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Anthelmintics for people with neurocysticercosis (Review)

Abba K, Ramaratnam S, Ranganathan LN

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[Intervention Review]

Anthelmintics for people with neurocysticercosis

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ABSTRACT

Background

Neurocysticercosis is an infection of the brain by the larval stage of the pork tapeworm. In endemic areas it is a common cause of epilepsy. Anthelmintics (albendazole or praziquantel) may be given to kill the parasites. However, there are potential adverse effects, and the parasites may eventually die without treatment.

Objectives

To assess the effectiveness and safety of anthelmintics for people with neurocysticercosis.

Search methods

In May 2009 we searched the Cochrane Infectious Diseases Group Specialized Register, CENTRAL (*The Cochrane Library* 2009, Issue 2), MEDLINE, EMBASE, LILACS, and the *m*RCT.

Selection criteria

Randomized controlled trials comparing anthelmintics with placebo, no anthelmintic, or other anthelmintic regimen for people with neurocysticercosis.

Data collection and analysis

Two authors independently selected trials, extracted data, and assessed each trial's risk of bias. We calculated risk ratios (RR) for dichotomous variables, with 95% confidence intervals (CI). We pooled data from trials with similar interventions and outcomes.

Main results

For viable lesions in children, there were no trials. For viable lesions in adults, no difference was detected for albendazole compared with no treatment for recurrence of seizures (116 participants, one trial); but fewer participants with albendazole had lesions at follow up (RR 0.56, 95% CI 0.45 to 0.70; 192 participants, two trials).

For non-viable lesions in children, seizures recurrence was less common with albendazole compared with no treatment (RR 0.49, 95% CI 0.32 to 0.75; 329 participants, four trials). There was no difference detected in the persistence of lesions at follow up (570 participants, six trials). For non-viable lesions in adults, there were no trials.

In trials including viable, non-viable or mixed lesions (in both children and adults), headaches were more common with albendazole alone (RR 9.49, 95% CI 1.40 to 64.45; 106 participants, two trials), but no difference was detected in one trial giving albendazole with corticosteroids (116 participants, one trial).

Authors' conclusions

In patients with viable lesions, evidence from trials of adults suggests albendazole may reduce the number of lesions. In trials of non-viable lesions, seizure recurrence was substantially lower with albendazole, which is counter-intuitive. It may be that steroids influence headache during treatment, but further research is needed to test this.

22 March 2019

Update pending

Authors currently updating

The update is due to be published in 2019.

PLAIN LANGUAGE SUMMARY

Treatment for illness caused by tapeworm larvae in the brain

If people eat eggs from the pork tapeworm (Taenia solium), these eggs can move from the gut and then lodge in different tissues of the body forming cysts. When these cysts form in the brain, this is called neurocysticercosis. Some people may have no symptoms if this happens, but others may suffer from seizures, headaches, or more rarely from confusion, loss of balance or brain swelling. More rarely still, someone may die.

The condition is mainly found where people live in close contact with pigs and where the sanitation is poor. It affects around 50 million people worldwide, and in some areas is the leading cause of adult-onset epilepsy.

The number, size and location of the cysts help to guide treatment of neurocysticercosis, as do the patient's symptoms; for example, giving anticonvulsants to someone with seizures. Two drugs, praziquantel and albendazole, can be used specifically in neurocysticercosis to help kill the parasite; these drugs are known as anthelmintics. Some cysts, called non-viable lesions are generally in the process of degenerating and resolving spontaneously; many experts recommend not treating this type of cyst. However, treating viable lesions (ie those lesions that may or may not resolve spontaneously) with these drugs may help kill the parasite, although treatment remains controversial due to the potential side effects and the fact the parasite may die without treatment.

In this review of 21 relevant randomized controlled trials, most studies examined the effects of albendazole. In patients with viable lesions, there is only evidence available for adult patients; this suggests that albendazole may reduce the number of lesions. In patients with non-viable lesions, there is only evidence available for children; this suggests that seizure recurrence was lower with albendazole, which goes against the opinions of some experts. There is insufficient evidence available to assess praziquantel.

BACKGROUND

Neurocysticercosis is an infection of the central nervous system by the larval stage of the pork tapeworm*Taenia solium.* If eggs (cysticerci) from the faeces of humans infected with the intestinal parasites are ingested, they can migrate from the gut to lodge in various tissues of the body, where they form cysts (cysticercosis). This review is confined to treating neurocysticercosis, where the cysts lodge in the brain.

