is it likely that participants received an unintended intervention (contamination or co-intervention) that may have influenced the results?	No	182 (100%)
H. Analyses		
(Q1) Unit of allocation	Individual	182 (100%)
(Q2) Unit of analysis	Individual	182 (100%)

Table 3. Summary of EPHPP tool quality assessment component ratings (*Continued*)

(Q3) Are the statistical methods appropriate for the study design?	Yes	159 (87%)
	No stats	23 (13%)
(Q4) Is the analysis performed by intervention allocation status (i.e. intention-to-treat) rather than by the actual intervention received?	Yes	182 (100%)
Global rating	**Strong**	**5 (3%)**
	Moderate	**79 (43%)**
	Weak	**98 (54%)**

EPHPP: Effective Public Health Practice Project.

Table 4. Risk of bias assessment of six randomised controlled trials

Study	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants, personnel, and outcome assessors (performance and detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Alonso-Vanegas 2018: judgement	Low	Unclear	High	Low	Low	Low
Support for judgement	Computer generated randomisation list	No information provided	Not blinded	No exclusions or withdrawals stated, all randomised patients seem to be included	Seizure outcome and safety outcomes described in the methods section well reported in the results. No protocol available to assess planned outcomes a priori	No other bias detected
Barbaro 2018: judgement	Unclear	Unclear	Low	Low	Low	Low

Table 4. Risk of bias assessment of six randomised controlled trials (*Continued*)

Support for judgement	Described as randomised but no further details provided	No information provided	Single-blinded, outcome assessors were blinded	Attrition rates clearly stated, all participants included in seizure remission analysis up to 36 months	Seizure outcome, cognition and quality of life outcomes described in the methods section well reported in the results. No protocol available to assess planned outcomes a priori	No other bias detected
Ding 2016 : judgement	High	High	Unclear	Low	Low	Low
Support for judgement	Quasi-randomisation based on odd or even patient ID number; not an adequate method of randomisation	Quasi-randomisation meaning that allocation was not concealed	No information provided	All participants followed for 3 years and included in the outcome at 3 years; attrition at 5 years clearly reported	Seizure outcome, complications, and intelligence /quality of life changes described in the methods section well reported in the results. No protocol available for assessment of planned outcomes a priori	No other bias detected
Dwivedi 2017 : judgement	Low	Low	Low	Low	Low	Low
Support for judgement	Computer-generated non-stratified randomisation	Allocation concealed with sealed opaque envelopes	Primary outcome measure of freedom from seizures assessed in a blinded manner	All participants followed for 12 months and included in the outcome at 12 months	Protocol available as an online supplement to the publication. All prespecified outcomes reported	No other bias detected
Liang 2012: judgement	High	High	Unclear	Low	Low	Low
Support for judgement	Quasi-randomisation based on odd or even patient ID num-	Quasi-randomisation meaning that al-	No information provided	All participants followed for 2 years	Seizure outcome, complications,	No other bias detected

Table 4. Risk of bias assessment of six randomised controlled trials (*Continued*)

	ber; not an adequate method of randomisation	location was not concealed		and included in the outcome at 2 years	and behavioural changes described in the methods section well reported in the results. No protocol available for assessment of planned outcomes a priori	
Schramm 2011: judgement	Low	Low	Low	Low	Low	Low
Support for judgement	Computer-generated blocked randomisation list prepared	Each centre received the randomisation codes in numbered and sealed envelopes, with each envelope allocating the extent of resection for 1 particular participant at that centre. Envelopes were to be used in the given sequence for participants as they were included into the study. Envelopes had to be opened in the OR not before the morning of surgery. Thus, the type of surgery (selective amygdalohippocampectomy or lobectomy) was determined before the envelope was opened, but the content of the	Neither study participants nor epileptologists assessing outcomes were told of the result of the randomisation (i.e. they were not aware whether a short or a long resection had been done); the only person who knew this was the surgeon. OR notes did not mention the planned resection extent. In particular, persons performing MRI volumetry were blinded to group assignment	No losses to follow-up; all participants included in analysis of outcome at 1 year	Seizure outcome, extent of resection, and complications described in the methods section well reported in the results. No protocol available for assessment of planned outcomes a priori	No other bias detected

