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Antiepileptic drugs for seizure control in people with neurocysticercosis (Review)

Walton D, Castell H, Collie C, Wood GK, Sharma M, Singh T, Michael BD

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[Intervention Review]

Antiepileptic drugs for seizure control in people with neurocysticercosis

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ABSTRACT

Background

Neurocysticercosis is the most common parasitic infection of the brain. Epilepsy is the most common clinical presentation, though people may also present with headache, symptoms of raised intracranial pressure, hydrocephalus, and ocular symptoms depending upon the localisation of the parasitic cysts. Anthelmintic drugs, antiepileptic drugs (AEDs), and anti-oedema drugs, such as steroids, form the mainstay of treatment.

This is an updated version of the Cochrane Review previously published in 2019.

Objectives

To assess the effects (benefits and harms) of AEDs for the primary and secondary prevention of seizures in people with neurocysticercosis.

For the question of primary prevention, we examined whether AEDs reduce the likelihood of seizures in people who had neurocysticercosis but had not had a seizure.

For the question of secondary prevention, we examined whether AEDs reduce the likelihood of further seizures in people who had had at least one seizure due to neurocysticercosis.

As part of primary prevention studies, we also aimed to examine which AED was beneficial in people with neurocysticercosis in terms of duration, dose, and side-effect profile.

Search methods

For the 2021 update of this review, we searched the Cochrane Register of Studies (CRS Web), MEDLINE, and LILACS to January 2021. CRS Web includes randomised or quasi-randomised, controlled trials from CENTRAL, the Specialised Registers of Cochrane Review Groups, including Epilepsy, PubMed, Embase, ClinicalTrials.gov, and the World Health Organisation International Clinical Trials Registry Platform. We also checked the reference lists of identified studies, and contacted experts and colleagues in the field to search for additional and ongoing studies.

Selection criteria

Randomised and quasi-randomised controlled trials.

Single-blind, double-blind, or unblinded studies were eligible for inclusion.

Data collection and analysis

We followed standard methodological procedures expected by Cochrane. Two review authors independently selected trials for inclusion and extracted the relevant data. The primary outcomes of interest were: proportion of individuals experiencing seizures, and time to first seizure post randomisation. Secondary outcomes included: seizure freedom, number of withdrawals, side effects, number of people seizure free with short or long durations of treatment, quality of life, therapy costs, hospitalisations, and mortality.

We used an intention-to-treat analysis for the primary analysis. We calculated odds ratio (OR) for dichotomous data (proportion of individuals who experienced seizures, were seizure free for a specific time period (12 or 24 months), withdrew from treatment, developed drug-related side effects or complications, were seizure-free with each treatment policy, mortality), and planned to use mean difference (MD) for continuous data, if any continuous data were identified (quality of life, cost of treatment). We intended to evaluate time to first seizure after randomisation by calculating hazard ratios (HRs). We assessed precision using 95% confidence intervals (CIs). We stratified the analysis by treatment comparison. We also considered the duration of drug usage, co-medications, and the length of follow-up.

Main results

We did not find any trials that investigated the role of AEDs in preventing seizures among people with neurocysticercosis, presenting with symptoms other than seizures.

We did not find any trials that directly compared individual AEDs for primary prevention in people with neurocysticercosis.

We included four trials that evaluated the efficacy of short-term versus longer-term AED treatment for people with solitary neurocysticercosis (identified on computed tomography (CT) scan) who presented with seizures. In total, 466 people were enrolled. These studies compared AED treatment durations of 6, 12, and 24 months.

The risk of seizure recurrence with six months of treatment compared with 12 to 24 months of treatment was inconclusive (odds ratio (OR) 1.34, 95% confidence interval (CI) 0.73 to 2.47; three studies, 360 participants; low-certainty evidence). The risk of seizure recurrence with six to 12 months of treatment compared with 24 months of treatment was inconclusive (OR 1.36, 95% CI 0.72 to 2.57; three studies, 385 participants; very low-certainty evidence).

Two studies compared seizure recurrence with CT findings, and suggested that persistent and calcified lesions had a higher recurrence risk, and suggest longer duration of treatment with AEDs. One study reported no side effects, while the rest did not comment on side effects of the drugs.

None of the studies addressed the quality of life of the participants. These studies had methodological deficiencies, such as small sample sizes, and a possibility of bias due to lack of blinding, which affect the results of the review.

Authors' conclusions

Despite neurocysticercosis being the most common cause of epilepsy worldwide, there is currently no evidence available regarding the use of AEDs as seizure prophylaxis among people presenting with symptoms other than seizures. For those presenting with seizures, there is no reliable evidence regarding the duration of treatment required. Therefore, there is a need for large scale randomised controlled trials to address these questions.

PLAIN LANGUAGE SUMMARY

Treatment of epilepsy in people with neurocysticercosis

Background

Neurocysticercosis is a common infection of the brain. It is caused by the larvae of the pork tapeworm that migrate to the brain and form an enclosed sac around themselves (called a cyst). Seizures are the most common symptoms, although some people may present with headache, vomiting, or other symptoms of brain swelling.

This review investigated the usefulness of antiepileptic drugs (AEDs) in preventing seizures in people who did not have seizures to start with, but presented with these other symptoms. We also examined the usefulness of AEDs in people with epilepsy due to neurocysticercosis, in terms of choice of drug, dosage, duration of treatment, side effects, and the quality of life.

Study characteristics

We included four trials, with a total of 466 participants, which focused on the comparison of short-duration and long-duration of AED treatment in people with a single brain cyst. The trials considered six to 12 months as short-duration treatment, and 12 to 24 months as long-duration treatment.

Key results

There were inconclusive results for the benefit of one duration of AED over the other (six, 12, or 24 months) for people with a single cyst. In people with calcified cysts, longer duration of therapy may be preferable.

All four included trials enrolled people with a single brain lesion. The findings of our review cannot be generalised to people with multiple cysts, or with cysts in unusual parts of the brain.

The evidence is current to January 2021.

SUMMARY OF FINDINGS

Summary of findings 1. Short-duration antiepileptic drug treatment compared with long-duration antiepileptic drug treatment for people with neurocysticercosis

Short-duration antiepileptic drugs**compared with long-duration** antiepileptic drugs**for seizure control in people with neurocysticercosis**

Patient or population: people with neurocysticercosis
Settings: outpatients, in India
Intervention: short-duration antiepileptic drugs (6-month AED treatment)
Comparison: long-duration antiepileptic drugs (12- to 24-month AED 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				
	Long-duration AEDs (12 to 24 months)	Short duration AEDs (6 months)				
Seizure control (seizure recurrence) Follow-up: median 12 months	**Study population**		OR 1.34 (95% CI 0.73 to 2.47)	360 (3 studies)	⊕⊕⊖⊖ **low** [a]	OR > 1 indicates seizure recurrence is more likely on short duration AEDs (6 months); CI makes this inconclusive.
	121 per 1000	**162 per 1000** (88 to 299 per 1000)				

Assumed risk: the event rate in the long duration AED group multiplied by 1000. The event rate is the proportion of the total population in which the event occurred.

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; **OR:** odds ratio;

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

[a]Downgraded twice due to lack of blinding of participants and researchers in all the included studies, unclear risk of bias in participant concealment, and lack of applicability.

Summary of findings 2. Six- to 12-month antiepileptic drug treatment compared with 24-month antiepileptic drug treatment for seizure control in neurocysticercosis

Six- to 12-month antiepileptic drug**treatment compared with 24-month** antiepileptic drug**treatment for seizure control in people with neurocysticercosis**

Patient or population: people with neurocysticercosis
Settings: outpatients, in India
Intervention: 6 to 12 months of antiepileptic drug (AED) treatment
Comparison: 24 months of AED 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				
	24-month AED treatment	6- to 12-month AED treatment				
Seizure control (seizure recurrence) Follow-up: 18 months	**Study population**		OR 1.36 (95% CI 0.72 to 2.57)	385 (3 studies)	⊕⊕⊕⊖ **very low** [a,b]	OR > 1 indicates seizure recurrence is more likely on 6 to 12 months AED treatment; CI makes this inconclusive.
	103 per 1000	**140 per 1000** (74 to 264 per 1000)				

Assumed risk: the event rate in the long-duration AED group multiplied by 1000. The event rate is the proportion of the total population in which the event occurred.

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; **OR:** odds ratio

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

[a]Downgraded twice due to lack of blinding of participants and researchers in all the included studies, unclear risk of bias in participant concealment, lack of applicability, and high probability of publication bias.
[b]Inconsistency in report of withdrawals and reasons for them.

BACKGROUND

This is an updated version of the Cochrane Review previously published in 2019 (Frackowiak 2019).

Description of the condition

Neurocysticercosis is an infection of the central nervous system, caused by the *Taenia solium cysticerci*. *Taenia solium* is an intestinal parasite that infests animals, such as pigs, and has a secondary life cycle in human beings. Ingestion of the parasite eggs, excreted in the faeces of the pig or an infested human host, can result in cysticercosis. After ingestion, the eggs can migrate from the gut to lodge in various tissues of the body, where they form cysts. Cysticercosis is usually asymptomatic. When symptoms of cysticercosis do develop, it is usually due to cysticercal invasion of the central nervous system and eyes.

Neurocysticercosis is the most common parasitic infection of the brain. The prevalence of neurocysticercosis is high in low- and middle-income countries, particularly in populations in which there is close proximity between humans and pigs; it is common in much of South and Central America, China, the Indian subcontinent, South-East Asia, and sub-Saharan Africa. It affects around 50 million people worldwide, with men and women equally affected (Dhawan 2011), and has a peak incidence between the ages of 30 to 40 years (Zafar 2013). However, migration of populations has changed the epidemiology of the disease, and its prevalence in high-income countries is now increasing.

The presentation of neurocysticercosis is related to the site of invasion by the cyst, the stage of the parasite, and the host immune response. Cysts in the cerebral parenchyma are noted to have four stages – vesicular stage, colloidal stage, granulomatous stage, and calcified stage (DeGiorgio 2004; García 2002). The vesicular stage is the viable cyst, which is associated with minimal immune response, and hence shows limited enhancement after intravenous contrast in neuroimaging, although an eccentric scolex may be seen with magnetic resonance imaging (MRI) within the cyst at this stage. The second stage is when the viable cyst ruptures to release its fluid into the surrounding parenchyma. This fluid stimulates an intense immune response in the host, and results in perilesional oedema, which is associated with contrast enhancement on MRI. This is the most common clinically evident stage of neurocysticercosis. Cellular response to this stage results in the next stage (granulomatous, or nodular), during which some perilesional oedema may still be visible. The final stage of destruction and calcification may result in permanent calcific lesions in the parenchyma. There may also be a conglomeration of cysts in the basal cisterns (termed racemose cysts). Single cysts are usually up to 20 mm in diameter. Giant cysts, measuring more than 50 mm in diameter may produce space-occupying effects. Cysts may also occur within the ventricles or in the spinal cord.

Epilepsy is an important neurological condition, characterised by recurrent seizures. It has an estimated annual incidence of 50/100,000, and a prevalence of 5/10,000 to 10/1000 in the 'developed' world (Sander 1996). Approximately 3% of the population will suffer from seizures at some point in their lives (Hauser 1992). Epilepsy can have several causes, for example head injury, infections of the brain, tumours, infarcts, and haemorrhage. Neurocysticercosis is an important cause of symptomatic seizures, or secondary epilepsy among children and adults in many low- and middle-income countries. In some countries, neurocysticercosis has been reported to be the cause of 20% to 70% of cases of symptomatic epilepsy (Daniels 2006; Del Brutto 2005; Palacio 1998; Rajshekhar 2006). In some Asian countries, neurocysticercosis causes up to 50% of cases of epilepsy (Rajshekhar 2003), and up to 90% of cases of symptomatic seizures in children (Singhi 2000).

Seizures are the most common first presenting feature of neurocysticercosis, occurring in nearly 70% to 90% of affected people (DeGiorgio 2004). The seizures are usually focal seizures, with or without secondary generalisation (Del Brutto 1992; Singhi 2000). Host immune response (resulting in oedema or gliosis (or both) surrounding the cysts) and calcification are the reasons for epileptogenesis (the gradual process during which a previously normal brain develops epilepsy) in neurocysticercosis (Pradhan 2000). Multiple parenchymal cysts are associated with more frequent seizures (Ferreira 2002). A smaller, but significant number of people may present with severe and recurrent headaches. Localisation in the ventricles or in the basal cisterns may result in the development of hydrocephalus, causing severe headache and features of raised intracranial pressure. Cysticercostic encephalitis is a rare clinical presentation of neurocysticercosis (García 2002).