The cysts naturally evolve, over a period of years, through stages beginning with viable larvae and ending with the death of the parasite and resorption or calcification of the cyst. Individuals may have one or more cysticerci in the brain. The following types of neurocysticercosis have been recognized, depending on where the cysts are lodged: parenchymal; intraventricular; racemose type found in the basal cisterns; and spinal. Symptoms may or may not occur, depending on the number, location, and stage of the cysts, as well as the infected person's immune response. Seizures are the most common symptom, present in most of the presenting cases, followed by headaches. Rarely, it causes confusion, lack of attention to people and surroundings, difficulty with balance, paralysis, swelling of the brain, and very rarely, death. Symptoms may be associated with the host's immune response or due to calcifications left once the cysts have been eliminated (Leite 2000).

The condition is found where people live in close contact with pigs and where sanitation is poor. It is common in much of South and Central America, China, the Indian subcontinent and South-East Asia, and sub-Saharan Africa. It affects around 50 million people worldwide (Kossoff 2005), with men and women equally affected, and has a peak of incidence at the ages of 30 to 40 years (Burneo 2005). In endemic areas, it is the leading cause of adult-onset epilepsy and an important cause of seizures in children (Roman 2000). It has also been estimated to cause at least 50,000 deaths worldwide each year (Roman 2000). It is therefore a significant public health problem, with significant associated costs in health care and lost productivity.

The cysts in the brain can be visualized using CT or MRI scanning. Over the course of the infection, radiological images change from 'non-enhancing' (after intravenous injection of a radiographic contrast), indicating a viable cyst with little host immune response, to 'ring-enhancing' indicating a degenerating cyst with surrounding immune response, to calcification or total resolution (DeGiorgio 2004). Cysts may be located in the parenchyma (brain tissue) or within structures and spaces around the brain (extraparenchymal cysts). Infection burden varies widely; a recently published guideline classified infection burdens from mild (one to five cysts) to moderate (five to 99 cysts) to heavy (more than 100 cysts) (Garcia 2002).

Treatment options depend on the number, size, and location of the cysts, and on the symptoms. Initial symptomatic treatment includes anticonvulsant drugs for seizures and analgesics for headache. Some extraparenchymal cysts are treated with surgery, either to remove the cyst or to relieve intracranial pressure. Where serious inflammation of the brain is present (usually associated with degeneration of the cysts), corticosteroids may be prescribed.

Cysts may degenerate and resolve spontaneously. For this reason, specific anthelmintics are usually considered for people with viable cysts, as the treatment may help kill the parasites. When lesions are non-viable, many experts do not recommend these drugs.

There are two anthelmintics used in neurocysticercosis: praziquantel, available since 1979, and albendazole, available since 1987. If anthelmintics are used, corticosteroids are often prescribed with them to prevent inflammation of the brain caused by the host immune response to the destroyed parasites.

Treatment with anthelmintics remains controversial, due to potential adverse events and the natural history of the parasite, which may eventually die without treatment. The original version of this Cochrane Review found no evidence that the potential benefits of treatment outweigh the potential harms (Salinas 1999). This review was undertaken as a substantive update of the original Cochrane Review to take trials published since 1999 into account. We have stratified patients by age (children and adult) and by whether patients have predominantly viable or non-viable cysts, given the natural history and assumptions about when anthelmintics may or may not be effective.

OBJECTIVES

To assess the effects of anthelmintics for people with neurocysticercosis.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized controlled trials.

Types of participants

People with symptomatic or asymptomatic neurocysticercosis defined by viable or non-viable lesions in the brain, identified as 'non-enhancing' or 'ring-enhancing' on medical imaging..

Types of interventions

Intervention

- Anthelmintics plus usual treatment.
- Anthelmintics plus corticosteroids plus usual treatment.

Control

- Usual treatment only.
- Corticosteroids plus usual treatment.
- Another anthelmintic plus usual treatment.
- Another dose or duration of anthelmintic, plus usual treatment.

We included trials irrespective of the type of anthelmintic used, or the dosage and duration of treatment.

Types of outcome measures

Primary

- Free of seizures for one year after treatment.
- Recurrence of seizures at follow-up.
- Number of seizures during follow-up period.
- Seizure free at follow-up following withdrawal of anticonvulsant drugs.

Secondary

Health status indicators

- All-cause death.
- Hospital admission for any cause.
- Any neurological symptoms or signs (includes headache, paralysis, visual disturbance).
- Need for surgery.
- Resumption of normal activities at follow up; or time to resumption of normal activities.
- Resolution of symptoms.

Radiological changes at follow up

- Persistence of lesions.
- Reduction in number of lesions.
- Reduction in ventricular size.

Adverse events

- Any adverse events.
- Adverse event requiring withdrawal of anthelmintic drugs.

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).