Table 4. Risk of bias assessment of six randomised controlled trials (*Continued*)

		envelope determined the mesial extent of resection				
Vogt 2018: judgement	Low	Low	Unclear	High	Low	Low
Support for judgement	Computer generated randomisation list	Allocation communicated to the surgeon after the patient was brought into the operating theatre	No information provided	Seven out of 54 (13%) randomised participants who did not complete neuropsychological assessments at 1 year were excluded from all analyses	Seizure outcome and neuropsychological outcomes described in the methods section well reported in the results. No protocol available to assess planned outcomes a priori	No other bias detected
Wiebe 2001: judgement	Unclear	Low	Unclear	Low	Low	Low
Support for judgement	Participants "randomly assigned…after stratification according to the presence or absence of generalized motor seizures"; no further information given	Random assignments prepared outside the study centre and delivered in sealed, opaque, sequentially numbered envelopes	Blinding not possible for anyone involved (surgical vs medical treatment); unclear whether outcome was influenced by this	Full details of attrition given: "No patients were lost to follow-up. There were no crossovers from the medical group to the surgical group. One patient in the medical group died (a sudden, unexplained death) 7.5 months into the study. No deaths occurred in the surgical group." Intention-to-treat approach taken	Seizure outcome and quality of life described in the methods section well reported in the results. No protocol available for assessment of planned outcomes a priori	No other bias detected
Wyler 1995: judgement	Unclear	Unclear	Low	Low	Low	Low

Table 4. Risk of bias assessment of six randomised controlled trials (*Continued*)

Support for judgement	Study described as randomised; no further information given	No information provided	Participants and outcome assessors blinded; not possible to blind surgeons by design	All participants included in assessment of outcome at 1 year; intention-to-treat approach taken	Seizure outcome and neuropsychological outcomes described in the methods section well reported in the results. No protocol available for assessment of planned outcomes a priori	No other bias detected

ID: identification.
MRI: magnetic resonance imaging.
OR: operating room.

Table 5. Risk of bias in prognostic studies according to QUIPS tool

Author	1. Study participation		2. Study attrition		3. Prognostic factor measurement		4. Outcome measurement		5. Study confounding		6. Statistical analysis and reporting	
	Judgement	**Risk of bias**	**Judgement**	**Risk of bias**	**Judgement**	**Risk of bias**	**Judgement**	**Risk of bias**	**Judgement**	**Risk of bias**	**Judgement**	**Risk of bias**
Althausen 2013	Population of interest well described and sample recruited seems to match this; however sample restricted	**moderate**	Retrospective, so NA	**NA**	Most variables well defined, some not; unclear how data were collected and whether data were	**moderate**	Outcome patient-reported, therefore likely to be highly subjective; also unclear when outcome	**high**	Most variables well defined, some not; unclear how data were collected and whether data	**moderate**	Insufficient information provided in the methods; some variables included in the model	**high**

Table 5. Risk of bias in prognostic studies according to QUIPS tool (*Continued*)

	to those who returned postoperative questionnaires; may exclude some of those with poorer intellectual/ seizure outcomes?				complete		was measured and if additional medical records were used for some/ all participants		were complete; some adjustment seems to have been done but not for all relevant variables		without prespecification and no definitions; results selectively reported	
Boesebeck 2007	Population of interest well described and sample seems to match this, but unclear on recruitment methods and inclusion criteria	**moderate**	Retrospective, so NA	**NA**	Prognostic factors entering the model well described, but not much information given on how these data were collected	**moderate**	Difficult outcome to measure in a valid and reliable way, but outcome definition is clear and the same for all participants; method of collecting outcome data	**moderate**	NA for studies of a single-group design	**NA**	Model well described and based on clinical value rather than statistical significance; however not all P values reported and regression coefficients re-	**moderate**

Table 5. Risk of bias in prognostic studies according to QUIPS tool (*Continued*)

							not specified				ported rather than meaningful effect sizes	
Cossu 2008	Population of interest well described; sample well described; sample representative of the source population	**low**	Retrospective, so NA	**NA**	All variables well described; measurement techniques specified and patients all came from a single centre, so likely followed the same protocol	**low**	Difficult outcome to measure in a valid and reliable way; measured on a known scale; last follow-up meaning variability across measurement times	**moderate**	Age at surgery and pathology seem to have been considered as confounders; unclear what are confounders and what are prognostic factors	**moderate**	Analysis described clearly, but variables in the model based on statistical significance; results presented only for statistically significant variables	**high**
Cossu 2005	Population of interest well described and original sample matches this population; how-	**moderate**	Retrospective, so NA	**NA**	Variables well defined, but very little information provided on how data	**moderate**	Difficult outcome to measure in a valid and reliable way; information	**moderate**	NA for studies of a single-group design	**NA**	Methods well described on the model and variables, but reporting of	**moderate**