The diagnosis of neurocysticercosis is established on the basis of clinical presentation and computed tomography (CT) scan or MRI. Diagnostic criteria proposed by Rajshekhar and Brutto include these features, and can be used to define the disease (Del Brutto 2001; Rajshekhar 2003). The clinical and radiological diagnosis can be supported by serological tests, such as enzyme-linked immunosorbent assay (ELISA) and enzyme-linked immuno transfer blot test (ELITB), which have been found to be highly specific for the diagnosis (Dhawan 2011).

Description of the intervention

As seizures are the most common presentation of neurocysticercosis, antiepileptic drugs (AEDs) are often used. The duration of AED therapy has been based on expert opinions or consensus. Most experts recommend that AEDs be continued until the epileptogenic focus, in the form of the oedema or the degenerating cyst, resolves completely. This may take up to six months. However, as some of the lesions may resolve as a calcified lesion in the parenchyma, they may continue to be a focus for seizures. The benefit of longer-term AED therapy on seizure frequency has not been established (Gupta 2002; Thussu 2002; Verma 2006). Seizure recurrence in people with neurocysticercosis is usually associated with the presence of multiple parenchymal cysts, frequent seizures before the start of treatment with AEDs, and persistent calcification (Del Brutto 1996; Gupta 2002; Rajshekhar 2004; Thussu 2002). Monotherapy with carbamazepine or phenytoin is the common choice for seizure control. A small proportion may require polytherapy (Rajshekhar 2004).

How the intervention might work

AEDs are important in the control of seizures, which are the most common presentation of neurocysticercosis. These drugs help to prevent the recurrence of seizures in people with symptomatic epilepsy secondary to neurocysticercosis, and may have a role in primary prevention of seizures in people with neurocysticercosis who present with features other than seizures, such as headache or altered behaviour.

Why it is important to do this review

The management of an individual with neurocysticercosis imposes a great burden on the economy of the world. One treatment for each person with neurocysticercosis in India costs an estimated 0.0037% of the gross national product (Murthy 2007; Pal 2000). Solitary neurocysticercosis is essentially self-limiting, and presents clinically when the viable cysts actually start degenerating to produce an immune response. The use of anthelmintic treatment has been a subject of debate, and is the topic of another Cochrane Review (Abba 2010). Short courses of steroids (oral prednisolone) are used to control the host response and pericystic oedema.

For people with symptomatic epilepsy secondary to neurocysticercosis, there are no systematic reviews to inform their clinicians on which AED to use, what dosage to prescribe, or how long to administer the AED. For those with neurocysticercosis who present with symptoms other than seizures, there are no systematic reviews to inform their clinicians on the use of AEDs to prevent seizures. Hence, we undertook a systematic review of the role of AEDs in the treatment of people with neurocysticercosis presenting, with or without seizures.

OBJECTIVES

To assess the effects (benefits and harms) of antiepileptic drugs (AEDs) for the primary and secondary prevention of seizures in people with neurocysticercosis.

1. For the question of primary prevention, we examined whether AEDs reduced the likelihood of seizures in people who had neurocysticercosis, but had not had a seizure.
2. For the question of secondary prevention, we examined whether AEDs reduced the likelihood of further seizures in people who had had at least one seizure due to neurocysticercosis.
3. As part of primary prevention studies, we also aimed to examine which AED was beneficial in people with neurocysticercosis in terms of duration, dose, and side-effect profile.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised and quasi-randomised controlled trials.

Single-blind, double-blind, or unblinded studies were eligible for inclusion.

For studying primary prevention, we planned to include studies in which individuals with neurocysticercosis presented with symptoms other than seizures, such as headache or behavioural changes.

For secondary prevention, we planned to include studies in which the participants had neurocysticercosis with seizures prior to randomisation.

Types of participants

We included studies of people with neurocysticercosis, diagnosed on the basis of neuroimaging findings, with or without additional serological or histopathological confirmation.

The participants were of all age groups (children and adults) and both genders. The participants experienced any type of seizure associated with neurocysticercosis, or presented with symptoms other than seizures.

We excluded studies on neurocysticercosis at extracerebral sites.

Types of interventions

The intervention group may have received any of the currently marketed antiepileptic drugs (AED), in addition to the usual treatment for neurocysticercosis (anthelmintics, steroids, or both). The controls may have received placebo, or the usual treatment for neurocysticercosis without AEDs. The AEDs may have been a single drug (monotherapy) or a combination of AEDs. The duration of treatment may have been short (a few weeks or months) or prolonged (years). A follow-up period of 12 months is required for inclusion.

Types of outcome measures

Primary outcomes

1. Proportion of individuals experiencing seizures
2. Time to first seizure post randomisation

Secondary outcomes

1. Proportion of individuals who were seizure free for a specific time period (12 or 24 months)
2. Proportion of individuals who withdrew from treatment
3. Proportion of individuals who developed drug-related side effects or complications
4. For studies comparing short versus long duration of treatment, proportion of individuals who were seizure free with each treatment policy
5. Quality of life (measured by validated scales)
6. Cost of therapy
7. Requirement for hospitalisation, need for intensive care treatment, and length of hospitalisation
8. Mortality

Search methods for identification of studies

We attempted to identify all relevant trials, regardless of language or publication status (published or unpublished, in press, or in progress).

Electronic searches

We ran the searches for the original review in April 2014. We ran subsequent searches in May 2015, December 2016, June 2018, and July 2019. For the latest update, we searched the following databases:

1. Cochrane Register of Studies (CRS Web; searched 14 January 2021), using the search strategy outlined in Appendix 1;
2. MEDLINE Ovid (1946 to 14 January 2021), using the search strategy outlined in Appendix 2;
3. LILACS (1982 to 14 January 2021), using the search strategy outlined in Appendix 3.

CRS Web includes randomised or quasi-randomised, controlled trials from the Cochrane Central Register of Controlled Trials

(CENTRAL), and the Specialized Registers of Cochrane Review Groups, including Epilepsy, PubMed, Embase, ClinicalTrials.gov, the World Health Organization International Clinical Trials Registry Platform (ICTRP).

Searching other resources

We also checked the reference lists in the selected studies, and tried to contact researchers in the field to look at unpublished data. We contacted experts in the field and colleagues, and asked if they were aware of any studies that we may have missed in our searches.

Data collection and analysis

We used Review Manager 5.4 (Review Manager 2020). We used an intention-to-treat analysis for the primary analysis. We calculated odds ratio (OR) for dichotomous data (proportion of individuals who experienced seizures, were seizure free for a specific time period (12 or 24 months), withdrew from treatment, developed drug-related side effects or complications, were seizure-free with each treatment policy, mortality), and planned to use mean difference (MD) for continuous data, if any continuous data were identified (quality of life, cost of treatment). We intended to evaluate time to first seizure after randomisation by calculating hazard ratios (HRs). We assessed precision using 95% confidence intervals (CIs).

We stratified the analysis by treatment comparison. We also considered the duration of drug usage, co-medications, and the length of follow-up.

Selection of studies

In the 2015 and 2019 reviews, review authors (MS, MF and BDM) independently screened all citations and abstracts, and evaluated the eligibility of each reference for the review. MS independently screened the initially identified 180 citations, MF and BDM independently screened the 48 citations identified for the 2019 update. In the 2021 review, two review authors (DW and BDM) screened all new citations and abstracts for eligibility.

We included studies on the basis of the criteria described in Criteria for considering studies for this review. We excluded studies that were not eligible, and documented the reasons for exclusion.

Data extraction and management

Two review authors (MS, AM) independently extracted data, using a tailored data extraction form. We summarised and coded data on study design, participant characteristics, interventions, and outcomes, and entered them into Review Manager 5 (Review Manager 2014). We resolved any discrepancies between data extracted by the two authors by discussion, and by referring to the third review author.

We extracted the following data.

1. Trial factors
   a. study setting, country and year of study
   b. study design
   c. randomisation method
   d. blinding
   e. duration of study
   f. duration of follow-up
2. Participants
   a. number in each group
   b. age and sex distribution per randomised group
   c. seizure type and frequency per randomised group
   d. number of seizures before randomisation in each group
   e. other neurologic deficits
   f. neuroimaging data: location of lesion(s), number of lesion(s) – solitary or multiple, nature of cyst(s) – live, dying, or calcified
3. Type of intervention
   a. AED studied, and dose
   b. number of drugs used
   c. duration of AED
   d. adjunctive medications used in each group
4. Outcome measures (as described earlier)
5. Withdrawals from study

Assessment of risk of bias in included studies

Two review authors (MS, AM) assessed each trial independently and resolved any disagreements by consensus, or with consultation of a third party (TS) in case of ongoing disagreement. We assessed risk of bias using Cochrane's RoB tool (Higgins 2011).

We used the following criteria.

1. Was the allocation sequence adequately generated?
2. Was the allocation adequately concealed?
3. Was knowledge of the allocated intervention adequately prevented during the study?
4. Were incomplete outcome data adequately addressed?
5. Are reports of the study free of suggestion of selective outcome reporting?
6. Was the study apparently free of other problems that could put it at a high risk of bias?

We used individual bias items, as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). Risk of bias summaries can be accessed here (Figure 1; Figure 2);

Figure 1. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies

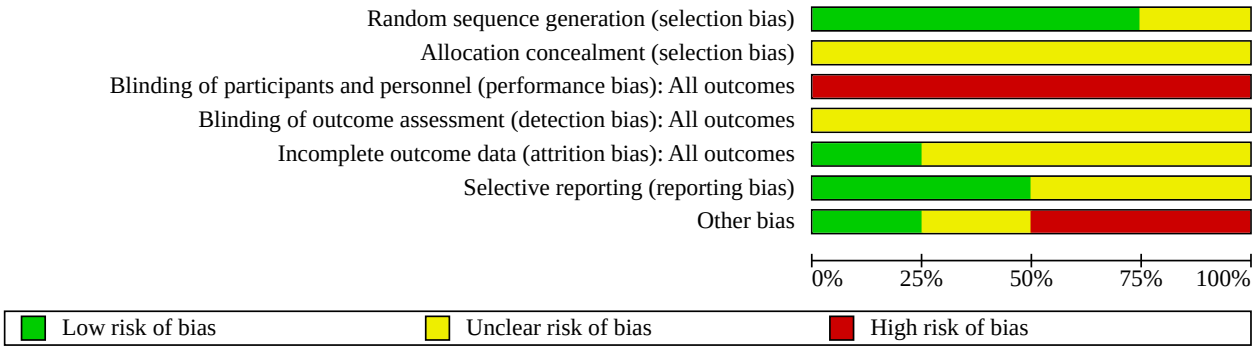
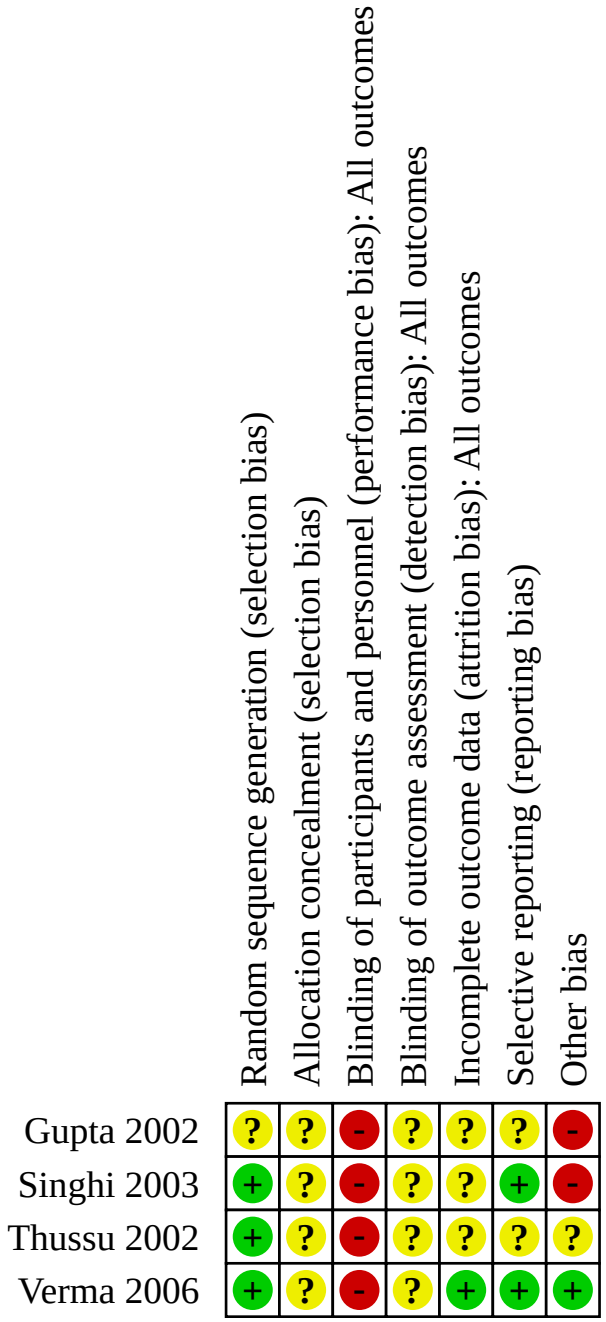


Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study



We planned to explore the influence of individual risk of bias criteria in a sensitivity analysis.