Databases

We searched the following databases using the search terms and strategy described in Appendix 1: the Cochrane Infectious Diseases Group Specialized Register (May 2009); the Cochrane Central Register of Controlled Trials (CENTRAL), published in *The Cochrane Library* (2009, Issue 2); MEDLINE (1966 to May 2009); EMBASE (1988 to May 2009); and LILACS (1982 to May 2009). We also searched the *meta*Register of Controlled Trials (*m*RCT) using the term 'neurocysticercosis' May 2009).

Reference lists

We also checked the reference lists of all trials and review articles identified by the above method.

Data collection and analysis

Selection of studies

Two authors (KA and LR) independently screened all citations and abstracts, using an eligibility form to apply the selection criteria to identify relevant studies. Where there was uncertainty over the eligibility of a particular study, we obtained the full-text article. We resolved any differences in opinion by discussion or, where necessary, by discussion with the third author (SR). We excluded studies that did not meet the criteria, and documented the reasons for exclusion in the table 'Characteristics of excluded studies'.

Data extraction and management

One author (KA) extracted data using a tailored data extraction form, and a second author (LR) checked this extracted data, after which any disagreements were resolved by discussion. We summarized data on study design, participant characteristics, interventions, and outcomes and entered these into Review Manager 5.

Assessment of risk of bias in included studies

Two review authors independently assessed the risk of bias of the included trials using a pro forma. In case of disagreement, we planned to consult a third person. We categorized the generation of the allocation sequence and allocation concealment as adequate, unclear, or inadequate as in Jüni 2001. We assessed whether the participants, care providers and investigators were blinded to which participants received which drug regimen. For all outcomes, we assessed that incomplete outcome data had been adequately addressed if 85% or more of the participants were included in the analysis, or if less than 85% were included but adequate steps were taken to ensure or demonstrate that this did not bias the results. We also examined the trial reports for any evidence of selective reporting of outcomes or any other issues that may bias the results. We reported the results of the assessment in a table.

Assessment of reporting biases

We planned to assess the probability of publication bias by examining the funnel plot for asymmetry, using one of the primary outcomes of seizure recurrence with the largest number of contributing trials. However, there were not enough trials reporting on the same primary outcomes to present a meaningful analysis.

Data synthesis

We analysed the data using Review Manager 5. We calculated risk ratio (RR) for dichotomous data and mean difference (MD) for continuous data. We measured precision using 95% confidence intervals (CI). Where more than one trial included similar participants and interventions, without significant clinical or methodological diversity or statistical heterogeneity, we undertook a meta-analysis using a fixed-effect model. Highly skewed data (where the standard deviation was greater than the mean) were presented in the text. Analyses were based on the number of available participants at each stage of follow up; there was no adjustment for loss to follow up.

We stratified the results by treatment comparison and type of lesion; viable (non-enhancing) or non-viable (enhancing).

Subgroup analysis and investigation of heterogeneity

We assessed heterogeneity between trials by examining the forest plot for overlapping confidence intervals, and using the I^2 statistic for heterogeneity. We investigated potential sources of heterogeneity by performing subgroup analyses by co-medications or treatments used and, where possible, length of follow up. We planned also to investigate potential sources of heterogeneity by performing subgroup analyses for participant age (adults or children), and number of lesions, but there were insufficient trials to enable this.

Sensitivity analysis

Where sufficient trial data were available, we undertook sensitivity analyses by excluding trials without adequate reported allocation concealment.

RESULTS

Description of studies

Eligibility

We included 21 completed trials. (see 'Characteristics of included studies') We excluded nine studies (see reasons in 'Characteristics of excluded studies'). Three studies are classified as awaiting assessment because it was unclear from the reports whether or not they were randomized. We have emailed and written to the authors for more detailed information about the methods.The search also identified one ongoing trial that met the inclusion criteria (see 'Characteristics of ongoing studies').

In detail, the search strategy identified 48 potentially relevant reports of completed studies; of these, 35 initially seemed relevant, and we obtained the full texts. One was in Portuguese (Antoniuk 1991), the others in English. We obtained the help of a Portuguese reader to assess the relevant report for inclusion. Two reports were unclear as to whether the groups were randomly allocated: we attempted to contact the trial authors for clarification but were unsuccessful; these trials are reported as 'awaiting classification'. Following inspection of the reference lists of the included reports, we identified a further two relevant trials for inclusion (Padma 1994; Sotelo 1990), and another report that initially seemed relevant but did not meet the inclusion criteria (Medina 1993).

Trial location and setting

The included trials were conducted in Ecuador (five trials), Mexico (three trials), Peru (two trials), and India (11 trials). All were carried out within hospital settings, with treatment provided on an in-patient basis.