Table 5. Risk of bias in prognostic studies according to QUIPS tool (*Continued*)

	ever not all from original sample included in final analyses, and characteristics not described for the subgroup of interest who did undergo surgery				were collected and analysed		provided on outcome classification, but not on when outcome was measured and how outcome was measured				results highly selective, with no useful information provided at all	
Elsharkav 2008a	Population of interest and sample well described; seem to match	**low**	Retrospective, so NA	**NA**	All variables well defined, pre-operative workup seems the same but data collected retrospectively in a variety of ways, which could have led to	**moderate**	Difficult variable to measure in a valid and reliable way; outcome well defined overall, but unclear at which time point modelling was conducted	**moderate**	Although all results presented according to "Group", differences between these groups do not seem to be considered; unclear if any variables	**moderate**	Model appropriate for the data, but variables included based on statistical significance and results selectively reported	**high**

Table 5. Risk of bias in prognostic studies according to QUIPS tool (*Continued*)

					variability across participants		and potential variability in data collection across participants		are being treated as confounders or as prognostic variables			
Elsharkav 2009a	Population of interest well defined, and sample recruited seems to match this; very clear how sample was recruited; large sample size	**low**	Retrospective, so NA	**NA**	Most variables well defined, and data recorded and collected following the same protocol; however definitions of some variables unclear due to variable terminology, which makes it unclear which variables have been analysed	**moderate**	Difficult outcome to measure in a valid and reliable way, but methods seem satisfactory (same time points, single protocol, multiple data sources)	**low**	NA for studies of a single-group design	**NA**	Model appropriate for the data but variables included based on statistical significance; some variable definitions unclear and results selectively reported	**high**

Table 5. Risk of bias in prognostic studies according to QUIPS tool (*Continued*)

Gelinas 2011	Population of interest and sample recruited well described and seem compatible; uncertainty only around the definition of "paediatric"	**moderate**	Retrospective, so NA	**NA**	All variables well defined and method of measurement seems valid and consistent for most; some variability possible for one of the most important variables in the study - subjective choice	**moderate**	Difficult outcome to measure in a valid and reliable way; measured at a single time point for analysis and judged by an expert, so seems reasonable	**low**	Potential "confounder"; type of surgery well defined but choice was subjective and likely to vary across participants; differences between groups considered, and this variable included in regression analysis	**moderate**	Results well reported, but unclear exactly how many variables went into the model	**moderate**
Janszky 2003a	Population of interest well described; however given the clinical question of interest, the sample seems	**high**	Retrospective, so NA	**NA**	Prognostic factors well defined including definitions of key variables (IEDs, CFCs); unclear whether	**moderate**	Difficult outcome to measure in a valid and reliable way; outcome recorded accord-	**moderate**	All apparent relevant confounders examined, well defined, and adjusted for in analysis of prog-	**moderate**	Methods describe models quite well; unclear how it was decided which variables went	**high**

Table 5. Risk of bias in prognostic studies according to QUIPS tool (*Continued*)

	quite selective				participants were submitted to 1 or 2 centres, so unclear if data collection methods are the same		ing to a known scale, but unclear when outcome was measured (possibly variable across participants); little detail given about how data were collected		nostic factors, but unclear whether participants were submitted to 1 or 2 centres, so unclear if data collection methods are the same		into the prognostic model; results selectively reported	
Jennum 1993	Population of interest well described, and sample seems to match this, but unclear on recruitment methods and inclusion criteria	**moderate**	Retrospective, so NA	**NA**	Prognostic factors entering the model mostly well described (except for extent of resection), but not much information given on how	**moderate**	Difficult outcome to measure in a valid and reliable way; however outcome data collected in the same way	**low**	NA for studies of a single-group design	**NA**	Very little information given about the model; only significant P values reported	**high**