Measures of treatment effect

We measured treatment effect as the proportion of individuals in each group who were seizure free for a specific time period (six, 12 or 24 months). We calculated ORs for dichotomous data, and

planned to use MD for continuous data. We assessed precision using 95% CIs.

We planned to measure the adverse effect of treatment as the proportion of individuals who withdrew from the study due to adverse effects of the drugs. We also planned to try to measure and compare the adverse effects between short and long duration of treatment in studies that compared short and long duration of treatment.

We carried out an analysis of three studies comparing six months AED with 12 to 24 months AED, and of three studies comparing six to 12 months versus 24 months AED therapy.

Unit of analysis issues

We intended to take into account the level at which randomisation occurred, such as cross-over trials, cluster-randomised trials, and multiple observations for the same outcome. However, none of the studies included in the review are cross-over or cluster-randomised trials.

Dealing with missing data

We procured the complete article for collection of data. In cases of missing data (number of patients excluded, reasons), we contacted the principal investigator of the study by email. Until the time of writing this review, we had not received any replies.

Assessment of heterogeneity

We assessed heterogeneity between trials by examining the forest plot, and using the I^2 statistic for heterogeneity, where an I^2 greater than 50% indicated substantial heterogeneity.

We assessed clinical heterogeneity by comparing the differences in demographics, type and number of seizures, type of AED used, dosages and duration of treatment, and radiological data in the various studies.

Assessment of reporting biases

We assessed the included studies for reporting bias by evaluating the exclusion criteria in the study, and by evaluating the dropout rate and noting the reasons for it. We also assessed the probability of publication bias by examining a funnel plot for asymmetry.

Data synthesis

We used Review Manager 5.4 (Review Manager 2020) software for all data synthesis. We analysed data as set out in Measures of treatment effect.

Subgroup analysis and investigation of heterogeneity

We had planned to undertake subgroup analysis for the following subgroups:

1. individuals with a single granuloma and those with multiple cerebral granulomas;
2. individuals with neurocysticercosis treated with monotherapy and polytherapy;

We did not find any studies comparing treatment in people with single and multiple granulomas, or that compared monotherapy versus polytherapy.

Sensitivity analysis

We did not carry out a sensitivity analysis to test the robustness of meta-analysis.

Summary of findings and assessment of the certainty of the evidence

We created two summary of findings tables; one for each comparison (six months AED treatment versus 12 to 24 months AED treatment, and six to 12 months AED treatment versus 24 months AED treatment) (Summary of findings 1; Summary of findings 2). The primary outcomes of the review, proportion of individuals experiencing seizures and time to first seizure after randomisation, were not reported in any of the included studies. If these outcomes are reported in included studies in future updates of the review, they will be added to the 'Summary of findings' tables. We determined the certainty of the evidence using the GRADE approach (GRADEpro GDT). We downgraded the evidence in the presence of high risk of bias in at least one trial, indirectness of the evidence, unexplained heterogeneity or inconsistency, imprecision of results, and high probability of publication bias. We downgraded the evidence by one level if we considered the limitation to be serious, and two levels if we considered it to be very serious.

RESULTS

Description of studies

Results of the search

In the 2019 review, we identified a total of 228 records through database searching; 48 identified trials and a further three records were identified through other sources. We removed duplicate citations and obviously irrelevant items (i.e. not reports of trials), trials studying the use of albendazole, praziquantel, and their combinations, and trials studying various protocols of steroids for people with neurocysticercosis. Of the 85 remaining records, we excluded 78, as they were studies that addressed laboratory diagnosis of neurocysticercosis, or trials for which the outcomes reported were an assessment of the impact of non-antiepileptic drugs (AED), such as anthelmintics, steroids, or both.

We found seven potentially relevant studies for the 2019 review, and reviewed their full, published texts. We excluded three, and we finally included four studies. The review authors decided which studies should be included for the review after discussion. They graded the inclusion, exclusion criteria, and methodological quality on a pre-designed format. The review authors were not blinded to the study authors names, institute of the studies, or the journal of publication.

For this review update (2021) we identified a total of nine new trials. After removing duplicate and irrelevant records, two studies remained for consideration. The first was an ongoing study (CTRI/2019/01/017368), the other we excluded as it did not have the minimum of 12 month follow-up data required (Santhosh 2021). The search results are shown in Figure 3.

Figure 3. Study flow diagram for the 2021 review update

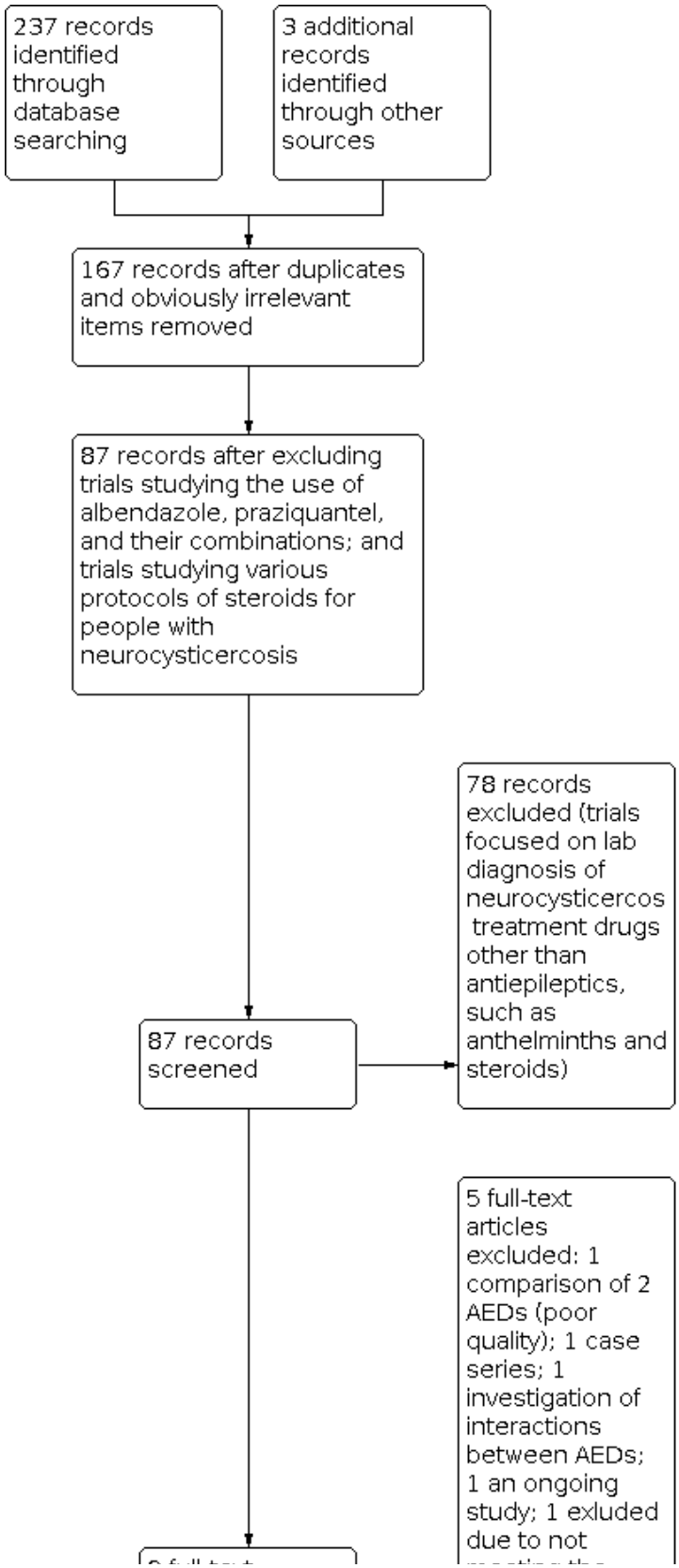
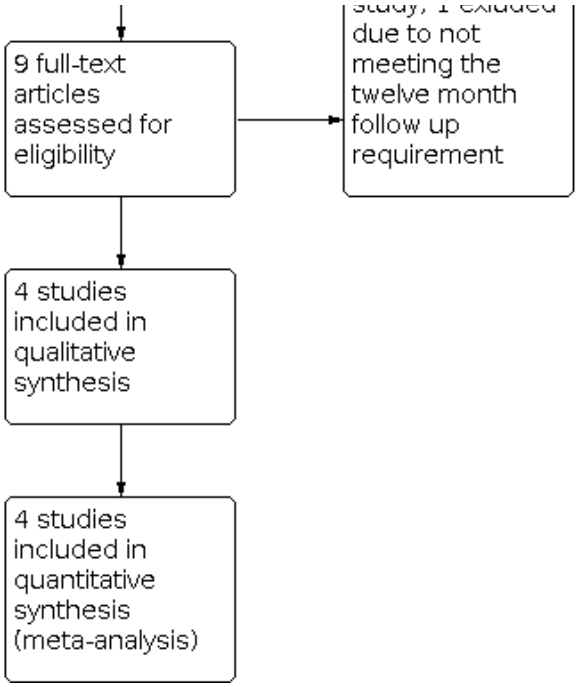


Figure 3. (Continued)



Included studies

We included four studies, which together enrolled 466 participants with neurocysticercosis. One study included children between the ages of three and 14 years (Singhi 2003); one study included adults (age not specified (Verma 2006)); one study included both children and adults, with ages ranging from four to 52 years (Thussu 2002); and one study did not clearly mention the age range of participants included in the study (Gupta 2002). Three studies enrolled patients from outpatient clinics (Singhi 2003; Thussu 2002; Verma 2006); Gupta 2002 did not mention the source of participants.

Of the 466 people involved, one study did not include the gender of 81 people (Gupta 2002). Of the rest, 237 were male and 148 were female. Focal seizures were the commonest form of seizures. Forty-two participants had primary generalised seizures, and 343 participants had focal seizures. Gupta 2002 did not elaborate on the type of seizures or drugs given. In the other three studies, 299 participants were given carbamazepine, and 105 participants received phenytoin.

All included studies were single-centre studies, carried out at various centres in India. They compared the efficacy of different durations of AED therapy (six, 12, and 24 months). Three studies considered six months of AED treatment to be short duration (Gupta 2002; Thussu 2002; Verma 2006); one study considered 12 months of treatment to be short duration (Singhi 2003). Gupta 2002 considered twelve months to be long duration of treatment; and three studies considered 24 months to be long duration of treatment (Singhi 2003; Thussu 2002; Verma 2006). One hundred and eighty-six participants in three studies received six months of AED treatment (Gupta 2002; Thussu 2002; Verma 2006), and 55 people in one study received 12 months of AED treatment as short duration (Singhi 2003). One hundred and eighty-five participants in three studies received 24 months of AED treatment as long duration (Singhi 2003; Thussu 2002; Verma 2006), and 40 participants in one study received 12 months of AED as long-duration treatment (Gupta 2002).

Participants were followed for 12 months after randomisation in three studies (Gupta 2002; Singhi 2003; Thussu 2002), and for 18 months after randomisation in one (Verma 2006). Repeat neuroimaging, after an initial scan at randomisation, was performed in three studies: at three or six months later in two studies (Gupta 2002; Verma 2006), and at 12 months later in one study (Singhi 2003).

The common AEDs used were carbamazepine or phenytoin. Two studies stated that the choice of drug was decided by the treating physician, and was possibly affected by cost of treatment (Singhi 2003; Verma 2006). One study did not state the reason, if any, for choice of a particular AED (Thussu 2002). The fourth study focused on the comparison of the duration of the AED given, but did not state which drug was given (Gupta 2002). This adds an element of bias in the choice of therapy, and affects the outcome, and we judged it as high risk of other bias.

Details of each of the included studies are further described in Characteristics of included studies.