Table 5. Risk of bias in prognostic studies according to QUIPS tool (*Continued*)

					these data were collected		for all participants and measured at the same time					
Kim 2009	Population of interest well described; sample well described; seem to match	**low**	Retrospective, so NA	**NA**	Definitions and measurements of some factors unclear	**moderate**	Difficult outcome to measure in a valid and reliable way; not defined according to a scale such as Engel Class; no information on when outcome is measured	**high**	NA for studies of a single-group design	**NA**	Methods well described, but variables entered into the model based on statistical significance and results selectively reported	**high**
Kim 2010a	Population of interest and sample well defined, but unclear whether patients were re-	**moderate**	Retrospective, so NA	**NA**	Most variables well described but technical; not clear if participants	**moderate**	Seizure outcome defined, but not the time point measured;	**moderate**	NA for studies of a single-group design	**NA**	Unclear which variables went into the model; results selectively	**moderate**

Table 5. Risk of bias in prognostic studies according to QUIPS tool (*Continued*)

	cruited from a single centre or from multiple centres, and if the type of epilepsy in the sample matches the population				came from a single centre, so different protocols may have been followed		unclear how data were collected				reported	
Lopez-Gonzalez 2012	Population of interest well defined, and sample recruited seems to match this; very clear how sample was recruited	**low**	Retrospective, so NA	**NA**	Variables well described; pre-operative evaluations carried out in standardised fashion, but unclear how retrospective analysis was carried out (patient records extracted, etc.)?	**moderate**	Outcome briefly defined but no further information provided; unclear how outcome data were collected; multiple time points for the analysis accounted for in the analysis	**moderate**	NA for studies of a single-group design	**NA**	Statistical methods well described; variables well defined (but based on statistical significance) and results clearly tabulated (unclear why RRs were reported)	**moderate**

Table 5. Risk of bias in prognostic studies according to QUIPS tool (*Continued*)

Madhavan 2007	Descriptions of population of interest and sample recruited not quite the same; inclusion criteria brief	**moderate**	Retrospective, so NA	**NA**	Likely that measurement of variables was different across centres; unclear how some variables have been defined and choice for analysis	**high**	Seizure outcome defined according to a known scale; time point not stated and unclear how outcome data were collected	**moderate**	NA for studies of a single-group design	**NA**	Unclear what kind of statistical model had been fitted; only significant variables entered into the model	**high**
McIntosh 2012	Population of interest well described; study sample matches population for characteristics of interest; all included in analysis	**low**	Retrospective, so NA	**NA**	Prognostic variables well defined; a lot of effort made to accurately collect data for all participants; participants came from a single centre	**low**	Difficult outcome to measure in a valid and reliable way, but a lot of effort made to correctly classify participants; outcome mea-	**low**	NA for studies of a single-group design	**NA**	Methods well described and results well reported; however, choice of variables and categories based on data and statistical significance	**moderate**

Table 5. Risk of bias in prognostic studies according to QUIPS tool (*Continued*)

							sured at 1 time point in primary analysis					
O'Brien 2000	Population of interest well defined and sample recruited seems to match this; very clear how sample was recruited	**low**	Retrospective, so NA	**NA**	Potential for misclassification due to the nature of the prognostic factors, but efforts made to reduce risk; definitions well described but unclear why some participants were not included in some analyses	**moderate**	Difficult outcome to measure in a valid and reliable way; measured according to a known scale; could have been different if a different time of measurement was chosen due to variability of outcome	**moderate**	NA for studies of a single-group design	**NA**	Statistical analysis described very well, with no selective reporting of results	**low**
Paolicchi 2000	Population of interest clear and sample seems to	**moderate**	Retrospective, so NA	**NA**	All definitions of variables seem clear; little to no vari-	**moderate**	Difficult outcome to measure in a valid and	**moderate**	NA for studies of a single-group design	**NA**	Unclear which variables have actually gone	**high**

Table 5. Risk of bias in prognostic studies according to QUIPS tool (*Continued*)

	match this; however insufficient information given regarding methods of recruitment				ation in collection/measurement methods seems to have occurred across participants, but unclear if participants came from a single centre		reliable way; unclear when the outcome was measured - probably variable across participants, who may have come from multiple centres				into the model, what "univariate conditions" means, and whether results are selectively reported	
Phi 2009	Population of interest well defined, and sample recruited seems to match this; very clear how sample was recruited	**low**	Retrospective, so NA	**NA**	Most variables well defined; some uncertainty on method of measurement for some variables and methods of analysis	**moderate**	Difficult outcome to measure in a valid and reliable way; unclear when the outcome was measured - probably variable across participants	**moderate**	NA for studies of a single-group design	**NA**	Methods section seems clear on methods and factor list, but unclear from the results exactly what has gone into the model	**moderate**