Excluded studies

We excluded four studies. One study was a small case series of add-on treatment with tiagabine, in adults with neurocysticercosis receiving AEDs for seizure control (Chang 1998). The second study compared the tolerability, efficacy, and safety of clobazam with phenytoin sodium (Kaushal 2006). The third study compared carbamazepine against levetiracetam as monotherapy for secondary prevention of seizures, in neurocysticercosis with seizures (Santhosh 2021). We excluded these studies as the study participants in these open-label trials were only observed for six months rather than the 12 months required for inclusion. The fourth study investigated the pharmacokinetic interactions

between AEDs and serum albendazole enantiomer concentrations, as opposed to the clinical seizure outcome measures required for this review (Lanchote 2002).

Details of each of the excluded studies are further described in Characteristics of excluded studies.

Risk of bias in included studies

The risks of bias are summarised in Figure 1 and Figure 2, and detailed below.

Allocation

Three studies stated the method used for randomisation; Gupta 2002 did not state the method of randomisation. Methods used for randomisation included a lottery system (Thussu 2002), coin toss (Verma 2006), and random number tables (Singhi 2003). We assumed that randomisation was done appropriately, and thus, there was a low risk of allocation bias.

There was an unclear risk of allocation concealment bias in all four studies, as concealment was not mentioned.

Blinding

None of the studies mention blinding of participants or treating physicians to the study arm, or to the antiepileptic agent used. In two studies, the choice of drug used depended upon the physician and affordability of the agent (Singhi 2003; Verma 2006). We assessed a high risk of performance bias, and an unclear risk of detection bias in all four studies.

Incomplete outcome data

One study detailed the number of participants excluded from the study due to loss to follow-up and fulfilment of exclusion criteria (Verma 2006). We judged a low attrition bias in this study. The other three studies, mentioned exclusion criteria, but did not detail the number of participants excluded in the final analysis. We judged a unclear attrition bias in these studies.

Selective reporting

The protocols of the selected studies were not available to compare with the final conduct of the studies. We judged two studies to have a low risk of reporting bias, as evident from the reported results in the studies (Singhi 2003; Verma 2006). We judged the other two studies to have an unclear risk of reporting bias.

Effects of interventions

See: **Summary of findings 1** Short-duration antiepileptic drug treatment compared with long-duration antiepileptic drug treatment for people with neurocysticercosis; **Summary of findings 2** Six- to 12-month antiepileptic drug treatment compared with 24-month antiepileptic drug treatment for seizure control in neurocysticercosis

All four included studies compared the effectiveness of short-term versus long-term antiepileptic drug treatment in seizure control in people with neurocysticercosis.

All included studies recruited participants with seizures prior to AED treatment. None of the included studies randomised individuals to specific AEDs, and none compared the proportion of individuals experiencing seizures between the AEDs prescribed. Therefore, analyses are of secondary prevention, rather than primary prevention.

Primary Outcomes

Proportion of individuals experiencing seizures

None of the included studies reported this outcome.

Time to first seizure post randomisation

None of the included studies reported this outcome.

Secondary Outcomes

Proportion of individuals who were seizure free for a specific time period (12 or 24 months)

None of the included studies reported this outcome.

Proportion of individuals who withdrew from treatment

Only one study documented the number of people lost to follow-up and number of people completing the study (Verma 2006). The other three studies did not comment on withdrawals (Gupta 2002; Singhi 2003; Thussu 2002).

Proportion of individuals who developed drug-related side effects or complications

Only one study mentioned that no side effects occurred in any participant (Verma 2006). The other three studies did not comment on side effects of AEDs (Gupta 2002; Singhi 2003; Thussu 2002). The dosage of drug used was mentioned in one study (Verma 2006); no information was provided on drug doses in the other three studies. Therefore, we did not carry out subgroup analyses of drug given or dosage for this review.

Short versus long duration of treatment - proportion of individuals who were seizure free with each treatment policy

Three studies considered six months as short-term treatment (Gupta 2002; Thussu 2002; Verma 2006); Singhi 2003 considered patients treated for 12 months as the short-term group. Gupta 2002 considered 12 months as the long-duration treatment arm and the other three studies considered 24 months treatment as the long-duration arm (Singhi 2003; Thussu 2002; Verma 2006). Three studies followed up participants for 12 months after stopping AED (Gupta 2002; Singhi 2003; Thussu 2002); one study followed participants for 18 months (Verma 2006). The outcome seizure recurrence was recorded from participants' reports on follow-up visits every two or three months after randomisation.We analysed data comparing six months AED treatment versus 12 to 24 months AED treatment (Gupta 2002; Thussu 2002; Verma 2006); and data comparing six to 12 months AED treatment versus 24 months AED treatment (Singhi 2003; Thussu 2002; Verma 2006).The odds ratio (OR) of seizure recurrence with six months of AED treatment, compared with 12 to 24 months of AED treatment was inconclusive (OR 1.34, 95% CI 0.73 to 2.47; three studies; 360 participants; low-certainty evidence; Analysis 1.1; Figure 4). The risk of seizure recurrence with six to 12 months AED treatment compared with 24 months AED treatment was also inconclusive (OR 1.36, 95% CI 0.72 to 2.57; three studies, 385 participants; very low-certainty evidence; Analysis 2.1; Figure 5).Two studies correlated seizure recurrence with CT findings (Singhi 2003; Verma 2006; 312 participants). Both studies suggested that prolonged AED treatment may be required for people with

persistent lesions or calcification, based on seizure recurrence and follow-up CT scanning.

Figure 4. Forest plot of comparison: 2. 6 months AED treatment versus 12 to 24 months AED treatment, outcome: 2.1 Seizure recurrence

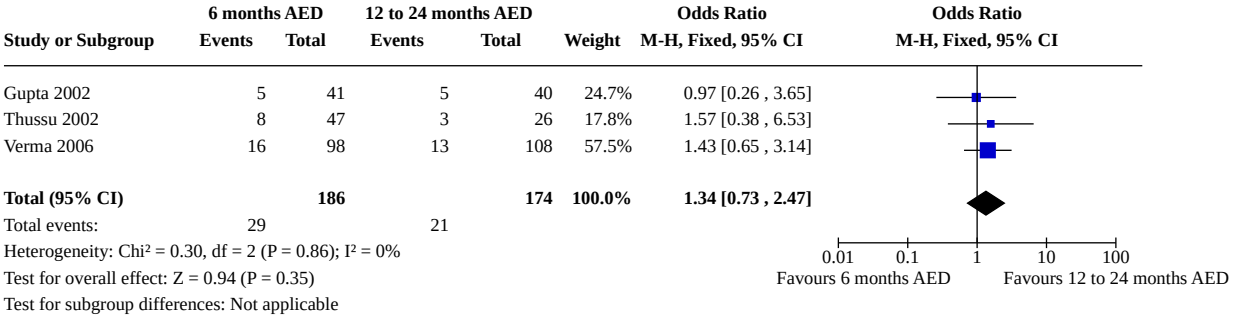
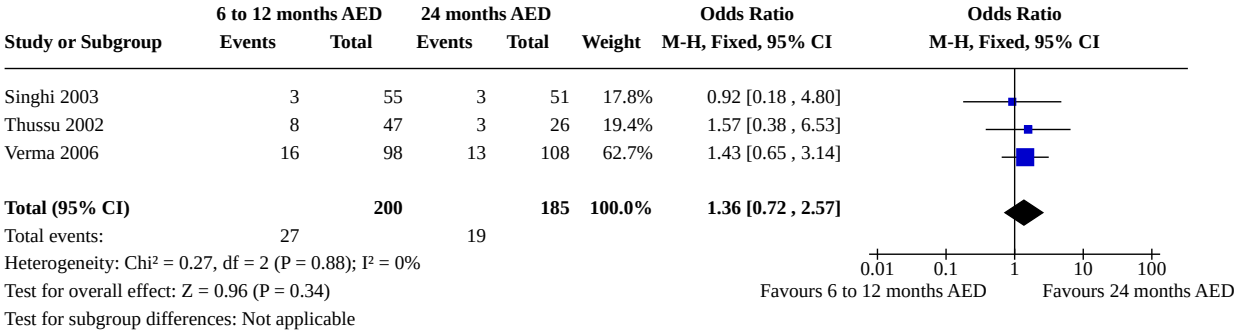


Figure 5. Forest plot of comparison: 2. 6 to 12 months AED treatment versus 24 months AED treatment, outcome: 2.1 Seizure recurrence



Quality of life (measured by validated scales)

None of the included studies reported this outcome.

Cost of therapy

None of the included studies reported this outcome.

Requirement for hospitalisation, need for intensive care treatment, and length of hospitalisation

None of the included studies reported this outcome.

Mortality

None of the included studies reported this outcome.

DISCUSSION

We intended to look at trials evaluating the efficacy of various antiepileptic drugs (AEDs) for seizure control in people with neurocysticercosis. For primary prevention, we intended to look at people with neurocysticercosis presenting with problems other than seizures, for example, headache, diplopia (double vision), etc. However, in our electronic search, we did not find trials addressing the above. This finding indicates a gap in our knowledge base, and the need for randomised controlled trials to address this issue.

For secondary prevention, we aimed to look at studies that considered whether AEDs decrease the likelihood of further seizures in people who had experienced at least one seizure.

Summary of main results

The four studies included in the review compared the use of short duration and long duration AED treatment in control of seizures in people with a single cerebral cysticercal cyst.

Four hundred and sixty-six people with neurocysticercosis participated in the four included studies (Gupta 2002; Singhi 2003; Thussu 2002; Verma 2006). These studies examined seizure recurrence with varying durations of AED treatment (six or 12 or 24 months).

The odds ratio (OR) of seizure recurrence with six months AED treatment compared with 12 to 24 months treatment was inconclusive (OR 1.34; 95% CI 0.73 to 2.47; three studies, 360 participants (186 participants for six months treatment and 174 participants for 12 to 24 months treatment); Analysis 1.1). The risk of seizure recurrence with six to 12 months AED treatment compared with 24 months treatment was inconclusive (OR 1.36; 95% CI 0.72 to 2.57; three studies, 385 participants (200 participants randomised to six to 12 months treatment and 185 participants to 24 months treatment); Analysis 2.1).

Two studies indicated that in cases where a persistence of lesion or calcification is found on review computed tomography (CT) scans, prolongation of AED treatment may be effective in optimal seizure control (Singhi 2003; Verma 2006).

Overall completeness and applicability of evidence

A major drawback of the four included studies, comparing short-duration and long-duration treatments, is that none of the studies sought to establish the effectiveness of the specific AED being given; they did not analyse the choice of drug, dosage, compliance, or side-effect profiles. All four studies solely focused on comparing the duration of drugs being given. Therefore, the results have limited applicability to inform physicians on the choice of AEDs. The study design and implementation of Santhosh 2021 addressed the aforementioned effectiveness of two AEDs being given (please refer to Characteristics of excluded studies) but was excluded due to its limited follow-up period.

With the exception of Verma 2006, where exclusions and losses were detailed, none of the included studies mentioned the exact number of people excluded from the trial and why.

Most studies mentioned that neurocysticercosis is a benign and often a self-limiting condition. Thus participant selection may affect the final outcome of the studies. Two studies excluded people who had a persistence of a lesion, which is actually a high risk for seizure recurrence, implying that people selected for the study had a low risk of seizure recurrence in the first place (Thussu 2002; Verma 2006).

Most of the studies included in the review excluded people with persistent lesions and those needing albendazole therapy, some of whom may have actually been at high-risk for seizure recurrence. As a result, the study inferences prevent generalisation to all people will neurocysticercosis, focusing instead on people with inactive parasitic cysts.

All of the included studies focused on people with a solitary cerebral lesion. These factors limit the applicability and generalisation of the study results for future use in people with neurocysticercosis who may have multiple cysts, or have a lesion that is situated in unusual locations, for example, intra ventricular cysts, brainstem cysts, etc.

Three of the studies correlated seizure recurrence and the need for prolonged therapy with the presence of a calcified lesion (Gupta 2002; Singhi 2003; Verma 2006). They suggested that people with calcified lesions would benefit from a longer duration of AEDs, and by repeated neuroimaging to check the status of the lesion. This suggestion is useful in practice.

Quality of the evidence

The included studies that compared short-duration and long-duration AEDs have methodological deficiencies, such as lack of blinding, small sample sizes, reporting biases, and lack of description of withdrawals from the study. We judged the overall quality of the evidence as low. All the included studies had an inherent bias in patient allocation and blinding. Though not clearly mentioned, it can be assumed that the treating physicians and participants were not blinded to the study drug and study arm being studied. This also adds a possibility of a reporting bias, all of which together affects the quality of evidence provided by the study results.