Table 5. Risk of bias in prognostic studies according to QUIPS tool (*Continued*)

Radhakrishnan 1998	Sample recruited well described and seems representative of the population of interest; however unclear whether participants were recruited prospectively or retrospectively, and how complete follow-up information was	**moderate**	Unclear whether participants were recruited prospectively or retrospectively (or both). 15 participants excluded for less than 2 years of follow-up, or missing data from all consecutive participants; no withdrawals mentioned (but implied), and no fixed study duration, so whether participants	**high**	Variables seem to be measured in the same way for all participants and defined clearly; some variables subjective and taken from participant surveys by definition, so could induce bias; quantity of missing data unclear, as is how this was handled in analysis	**moderate**	Difficult outcome to measure in a valid and reliable way; could have been different if a different time of measurement was chosen due to variability of outcome	**moderate**	NA for studies of a single-group design	**NA**	Appropriate model, well described; however, unclear which variables had been entered into the multivariate model (based on univariate analyses?) and if all results have been reported	**moderate**

Table 5. Risk of bias in prognostic studies according to QUIPS tool (*Continued*)

			completed the study is NA; unclear how complete follow-up information was, and if this impacted analysis									
Rossi 1994	Population of interest vague and unclear, so uncertain if the sample represents this; little information about how the sample was recruited; analysis performed on a subset of this sample	**high**	Retrospective, so NA	**NA**	Variables well defined and methods/ setting described in some detail, but unclear how the retrospective review was carried out; large proportion of missing data likely to have	**high**	Difficult outcome to measure in a valid and reliable way; outcome measured at the same time point by a well-defined scale, but no details provided regard-	**moderate**	NA for studies of a single-group design	**NA**	Some uncertainty over exactly what has been done in terms of modelling; variables entered based on statistical significance; only P values reported without inter-	**high**

Table 5. Risk of bias in prognostic studies according to QUIPS tool (*Continued*)

					impacted the generalisability of analyses		ing data collection				pretation	
Sagher 2012	Population of interest well described; sample recruited well described; seem to match	**low**	Retrospective, so NA	**NA**	All variables well described; multiple study authors classified some variables, and data likely to have been collected in the same way for participants from a single centre	**low**	Seizure outcome measured according to a known scale at specific time points; model builds in all follow-up of participants and data collected in the same way; participants from a single centre	**low**	Variables well defined and separated by the 2 types of surgery; differences between variables mostly not tested; type of surgery included in GEE model	**moderate**	Statistical methods well described, but unclear which variables went into the model and how effect sizes should be interpreted	**moderate**
Sarkis 2012	Population of interest well described; sample recruited well de-	**low**	Retrospective, so NA	**NA**	All variables well described; data likely to have been col-	**low**	Seizure outcome defined according to a known scale; not	**moderate**	NA for studies of a single-group design	**NA**	Statistical methods well described; however	**high**

Table 5. Risk of bias in prognostic studies according to QUIPS tool (*Continued*)

	scribed; seem to match				lected in the same way, with participants from a single centre		completely clear how outcome data were collected; statistical model will account for variable follow-up length				variables selected based on statistical significance and results selectively reported	
Schramm 2011	Large sample recruited; seems representative of the population of interest; however 35% of potentially eligible individuals not included for varying reasons	**moderate**	All participants in the study contributed data from 1 year and were included in an intention-to-treat analysis; secondary analysis was planned in the case of drop-outs	**low**	Clinical/ demographic data seem to have been collected in a reliable and valid way under the same protocol for all patients; however unclear what	**moderate**	Difficult outcome to measure in a reliable and valid way but seems satisfactory; measured by a known scale at a single time point in the same way for all	**low**	Clinical/ demographic data seem to have been collected in a reliable and valid way under the same protocol for all participants; however	**moderate**	Unclear which variables have been included in the model, exactly what type of analysis has been performed, and whether all results have been re-	**moderate**