We evaluated the included studies for heterogeneity using the I^2 statistic (I^2 = 0%). The studies included in the meta-analysis were homogenous with respect to diagnostic criteria used, method of sampling, method of observation, follow-up, and analysis of results.

An analysis of the findings is shown in the Summary of findings 1 and Summary of findings 2.

Potential biases in the review process

Potentially, studies may have been missed by the search strategy if smaller studies were presented at clinical conferences, but not in the literature identified through the search engines employed.

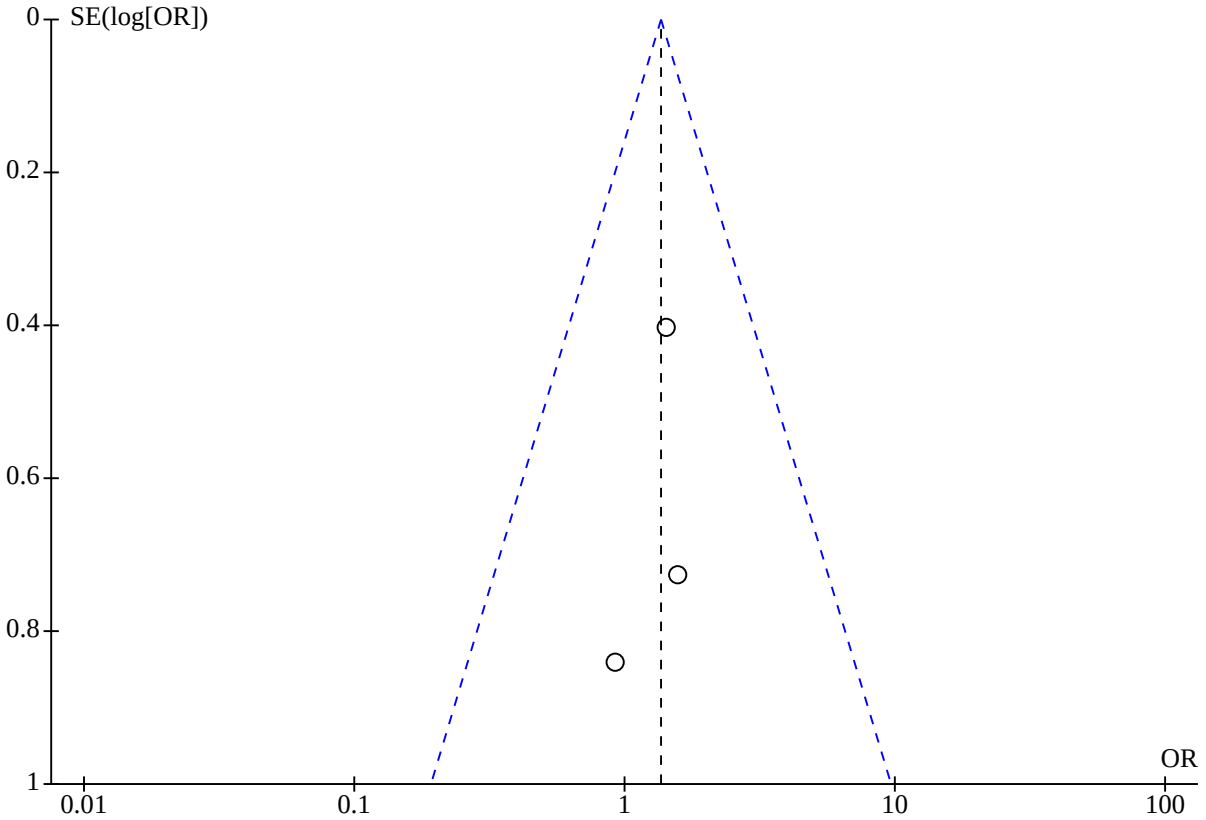
None of the identified studies reported the primary outcome measures of the proportion of individuals experiencing seizures or the time to first seizure between AED treatment groups. We contacted the authors to attempt to obtain these data but did not receive them data to enable us to undertake these analyses. Nevertheless, had these data been made available, there would potentially be significant bias, as the prescription of AEDs was not randomised but rather determined by the clinician, which reflects clinical and potentially financial bias.

Study selection potentially could have introduced bias, as we limited our inclusion to studies with at least 12 months of data, therefore we are unable to comment on the efficacy of AEDs in the first six months of therapy. Santhosh 2021 provided a well-designed study comparing the effectiveness of carbamazepine and levetiracetam, but was excluded due to its limited follow-up data of only six months.

All four included studies were single-centre studies from various parts of India. The geographic location and disease behaviour outcomes may be different in the subcontinent versus other regions of the world where neurocysticercosis is equally prevalent. We cannot rule out a regional bias in this review.

We generated a funnel plot, indicating a publication bias in the included studies (Figure 6). The quality of the trials included is not uniform, in terms of study design. For example, one study enrolled children only (Singhi 2003), one study included only adults (Verma 2006). One included people of all age ranges, but the mean age of participants was in the adult range (Thussu 2002). The fourth study did not specify details of the enrolled participants, such as age, gender, or type of seizures (Gupta 2002). This factor affected the results of this review.

Figure 6. Funnel plot of comparison: 2. 6 to 12 months AED treatment versus 24 months AED treatment, outcome: 2.1 Seizure recurrence



Agreements and disagreements with other studies or reviews

So far, there have been reviews on treatment of people with neurocysticercosis, highlighting anthelmintic therapy, anti-oedema measures, such as steroids, and various combinations of these measures in attempts to control seizures (Abba 2010; García 2002; Zafar 2013). While most of these reviews mention the need for AEDs in people presenting with seizures, there are no reviews dedicated to the use of AEDs, with respect to drug choices, duration of treatment, side-effect profiles, etc.

AUTHORS' CONCLUSIONS

Implications for practice

The initial research question for this review was: 'Do antiepileptic drugs (AEDs) influence seizure control in people with neurocysticercosis with respect to the drug used, dose, and duration?' We also intended to look at primary prevention in people with symptoms other than seizures. We do not know whether prophylactic AED therapy is useful in preventing seizures in people with neurocysticercosis who present with symptoms other than seizures, since no randomised controlled trials are available at present.

We did not find any studies that measured superiority of one AED over another at 12-month follow-up.

Our analysis does not suggest a clear benefit of short (six to 12 months) or longer duration of AED treatment (12 to 24 months) for people with a single cerebral cyst. In people with persistent cysts or calcification, two studies suggested that a longer duration of AED treatment may reduce seizures compared to a shorter duration of AED treatment.

Implications for research

Further studies are needed to determine which AED is more suitable for people with seizures (or epilepsy) due to neurocysticercosis, and the optimal dose range and duration of treatment for each AED. Studies are needed to address the issue of whether prophylactic treatment with AEDs reduces the occurrence of seizures. The effect of AED treatment on quality of life for people with neurocysticercosis also needs to be investigated.

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We would like to thank Dr Amrith Mathew for his contributions to the original review protocol and to previous versions of the review.

We would also like to thank Marta Frackowiak for her contribution to the 2019 review update.

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CHARACTERISTICS OF STUDIES

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

Gupta 2002

Study characteristics	
Methods	Randomised trial Method of randomisation not stated Single centre in New Delhi, India Total duration of trial 1.5 to 2 years in both study groups Ethical approval/consents not stated
Participants	81 participants, 41 people with NCC treated for 6 months in group A, 40 people with NCC treated for a period of 12 months in group B Diagnostic criteria based on CT scan findings Age and sex distribution not stated Inclusion criteria: all people with epilepsy and diagnostic CT findings, only people with a single lesion Exclusion criteria: suspected tuberculoma and people with NCC treated with albendazole Follow-up: 12 months after drug withdrawal
Interventions	AED treatment for seizure control for 6 months in group A, and 12 months in group B Details of drug used, dosage in either group not stated
Outcomes	Seizure recurrence after stoppage of treatment
Notes	Single outcome studied. Withdrawals and exact number of excluded participants not stated. Choice of AED not mentioned. Dosage, side effects, cost, and impact on quality of life not studied.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of randomisation not detailed
Allocation concealment (selection bias)	Unclear risk	Exact methodology not detailed in the article
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not mentioned in article, probably not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Method of outcome recording not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Withdrawals, exclusions, and reasons (if any) not stated

Gupta 2002 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Protocol not available. Insufficient information to comment on reporting
Other bias	High risk	AED used, formulation, and dosage not stated in the article

Singhi 2003

Study characteristics	
Methods	Randomised controlled trial Single centre in India Total duration of trial 2 to 3 years in both comparison groups
Participants	Children with NCC Diagnostic criteria based on CT Scan findings, only single lesions included 55 children treated with AEDs for 1 year as group A, 51 children treated for 2 years as group B. Age range: 3 to 14 years; 61 boys, 45 girls Demographically comparable groups Inclusion criteria: children with seizures and CT scan diagnosis of NCC Exclusion criteria: children with multiple or calcified CT lesions, static or progressive neurological disorder, any systemic or chronic illness, any clinical or ancillary evidence of tuberculosis 55% also received albendazole within 3 months of presentation Follow-up: 12 months after drug withdrawal
Interventions	AEDs for 12 months in group A, and 24 months in group B All children received monotherapy 80% received carbamazepine, 18% received dilantin Formulations, dosage, group-wise distribution not stated
Outcomes	Seizure recurrence during and after drug withdrawal Association of seizure recurrence with clinical variables (type and frequency of seizures) Association of seizure recurrence with CT and EEG abnormalities
Notes	

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random sequence tables used for randomisation Demographic variables of children in both groups comparable Type and frequency of seizures, AEDs given, EEG and CT scan observations detailed and comparable

Singhi 2003 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded to the intervention. Hence, we assume here that they were also not blinded to short- or long-duration treatment arms.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Withdrawals and reasons not stated
Selective reporting (reporting bias)	Low risk	Study protocol not available; all expected outcomes suitably detailed in the results section
Other bias	High risk	Dosage of AEDs given not stated

Thussu 2002

Study characteristics	
Methods	Randomised clinical trial Single centre in India Duration of trial 1.5 to 3 years in two groups
Participants	People with seizures and CT scan suggestive of NCC Age range: 4 to 52 years, mean ages in group A 19.5 ± 8.79 years and in B 25.6 ± 12.5 years; 53% of patients were males Total: 73 people, 47 in group A treated with AEDs for 6 months, 26 in group B treated for 24 months Follow-up: every 2 months for 12 months after withdrawal of drugs Exclusion criteria: people with persistent lesions requiring albendazole therapy
Interventions	AEDs for 6 months in group A, 24 months in group B Group A: 25 received carbamazepine, 22 received phenytoin Group B: 13 each received carbamazepine and phenytoin Exact dosage and formulations not stated. Stated to have received: "therapeutic dosage according to weight".
Outcomes	Seizure recurrence after withdrawal of AED Correlation of seizure recurrence with CT scan findings
Notes	
Risk of bias	

Thussu 2002 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation based on lottery system
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not stated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number of participants excluded or withdrawing from the study not mentioned
Selective reporting (reporting bias)	Unclear risk	Protocol not available. Insufficient information to confirm reporting bias.
Other bias	Unclear risk	Seizure recurrence discussed but timing of recurrence, i.e. during or after AED therapy, not clear

Verma 2006

Study characteristics	
Methods	Randomised clinical trial Single centre in India Duration of trial: 2 to 3.5 years in two groups
Participants	227 people with NCC, 206 randomised Inclusion criteria: people with epilepsy with CT scan criteria of Del Brutto 2001. Only people with complete resolution of lesion at 3- to 6-month CT scan, or presence of calcified residua included Exclusion criteria: persistent lesions on repeat CT scan at 3 to 6 months interval Mean age: 21.8 ± 6.1 years in group A, 19.5 ± 8.8 years in group B Sex distribution in two groups comparable Seizure type, duration at randomisation, and frequency comparable in the two groups Follow-up for a minimum of 18 months after drug withdrawal
Interventions	AEDs for 6 months in Group A and 24 months in Group B 176 people treated with carbamazepine (600 mg/day to 1000 mg/day) 51 people treated with phenytoin (300 mg/day to 400 mg/day)

Verma 2006 *(Continued)*

Outcomes	Seizure recurrence during and after withdrawal of AED Severe side effects to AED Correlation of seizure recurrence with CT scan finding in follow-up scans
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Simple random sampling by coin toss method
Allocation concealment (selection bias)	Unclear risk	Authors did not detail the conduct of the coin toss, and whether result of the coin toss was visible to the researchers or participants
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not stated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Number of people lost to follow-up in both groups, and number of people completing study mentioned in table 1
Selective reporting (reporting bias)	Low risk	Study protocol not available, no differences between planned and reported outcomes evident
Other bias	Low risk	Insufficient evidence to suggest risk of bias

AED: antiepileptic drug
CT: computed tomography
EEG: electroencephalography
NCC: neurocysticercosis

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

Study	Reason for exclusion
Chang 1998	Case series study of 4 adults with NCC with epilepsy. Tiagabine HCL was used as an add-on drug (2 on carbamazepine and 2 on phenytoin).
Kaushal 2006	Comparison of clobazam with phenytoin sodium for prevention of seizures in people with single NCC. This was an underpowered study, which was prematurely terminated due to relocation of one of the authors. The reason for the difference in numbers between the two comparison groups was not clear. It was not clear whether the two groups were balanced as far as the prognostic variables were concerned. The number of participants randomised to phenytoin and clobazam differ in the text and in the CONSORT flow chart. The study planned to enrol 135 participants in each of the two groups, in order to provide sufficient power to detect 10% difference in the primary outcome mea-

Study	Reason for exclusion
	sure with 90% confidence. However, the numbers accrued fell short, on account of premature termination of the study.
Lanchote 2002	The objective of this study was to determine the interaction between the AEDs and the selective metabolism of albendazole. In this study, plasma concentrations of albendazole sulfoxide (ASOX) and albendazole sulphone (ASON) metabolites were measured in 32 adults who received phenytoin, carbamazepine, phenobarbital, or no AED. None of the primary or secondary outcome measures in this review were assessed.
Santhosh 2021	This open label, randomised study in India compared carbamazepine against levetiracetam as a monotherapy for the secondary prevention of seizures in people with neurocysticercosis. They enrolled 99 drug naive individuals over the age of 14, with radiologically identified neurocysticercosis of varying types, who had presented with a seizure. Participants were randomly allocated to receive either carbamazepine or levetiracetam. The primary outcome measure was seizure control over six months; the secondary outcome measures were drug-related side effects, and need for change of the drug. They found a non-statistically significant trend towards greater seizure control with carbamazepine compared to levetiracetam, but a worse side-effect profile with carbamazepine, which was statistically significant. However, a caveat to the seizure control fining is that a larger proportion of the carbamazepine treated arm received albendazole treatment (carbamazepine: 33/49; levetiracetam: 24/50; P = 0.07); they had a greater proportion of completely resolved lesions (carbamazepine: 41/49; levetiracetam: 32/50; P = 0.08), and were significantly younger (mean (± SD) age: carbamazepine: 22.51 ± 8.9 years; levetiracetam: 27.56 ± 10.7 years; P = 0.01). Despite this, the study was well designed, well documented, with good applicability due to the demographic and neurocysticercosis variety included. However, the follow-up in this study for all participants was only six months, which did not fulfil the secondary outcome measure of this review. Authors contacted to obtain further data, but we have not received a reply.

AED: antiepileptic drug
HCL: hydrochloride
NCC: neurocysticercosis

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

CTRI/2019/01/017368

Study name	A study comparing levetiracetam and valproic acid in preventing seizure in children diagnosed with neurocysticercosis
Methods	Randomised, parallel-group, active controlled trial
Participants	All children diagnosed with neurocysticercosis aged 5 to 18 years, presenting with focal seizure/GTCS episode
Interventions	1. levetiracetam at 30 mg/kg 2. sodium valproate at 20 mg/kg
Outcomes	Primary: proportion of children with seizure recurrence at 3 months after starting treatment with study drug Secondary: Proportion of children who are seizure free for 6 months

CTRI/2019/01/017368 *(Continued)*

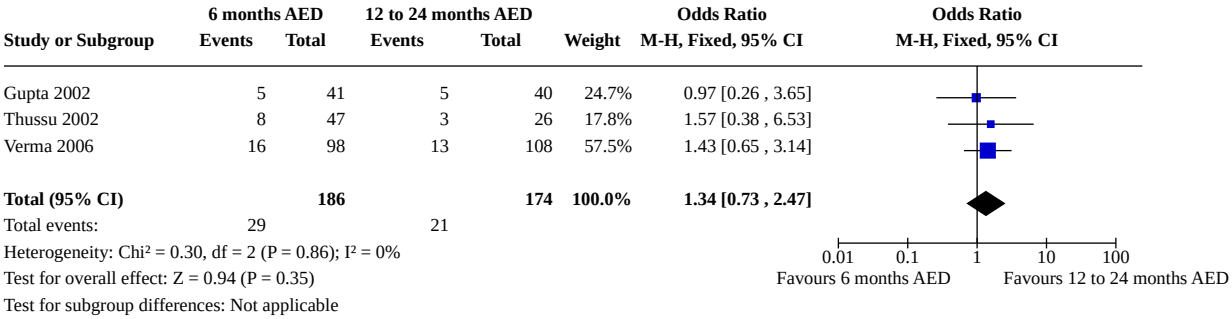
Starting date	31 January 2019
Contact information	C. Nanda
Notes	Authors contacted: study not yet completed

DATA AND ANALYSES

Comparison 1. 6 months AED treatment versus 12 to 24 months AED treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Seizure recurrence	3	360	Odds Ratio (M-H, Fixed, 95% CI)	1.34 [0.73, 2.47]

Analysis 1.1. Comparison 1: 6 months AED treatment versus 12 to 24 months AED treatment, Outcome 1: Seizure recurrence



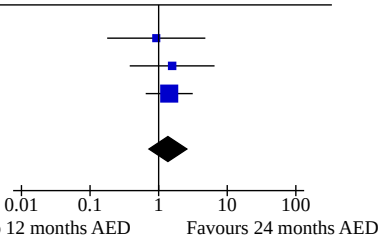
Comparison 2. 6 to 12 months AED treatment versus 24 months AED treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Seizure recurrence	3	385	Odds Ratio (M-H, Fixed, 95% CI)	1.36 [0.72, 2.57]

Analysis 2.1. Comparison 2: 6 to 12 months AED treatment versus 24 months AED treatment, Outcome 1: Seizure recurrence

Study or Subgroup	6 to 12 months AED Events	Total	24 months AED Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Singhi 2003	3	55	3	51	17.8%	0.92 [0.18 , 4.80]
Thussu 2002	8	47	3	26	19.4%	1.57 [0.38 , 6.53]
Verma 2006	16	98	13	108	62.7%	1.43 [0.65 , 3.14]
Total (95% CI)		**200**		**185**	**100.0%**	**1.36 [0.72 , 2.57]**
Total events:	27		19			

Heterogeneity: Chi² = 0.27, df = 2 (P = 0.88); I² = 0%
Test for overall effect: Z = 0.96 (P = 0.34)
Test for subgroup differences: Not applicable



APPENDICES

Appendix 1. CRS Web search strategy

1. MeSH DESCRIPTOR Neurocysticercosis Explode All AND CENTRAL:TARGET

2. neurocysticercosis AND CENTRAL:TARGET

3. MeSH DESCRIPTOR Taenia solium Explode All AND CENTRAL:TARGET

4. "Taenia solium" AND CENTRAL:TARGET

5. tapeworm OR "tape worm" AND CENTRAL:TARGET

6. #1 OR #2 OR #3 OR #4 OR #5 AND CENTRAL:TARGET

7. MeSH DESCRIPTOR Epilepsy Explode All WITH QUALIFIER DT AND CENTRAL:TARGET

8. MESH DESCRIPTOR Seizures EXPLODE ALL WITH QUALIFIER DT AND CENTRAL:TARGET

9. MeSH DESCRIPTOR Anticonvulsants Explode All AND CENTRAL:TARGET

10. (antiepilep* or anti-epilep* or anticonvulsant* or anti-convulsant* or AED or AEDs):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

11. #7 OR #8 OR #9 OR #10 AND CENTRAL:TARGET

12. MeSH DESCRIPTOR Midazolam Explode All AND CENTRAL:TARGET

13. (Dalam OR Dormicum OR Dormire OR Epistatus OR Fulsed OR Garen OR Hypnovel OR Ipnovel OR Midazolam* OR Nocturna OR Setam OR Terap OR Versed):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

14. #12 OR #13 AND CENTRAL:TARGET

15. MeSH DESCRIPTOR Methazolamide Explode All AND CENTRAL:TARGET

16. (Methazolamid* OR Methylacetazolamide OR Neptazane):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

17. #15 OR #16 AND CENTRAL:TARGET

18. MeSH DESCRIPTOR Propofol Explode All AND CENTRAL:TARGET

19. (Anepol OR Diprivan OR Disoprivan OR Disoprofol OR Fresofol OR Hypro OR Lipuro OR Plofed OR Profol OR Propofil OR Propofol* OR Propolipid OR Propovan OR Propoven OR Provive OR Recofol):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

20. #18 OR #19 AND CENTRAL:TARGET

21. MeSH DESCRIPTOR Temazepam Explode All AND CENTRAL:TARGET

22. (Dasuen OR Euhypnos OR Hydroxydiazepam OR Levanxol OR Methyloxazepam OR Nocturne OR Norkotral OR Normison OR Normitab OR Nortem OR Oxydiazepam OR Planum OR Pronervon OR Remestan OR Restoril OR Signopam OR Temaze OR Temazep* OR Temtabs OR Tenox):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

23. #21 OR #22 AND CENTRAL:TARGET

24. MeSH DESCRIPTOR Thiopental Explode All AND CENTRAL:TARGET

25. (Bomathal OR Farmotal OR Nesdonal OR Penthiobarbit* OR Pentothal OR Sodipental OR Thiomebumal OR Thionembutal OR Thiopent* OR Tiobarbital OR Tiopental* OR Trapanal):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

26. #24 OR #25 AND CENTRAL:TARGET

27. #11 OR #14 OR #17 OR #20 OR #23 OR #26 AND CENTRAL:TARGET

28. (Acemit OR Acetamide OR Acetazolamid* OR Avva OR Azm OR Azol OR Diacarb OR Diamox OR Diazomid OR Diluran OR Edemox OR Glaupax):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

29. (Barbexaclon*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

30. (Beclamid* OR Chloracon OR Hibicon OR Posedrine OR Nydrane OR Seclar):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

31. (Brivaracetam*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

32. (Bromide*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

33. (Carbamazepin* OR Carbamazepen* OR Carbamezepin* OR CBZ OR SPD417 OR "Apo-Carbamazepine" OR Atretol OR Biston OR Calepsin OR Carbagen OR Carbatrol OR Carbazepin* OR Carbelan OR Epitol OR Equetro OR Finlepsin OR Karbamazepin OR Lexin OR Neurotop OR "Novo-Carbamaz" OR "Nu-Carbamazepine" OR Sirtal OR Stazepin* OR "Taro-Carbamazepine" OR Tegretal OR Tegretol OR Telesmin OR Teril OR Timonil):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

34. (Carisbamat* OR Comfyde OR "RWJ-333369" OR "YKP 509"):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

35. (Cenobamat* OR Xcopri OR YKP3089):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

36. (Chlormethiazol* OR Distraneurin):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

37. (Aedon OR Anxirloc OR Castilium OR Chlorepin OR Clarmyl OR Clobam OR Clobamax OR Clobator OR Clobazam* OR Clofritis OR Clopax OR Clorepin OR Frisium OR Grifoclobam OR Karidium OR Lucium OR Mystan OR Noiafren OR Onfi OR Sederlona OR Sentil OR Urbadan OR Urbanil OR Urbanol OR Urbanyl):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

38. (Antelepsin OR Antilepsin OR Chlonazepam OR Cloazepam OR Clonazepam* OR Clonex OR Clonopin OR Iktorivil OR Klonopin OR Kriadex OR Landsen OR Paxam OR Petril OR Ravotril OR Rivatril OR Rivotril OR “ro 5-4023” OR “ro 54023”):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

39. (Calner OR Clorazepat* OR Justum OR Mendon OR "Novo-Clopate" OR Tranxene OR Tranxilium):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

40. (Diapam OR Diastat OR Diazemuls OR Diazepam* OR Nervium OR Relanium OR Valium):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

41. (Dimethadion* OR Dimethyloxazolidinedione):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

42. (Divalproex* OR Divalprax OR Ergenyl OR Valance OR Valcote OR Zalkote):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

43. (Eslicarbazepin* OR Exalief OR Stedesa OR Zebinix):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

44. (Esilgan OR Estazolam* OR Eurodin OR Nuctalon OR Prosom OR Tasedan):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

45. (Ethadion*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

46. (Aethosuximid* OR Emeside OR Ethosucci* OR Ethosuxide OR Ethosuximid* OR Etosuximid* OR Zarontin):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