Table 5. Risk of bias in prognostic studies according to QUIPS tool (*Continued*)

					are prognostic variables and what are confounding factors		participants		unclear what are prognostic variables and what are confounding factors; "confounders do not appear to be accounted for in the design, and unclear what type of analysis (if any) was done		ported	
Spencer 2005	Large sample size, which is representative of the population of interest, but unclear how many other eligible	**moderate**	Not enough information in the publications on participants lost to follow-up and those included in the	**moderate**	Complete data collected under the same protocol; some scope for variation between	**moderate**	Difficult outcome to measure in a reliable and valid way; relies on patient reporting and	**moderate**	NA for studies of a single-group design	**NA**	Unclear whether the analysis was appropriate, which variables were entered into the model, and	**high**

Table 5. Risk of bias in prognostic studies according to QUIPS tool (*Continued*)

	individuals declined to take part or were excluded from analyses		analyses unclear		participants; not all PF definitions are completely clear		does not use a known scale				whether results were selectively reported	
Tezer 2008	Population of interest and sample well described; sample seems to match population of interest	**low**	Retrospective, so NA	**NA**	Most variables well defined; unclear how some variables defined and analysed; a lot of effort made to avoid misclassification in data collection; participants came from a single centre	**moderate**	Difficult outcome to measure in a valid and reliable way, but a lot of effort made to correctly classify participants according to a known scale; however, outcome measured at variable time points	**moderate**	NA for studies of a single-group design	**NA**	Unclear which variables went into the model, what the outcome variable was, and results were selectively reported	**high**
Theodore 2012	Study sample seems to be repre-	**moderate**	Prospective study with	**moderate**	Exact prognostic factors of inter-	**moderate**	Difficult outcome to mea-	**moderate**	NA for studies of a single-group	**NA**	Unclear how variables	**high**

Table 5. Risk of bias in prognostic studies according to QUIPS tool (*Continued*)

	sentative of the population of interest; however not clear on how this sample was recruited, how many eligible participants declined to take part, whether any withdrawals occurred, etc		41 included participants; no fixed study length (duration of follow-up specified), so completing the study is not applicable; no drop-outs/ withdrawals/ losses to follow-up mentioned, and unclear if any occurred		est from the PET scans unclear		sure in a valid and reliable way; could have been different if a different time of measurement was chosen due to variability of outcome; not measured according to a known scale		design		are being analysed in the model and results selectively presented (no numerical results at all)	
Walz 2003	Sample recruited well described and seems representative of the population of in-	**moderate**	No losses to follow-up mentioned; reasons for exclusion from analysis given; not clear	**moderate**	Data seem to have been collected the same way for all participants, in a way that	**moderate**	Difficult outcome to measure in a valid and reliable way; could have been	**moderate**	NA for studies of a single-group design	**NA**	Statistical analysis appropriate and all results presented; however choice	**moderate**

Table 5. Risk of bias in prognostic studies according to QUIPS tool (*Continued*)

	terest; however unclear whether participants were recruited prospectively or retrospectively		if the study is of a prospective or retrospective design, so difficult to judge withdrawals and drop-outs		should minimise bias. Some variables by definition could be prone to recall/ misclassification biases, but clear definitions given (except dichotomis variables)		different if a different time of measurement was chosen due to variability of outcome; all participants from a single centre, and outcome measured according to a known scale				of variables for the multivariate model based on univariate results	
Wyler 1995	Population of interest not well defined; introduction refers more to surgical technique than to the population it is being	**moderate**	Outcome assessment at 1 year recorded for all participants; no drop-outs nor missing data	**low**	Variables entered into the logistic regression model well defined and seem to have been collected reliably,	**moderate**	Difficult outcome to measure in a valid and reliable way, but every effort seems to have been made to	**low**	Randomisation has balanced groups in terms of any confounding factors; therefore logistic	**low**	No statistical analysis described in the methods, only in the results; unclear exactly what has been	**moderate**

Table 5. Risk of bias in prognostic studies according to QUIPS tool (*Continued*)

	applied to				but unclear if all participants were from the sample centre and were following the same protocol		verify seizure outcomes of participants, and all outcomes measured at the same time		regression should allow for identification of prognostic factors without confounding		done and whether selective reporting occurred	
Yang 2011	Study sample appeared to be representative of the population of interest, but information is limited	**moderate**	Retrospective, so NA	**NA**	Definitions and measurements of some factors unclear	**moderate**	Difficult outcome to measure in a reliable and valid way but seems satisfactory and measured according to a known scale; variability in follow-up time handled in analysis	**low**	NA for studies of a single-group design	**NA**	Statistical methods unclear	**moderate**

CFC: complex febrile convulsion.
GEE: generalised estimating equation.