47. (Ethotoin* OR Peganone):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

48. (Felbamat* OR Felbatol OR Felbamyl OR Taloxa):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

49. (Flunarizin* OR Sibelium):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

50. (Cerebyx OR Fosphenytoin* OR Prodilantin):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

51. (Gabapentin* OR Aclonium OR Fanatrex OR Gabapetin OR Gabarone OR GBP OR Gralise OR Neogab OR Neurontin OR "Novo-Gabapentin" OR Nupentin):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

52. ("CCD-1042" OR Ganaxolon*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

53. (Erlosamide OR Harkoseride OR Lacosamid* OR Vimpat):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

54. (Lamotrigin* OR Elmendos OR Epilepax OR "GW 273293" OR Lamictal OR Lamictin OR Lamitor OR Lamitrin OR Lamogine OR Lamotrine OR LTG):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

55. (Levetiracetam* OR Keppra OR LEV OR Levitiracetam):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

56. (Ativan OR Intensl OR Loraz OR Lorazepam* OR Lormetazepam* OR Temesta):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

57. (Losigamon*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

58. ("Magnesium sulfat*" OR "Magnesium sulphat*"):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

59. (Medazepam* OR Nobrium OR Rudotel OR Rusedal):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

60. (Mephenytoin* OR Mesantoin):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

61. (Dapaz OR Equanil OR Meprobamat* OR Meprospan OR Miltown OR Tranmep OR Visano):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

62. (Celontin OR Mesuximid* OR Methsuximide OR Petinutin):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

63. (Mephobarbit* OR Mebaral OR Mephyltaletten OR Methylphenobarbit* OR Metilfenobarbital OR Phemiton OR Prominal):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

64. (Erimin OR Nimetazepam*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

65. (Alodorm OR Arem OR Insoma OR Mogadon OR Nitrados OR Nitrazadon OR Nitrazepam* OR Ormodon OR Paxadorm OR Remnos OR Somnite OR Pacisyn):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

66. (Oxcarbazepin* OR Actinium OR Barzepin OR Carbox OR Deprectal OR "GP 47680" OR Lonazet OR OCBZ OR Oxalepsy OR OXC OR Oxcarbamazepine OR Oxetol OR Oxpin OR Oxrate OR Oxtellar OR Oxypine OR Pharozepine OR Prolepsi OR Timox OR Trexapin OR Trileptal OR Trileptin):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

67. (Paraldehyd*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

68. (Paramethadion*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

69. (E2007 OR Fycompa OR Perampanel*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

70. (Phenacemid*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

71. (Ethylphenacemid* OR Pheneturid*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

72. (Adonal OR Aephenal OR Agrypnal OR Amylofene OR Aphenylbarbit OR Aphenyletten OR Barbenyl OR Barbinal OR Barbiphen* OR Barbipil OR Barbita OR Barbivis OR Barbonal OR Barbophen OR Bardorm OR Bartol OR Bialminal OR "Blu-Phen" OR Cabronal OR Calmetten OR Calminal OR Cardenal OR Chinoin OR Codibarbita OR Coronaletta OR Cratecil OR Damoral OR Dezibarbitur OR Dormina OR Dormiral OR Dormital OR Doscalun OR Duneryl OR Ensobarb OR Ensodorm OR Epanal OR Epidorm OR Epilol OR Episedal OR Epsylone OR Eskabarb OR Etilfen OR Euneryl OR Fenbital OR Fenemal OR Fenobarbital OR Fenosed OR Fenylettae OR Gardenal OR Gardepanyl OR Glysoletten OR Haplopan OR Haplos OR Helional OR Hennoletten OR Henotal OR Hypnaletten OR Hypnette OR "Hypno-Tablinetten" OR Hypnogen OR Hypnolone OR Hypnoltol OR Hysteps OR Lefebar OR Leonal OR Lephebar OR Lepinal OR Lepinaletten OR Linasen OR Liquital OR Lixophen OR Lubergal OR Lubrokal OR Lumen OR Lumesettes OR Lumesyn OR Luminal OR Lumofridetten OR Luphenil OR Luramin OR Molinal OR Neurobarb OR Nirvonal OR Noptil OR "Nova-Pheno" OR Nunol OR Parkotal OR PB OR Pharmetten OR "Phen-Bar" OR Phenaemal OR Phenemal* OR Phenobal OR Phenobarbit* OR Phenobarbyl OR Phenoluric OR Phenolurio OR Phenomet OR Phenonyl OR Phenoturic OR Phenylethylbarbit* OR Phenylethylmalonylurea OR Phenyletten OR Phenyral OR Phob OR Polcominal OR Prominal OR Promptonal OR "Seda-Tablinen" OR Sedabar OR Sedicat OR Sedizorin OR Sedlyn OR Sedofen OR Sedonal OR Sedonettes OR Sevenal OR Sinoratox OR Solfoton OR "Solu-Barb" OR Sombutol OR Somnolens OR Somnoletten OR Somnosan OR Somonal OR Spasepilin OR Starifen OR Starilettae OR Stental OR Talpheno OR Teolaxin OR Teoloxin OR Thenobarbital OR Theoloxin OR Triabarb OR Tridezibarbitur OR Triphenatol OR Versomnal OR Zadoletten OR Zadonal):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

73. (Phensuximid*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

74. (Aleviatin OR Antisacer OR Auranile OR Causoin OR Citrullamon OR Citrulliamon OR Comital OR Comitoina OR Convul OR Danten OR Dantinal OR Dantoin* OR Denyl OR "Di-Hydan" OR "Di-Lan" OR "Di-Phetine" OR Didan OR Difenilhidantoin* OR Difenin OR Difetoin OR Difhydan OR Dihycon OR Dihydantoin OR Dilabid OR Dilantin* OR Dillantin OR Dintoin* OR Diphantoin OR Diphedal OR Diphedan OR Diphenat OR Diphenin* OR Diphentoin OR Diphentyn OR Diphenylan OR Diphenylhydantoin* OR Diphenylhydatanoin OR Ditoinate OR Ekko OR Elepsindon OR Enkelfel OR Epamin OR Epanutin OR Epasmir OR Epdantoin* OR Epelin OR Epifenyl OR Epihydan OR Epilan OR Epilantin OR Epinat OR Epised OR Eptal OR Eptoin OR Fenantoin OR Fenidantoin OR Fenitoin* OR Fentoin OR Fenylepsin OR Fenytoin* OR "Gerot-epilan-D" OR Hidan OR Hidant* OR Hindatal OR Hydant* OR Ictalis OR Idantoi* OR Iphenylhydantoin OR Kessodanten OR Labopal OR Lehydan OR Lepitoin OR Lepsin OR Mesantoin OR Minetoin OR "Neos-Hidantoina" OR Neosidantoina OR Novantoina OR Novophenytoin OR "Om-hidantoina" OR "Om-Hydantoine" OR Oxylan OR Phanantin* OR Phenatine OR Phenatoine OR Phenhydan* OR Phenitoin OR Phentoin OR Phentytoin OR Phenytek OR Phenytex OR Phenytoin* OR PHT OR Ritmenal OR Saceril OR Sanepil OR Silantin OR Sinergina OR Sodanthon OR Sodanto* OR Solantin OR Solantoin OR Solantyl OR Sylantoic OR Tacosal OR Thilophenyl OR TOIN OR Zentronal OR Zentropil):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

75. (Lyrica OR Pregabalin*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

76. (Mysoline OR Primidon* OR Sertan):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

77. (Gabrene OR Garene OR Halogabide OR Halogenide OR Progabid*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

78. (Ecovia OR Remacemid*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

79. ("D-23129" OR "D23129" OR EZG OR Ezogabin* OR Retigabin* OR RTG OR Trobalt OR Potiga):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

80. (Rilutek OR Riluzol* OR Trifluoromethoxybenzothiazol*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

81. (Inovelon OR Rufinamid* OR Xilep):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

82. (Seletracetam*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

83. (Diacomit OR Stiripentol*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

84. (Sulthiam* OR Sultiam* OR Ospolot):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

85. (Talampanel*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

86. (Tiagabin* OR Gabitril):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

87. (Tiletamin*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

88. (Topiramat* OR Qudexy OR Tipiramate OR Topamax OR "Topiramic acid" OR TPM):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

89. (Tridione OR Trimethadion*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

90. (Valnoctamid*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

91. (Avugane OR Baceca OR Convulex OR Delepsine OR Depacon OR Depakene OR Depakine OR Depakote OR Deproic OR DPA OR Encorate OR Epiject OR Epilex OR Epilim OR Episenta OR Epival OR Ergenyl OR Mylproin OR Orfiril OR Orlept OR Selenica OR Stavzor OR Valcote OR Valparin OR Valpro* OR VPA):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

92. (Depamide OR Valpromid*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

93. (GVG OR Sabril OR Vigabatrin*):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

94. (Zonisamid* OR Exceglan OR Excegram OR Excegran OR ZNS OR Zonegran):AB,KW,KY,MC,MH,TI AND CENTRAL:TARGET

95. #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89 OR #90 OR #91 OR #92 OR #93 OR #94

96. #6 AND #95

Appendix 2. MEDLINE search strategy

This strategy includes a modification of the Cochrane Highly Sensitive Search Strategy for identifying randomised trials (Lefebvre 2021).

1. exp NEUROCYSTICERCOSIS/

2. neurocysticercosis.tw.

3. Taenia solium.tw.

4. exp Taenia solium/

5. (tape worm or tapeworm).tw.

6. 1 or 2 or 3 or 4 or 5

7. exp *Epilepsy/dt [Drug Therapy]

8. exp Seizures/dt [Drug Therapy]

9. exp Anticonvulsants/

10. (antiepilep$ or anti-epilep$ or anticonvulsant$ or anti-convulsant$ or AED or AEDs).tw.

11. exp Midazolam/

12. (Dalam or Dormicum or Dormire or Epistatus or Fulsed or Garen or Hypnovel or Ipnovel or Midazolam* or Nocturna or Setam or Terap or Versed).tw.

13. exp Methazolamide/

14. (Methazolamid* or Methylacetazolamide or Neptazane).tw.

15. exp Propofol/

16. (Anepol or Diprivan or Disoprivan or Disoprofol or Fresofol or Hypro or Lipuro or Plofed or Profol or Propofil or Propofol* or Propolipid or Propovan or Propoven or Provive or Recofol).tw.

17. exp Temazepam/

18. (Dasuen or Euhypnos or Hydroxydiazepam or Levanxol or Methyloxazepam or Nocturne or Norkotral or Normison or Normitab or Nortem or Oxydiazepam or Planum or Pronervon or Remestan or Restoril or Signopam or Temaze or Temazep* or Temtabs or Tenox).tw.

19. exp Thiopental/

20. (Bomathal or Farmotal or Nesdonal or Penthiobarbit* or Pentothal or Sodipental or Thiomebumal or Thionembutal or Thiopent* or Tiobarbital or Tiopental* or Trapanal).tw.

21. (Acemit or Acetamide or Acetazolamid* or Avva or Azm or Azol or Diacarb or Diamox or Diazomid or Diluran or Edemox or Glaupax).tw.

22. Barbexaclon*.tw.

23. (Beclamid* or Chloracon or Hibicon or Posedrine or Nydrane or Seclar).tw.

24. Brivaracetam*.tw.

25. Bromide*.tw.

26. (Carbamazepin* or Carbamazepen* or Carbamezepin* or CBZ or SPD417 or "Apo-Carbamazepine" or Atretol or Biston or Calepsin or Carbagen or Carbatrol or Carbazepin* or Carbelan or Epitol or Equetro or Finlepsin or Karbamazepin or Lexin or Neurotop or "Novo-Carbamaz" or "Nu-Carbamazepine" or Sirtal or Stazepin* or "Taro-Carbamazepine" or Tegretal or Tegretol or Telesmin or Teril or Timonil).tw.

27. (Carisbamat* or Comfyde or "RWJ-333369" or "YKP 509").tw.

28. (cenobamat* or Xcopri or YKP3089).tw.

29. (Chlormethiazol* or Distraneurin).tw.

30. (Aedon or Anxirloc or Castilium or Chlorepin or Clarmyl or Clobam or Clobamax or Clobator or Clobazam* or Clofritis or Clopax or Clorepin or Frisium or Grifoclobam or Karidium or Lucium or Mystan or Noiafren or Onfi or Sederlona or Sentil or Urbadan or Urbanil or Urbanol or Urbanyl).tw.

31. (Antelepsin or Antilepsin or Chlonazepam or Cloazepam or Clonazepam* or Clonex or Clonopin or Iktorivil or Klonopin or Kriadex or Landsen or Paxam or Petril or Ravotril or Rivatril or Rivotril or "ro 5-4023" or "ro 54023").tw.

32. (Calner or Clorazepat* or Justum or Mendon or "Novo-Clopate" or Tranxene or Tranxilium).tw.

33. (Diapam or Diastat or Diazemuls or Diazepam* or Nervium or Relanium or Valium).tw.

34. (Dimethadion* or Dimethyloxazolidinedione).tw.

35. (Divalproex* or Divalprax or Ergenyl or Valance or Valcote or Zalkote).tw.

36. (Eslicarbazepin* or Exalief or Stedesa or Zebinix).tw.

37. (Esilgan or Estazolam* or Eurodin or Nuctalon or Prosom or Tasedan).tw.

38. Ethadion*.tw.

39. (Aethosuximid* or Emeside or Ethosucci* or Ethosuxide or Ethosuximid* or Etosuximid* or Zarontin).tw.

40. (Ethotoin* or Peganone).tw.

41. (Felbamat* or Felbatol or Felbamyl or Taloxa).tw.

42. (Flunarizin* or Sibelium).tw.

43. (Cerebyx or Fosphenytoin* or Prodilantin).tw.

44. (Gabapentin* or Aclonium or Fanatrex or Gabapetin or Gabarone or GBP or Gralise or Neogab or Neurontin or "Novo-Gabapentin" or Nupentin).tw.

45. ("CCD-1042" or Ganaxolon*).tw.

46. (Erlosamide or Harkoseride or Lacosamid* or Vimpat).tw.

47. (Lamotrigin* or Elmendos or Epilepax or "GW 273293" or Lamictal or Lamictin or Lamitor or Lamitrin or Lamogine or Lamotrine or LTG).tw.

48. (Levetiracetam* or Keppra or LEV or Levitiracetam).tw.

49. (Ativan or Intensl or Loraz or Lorazepam* or Lormetazepam* or Temesta).tw.

50. Losigamon*.tw.

51. ("Magnesium sulfat*" or "Magnesium sulphat*").tw.

52. (Medazepam* or Nobrium or Rudotel or Rusedal).tw.

53. (Mephenytoin* or Mesantoin).tw.

54. (Dapaz or Equanil or Meprobamat* or Meprospan or Miltown or Tranmep or Visano).tw.

55. (Celontin or Mesuximid* or Methsuximide or Petinutin).tw.

56. (Mephobarbit* or Mebaral or Mephyltaletten or Methylphenobarbit* or Metilfenobarbital or Phemiton or Prominal).tw.

57. (Erimin or Nimetazepam*).tw.

58. (Alodorm or Arem or Insoma or Mogadon or Nitrados or Nitrazadon or Nitrazepam* or Ormodon or Paxadorm or Remnos or Somnite or Pacisyn).tw.

59. (Oxcarbazepin* or Actinium or Barzepin or Carbox or Deprectal or "GP 47680" or Lonazet or OCBZ or Oxalepsy or OXC or Oxcarbamazepine or Oxetol or Oxpin or Oxrate or Oxtellar or Oxypine or Pharozepine or Prolepsi or Timox or Trexapin or Trileptal or Trileptin).tw.

60. Paraldehyd*.tw.

61. Paramethadion*.tw.

62. (E2007 or Fycompa or Perampanel*).tw.

63. Phenacemid*.tw.

64. (Ethylphenacemid* or Pheneturid*).tw.

65. (Adonal or Aephenal or Agrypnal or Amylofene or Aphenylbarbit or Aphenyletten or Barbenyl or Barbinal or Barbiphen* or Barbipil or Barbita or Barbivis or Barbonal or Barbophen or Bardorm or Bartol or Bialminal or "Blu-Phen" or Cabronal or Calmetten or Calminal or Cardenal or Chinoin or Codibarbita or Coronaletta or Cratecil or Damoral or Dezibarbitur or Dormina or Dormiral or Dormital or Doscalun or Duneryl or Ensobarb or Ensodorm or Epanal or Epidorm or Epilol or Episedal or Epsylone or Eskabarb or Etilfen or Euneryl or Fenbital or Fenemal or Fenobarbital or Fenosed or Fenylettae or Gardenal or Gardepanyl or Glysoletten or Haplopan or Haplos or Helional or Hennoletten or Henotal or Hypnaletten or Hypnette or "Hypno-Tablinetten" or Hypnogen or Hypnolone or Hypnoltol or Hysteps or Lefebar or Leonal or Lephebar or Lepinal or Lepinaletten or Linasen or Liquital or Lixophen or Lubergal or Lubrokal or Lumen or Lumesettes or Lumesyn or Luminal or Lumofridetten or Luphenil or Luramin or Molinal or Neurobarb or Nirvonal or Noptil or "Nova-Pheno" or Nunol or Parkotal or PB or Pharmetten or "Phen-Bar" or Phenaemal or Phenemal* or Phenobal or Phenobarbit* or Phenobarbyl or Phenoluric or Phenolurio or Phenomet or Phenonyl or Phenoturic or Phenylethylbarbit* or Phenylethylmalonylurea or Phenyletten or Phenyral or Phob or Polcominal or Prominal or Promptonal or "Seda-Tablinen" or Sedabar or Sedicat or Sedizorin or Sedlyn or Sedofen or Sedonal or Sedonettes or Sevenal or Sinoratox or Solfoton or "Solu-Barb" or Sombutol or Somnolens or Somnoletten or Somnosan or Somonal or Spasepilin or Starifen or Starilettae or Stental or Talpheno or Teolaxin or Teoloxin or Thenobarbital or Theoloxin or Triabarb or Tridezibarbitur or Triphenatol or Versomnal or Zadoletten or Zadonal).tw.

66. Phensuximid*.tw.

67. (Aleviatin or Antisacer or Auranile or Causoin or Citrullamon or Citrulliamon or Comital or Comitoina or Convul or Danten or Dantinal or Dantoin* or Denyl or "Di-Hydan" or "Di-Lan" or "Di-Phetine" or Didan or Difenilhidantoin* or Difenin or Difetoin or Difhydan or Dihycon or Dihydantoin or Dilabid or Dilantin* or Dillantin or Dintoin* or Diphantoin or Diphedal or Diphedan or Diphenat or Diphenin* or Diphentoin or Diphentyn or Diphenylan or Diphenylhydantoin* or Diphenylhydatanoin or Ditoinate or Ekko or Elepsindon or Enkelfel or Epamin or Epanutin or Epasmir or Epdantoin* or Epelin or Epifenyl or Epihydan or Epilan or Epilantin or Epinat or Epised or Eptal or Eptoin or Fenantoin or Fenidantoin or Fenitoin* or Fentoin or Fenylepsin or Fenytoin* or "Gerot-epilan-D" or Hidan or Hidant* or Hindatal or Hydant* or Ictalis or Idantoi* or Iphenylhydantoin or Kessodanten or Labopal or Lehydan or Lepitoin or Lepsin or Mesantoin or Minetoin or "Neos-Hidantoina" or Neosidantoina or Novantoina or Novophenytoin or "Om-hidantoina" or "Om-Hydantoine" or Oxylan or Phanantin* or Phenatine or Phenatoine or Phenhydan* or Phenitoin or Phentoin or Phentytoin or Phenytek or Phenytex or Phenytoin* or PHT or Ritmenal or Saceril or Sanepil or Silantin or Sinergina or Sodanthon or Sodanto* or Solantin or Solantoin or Solantyl or Sylantoic or Tacosal or Thilophenyl or TOIN or Zentronal or Zentropil).tw.

68. (Lyrica or Pregabalin*).tw.

69. (Mysoline or Primidon* or Sertan).tw.

70. (Gabrene or Garene or Halogabide or Halogenide or Progabid*).tw.

71. (Ecovia or Remacemid*).tw.

72. ("D-23129" or "D23129" or EZG or Ezogabin* or Retigabin* or RTG or Trobalt or Potiga).tw.

73. (Rilutek or Riluzol* or Trifluoromethoxybenzothiazol*).tw.

74. (Inovelon or Rufinamid* or Xilep).tw.

75. Seletracetam*.tw.

76. (Diacomit or Stiripentol*).tw.

77. (Sulthiam* or Sultiam* or Ospolot).tw.

78. Talampanel*.tw.

79. (Tiagabin* or Gabitril).tw.

80. Tiletamin*.tw.

81. (Topiramat* or Qudexy or Tipiramate or Topamax or "Topiramic acid" or TPM).tw.

82. (Tridione or Trimethadion*).tw.

83. Valnoctamid*.tw.

84. (Avugane or Baceca or Convulex or Delepsine or Depacon or Depakene or Depakine or Depakote or Deproic or DPA or Encorate or Epiject or Epilex or Epilim or Episenta or Epival or Ergenyl or Mylproin or Orfiril or Orlept or Selenica or Stavzor or Valcote or Valparin or Valpro* or VPA).tw.

85. (Depamide or Valpromid*).tw.

86. (GVG or Sabril or Vigabatrin*).tw.

87. (Zonisamid* or Exceglan or Excegram or Excegran or ZNS or Zonegran).tw.

88. or/7-87

89. exp controlled clinical trial/ or (randomi?ed or placebo or randomly).ab.

90. clinical trials as topic.sh.

91. trial.ti.

92. 89 or 90 or 91

93. exp animals/ not humans.sh.

94. 92 not 93

95. 6 and 88 and 94

96. remove duplicates from 95

Appendix 3. LILACS search strategy

(anticonvulsant OR mh:("anticonvulsants")) AND (mh:("NEUROCYSTICERCOSIS" OR "TAENIA") OR neurocysticercosis OR taenia OR (tape AND worm) OR tapeworm)

WHAT'S NEW

Date	Event	Description
14 January 2021	New citation required but conclusions have not changed	Conclusions are unchanged.
14 January 2021	New search has been performed	Searches updated 14 January 2021; no new trials identified.

HISTORY

Protocol first published: Issue 3, 2011
Review first published: Issue 10, 2015

Date	Event	Description
8 July 2019	New citation required but conclusions have not changed	Conclusions are unchanged.
8 July 2019	New search has been performed	Searches updated 8 July 2019; no new trials identified.

CONTRIBUTIONS OF AUTHORS

MS independently screened all 180 citations and abstracts, and evaluated the eligibility of the studies for the 2019 review.
MF and BDM independently screened 48 identified citations and abstracts, and evaluated the eligibility of the studies for the review.

MS and AM independently extracted data, using a tailored data extraction form.
TS supervised data extraction, and resolved any discrepancies between MS and AM, if needed.
MS prepared the first draft of the review.
TS reviewed the final draft.

For the 2021 review update, both DW and BDM screened all newly identified citations and abstracts, and evaluated the eligibility of these studies for the review. DW, HC, CC and GKW prepared the final draft of the review, with direct critical input throughout from BDM.

DECLARATIONS OF INTEREST

DW: none known
HC: none known
CC: none known
GKW: none known
MS: none known
TS: none known
AM: none known
BDM: none known

SOURCES OF SUPPORT

Internal sources

- No sources of support provided

External sources

- National Institute of Health Research, UK

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In the protocol, we planned to analyse seizure control with AEDs over a specified period of time. We had also planned to look at studies comparing duration of treatment with respect to seizure control. A subgroup analysis between participants with single versus multiple cerebral lesions and monotherapy versus polytherapy was planned.

In the 2019 review, we were restricted to comparing short-duration versus long-duration therapy according to the studies identified and included in the review. All the included studies were carried out on people with single cerebral lesions, and all patients received monotherapy. Therefore, the intended subgroup analysis was not possible.

In the protocol, we had mentioned that we would exclude studies comparing two AEDs. However, we decided to include such studies after this oversight was pointed out during the review process. This was essential to answer our primary question of 'which AED is better for seizure control?'. Furthermore, we have limited our inclusion to studies with at least 12 months of follow-up data.

In the protocol, we intended to look at the effect of drugs in seizure control in a population with neurocysticercosis, and therefore, planned to calculate the risk ratio (RR). As we were only able to find studies that compared short-duration versus long-duration AED treatment, we calculated the odds ratio (OR) to look at the odds of seizure recurrence in long-duration of AED treatment against short-duration of treatment.

As far as the search methods, data collection, and analysis are concerned, we were able to proceed as per the protocol design.

INDEX TERMS

Medical Subject Headings (MeSH)

*Anticonvulsants [therapeutic use]; *Neurocysticercosis [complications] [drug therapy]; Quality of Life; Randomized Controlled Trials as Topic; Seizures [drug therapy] [prevention & control]; Single-Blind Method

MeSH check words

Humans