Trial participants

Viable lesions

Six trials included 322 participants (151 males, 148 females, 23 sex not reported) with viable lesions, or a combination of viable and non-viable lesions. Among these, four trials were conducted in adults (274 participants) and two trials included both children and adults (48 participants). Two trials did not specify the number of lesions, one trial included participants with up to three lesions, one trial with up to six lesions, and two trials with less than 20 lesions. All lesions in these studies were located in the parenchyma of the brain. None of the trials mentioned including or excluding people who were HIV positive.

Non-viable lesions

Nine trials included 941 participants (44 males, 321 females and 176 sex not reported) with non-viable lesions only. Among these, seven trials were conducted in children (763 participants) and two included both adults and children (178 participants). Six trials included only participants with single lesions, one trial included those with up to two lesions, one included those with up to three lesions, and one did not specify number of lesions. All lesions in these studies were located in the parenchyma of the brain. None of the trials mentioned including or excluding people who were HIV positive.

Mixed viable and non-viable lesions

Seven trials included 676 participants (392 male, 280 female and four sex not reported) whose type of lesion was unspecified. Among these five trials were conducted in adults (469 participants) and two trials included both adults and children (207 participants). Five trials did not specify the number of lesions in each participant, while two trials included only participants with more than one lesion. Five trials included parenchymal lesions only, while one included only subarachnoid and intraventricular lesions and another included parenchymal, subarachnoid and intraventricular lesions. None of the trials mentioned including or excluding people who were HIV positive.

Interventions

Viable lesions

The comparisons included in the trials included:

- Albendazole versus placebo or no drug (four trials) (Alarcon 1989; Garcia 1997; Alarcon 2001; Garcia 2004).
- Albendazole versus praziquantel (two trials) (Sotelo 1990; Del Brutto 1999).
- Albendazole: longer versus shorter duration of treatment (four trials) (Alarcon 1989; Sotelo 1990; Garcia 1997; Alarcon 2001).
- Praziquantel: same daily dose given for different durations (one trial) (Sotelo 1990).

In addition to anthelmintics, three trials also used corticosteroids; two in all the comparison groups (Garcia 1997; Del Brutto 1999) and one in the treatment groups only (Garcia 2004). Most trials reported providing anticonvulsant drugs for all patients who were having seizures, whichever treatment group they were randomized to.

Non-viable lesions

The comparisons included in the trials included:

- Albendazole versus placebo or no drug (six trials) (Padma 1994; Baranwal 1998; Singhi 2000; Gogia 2003; Kalra 2003; De Souza 2009).
- Albendazole plus praziquantel versus albendazole plus placebo (one trial) (Kaur 2009).
- Albendazole: longer versus shorter duration of treatment (one trial) (Singhi 2003).
- Albendazole with corticosteroids versus albendazole without corticosteroids (one trial) (Singhi 2004).

In addition to anthelmintics, five trials also used corticosteroids; three in the treatment and control groups (Baranwal 1998; Gogia 2003; Kaur 2009), one in the treatment groups only (Kalra 2003), and one in the control group and one of two intervention groups (Singhi 2004). Most trials reported providing anticonvulsant drugs for all patients who were having seizures, whichever treatment group they were randomized to.

Mixed viable and non-viable lesions

The comparisons included in the trials included:

- Albendazole versus placebo or no drug (five trials) (Sotelo 1988; Padma 1995; Garcia 1997; Das 2007; Carpio 2008).
- Praziquantel versus placebo or no drug (one trial) (Sotelo 1988).

- Albendazole versus praziquantel (one trial) (Sotelo 1988).
- Albendazole: longer versus shorter duration of treatment (two trials) (Cruz 1995; Garcia 1997).
- Albendazole: different doses given over a one-day period (one trial) (Gongora-Rivera 2006).

In addition to anthelmintics, five trials also used corticosteroids; three in the treatment and control groups (Garcia 1997; Gongora-Rivera 2006; Carpio 2008), one in the treatment groups only (Das 2007), and one in the control group only (Sotelo 1988). Most trials reported providing anticonvulsant drugs for all patients who were having seizures, whichever treatment group they were randomized to.

One ongoing study is comparing albendazole plus corticosteroid with placebo (Gilman 2007).

Outcomes

Viable lesions

Three of the included trials reported outcomes relating to the presence or severity of seizures at follow up. A further trial reported on the presence or severity of any symptoms. All the trials reported on radiologically visible changes to the numbers or sizes of lesions.

Non-viable lesions

Seven of the included trials reported outcomes relating to the presence or severity of seizures at follow up. All the trials reported on radiologically visible changes to the numbers or sizes of lesions.

Mixed viable and non-viable lesions

Three of the included trials reported outcomes relating to the presence or severity of seizures at follow up. A further two reported on the presence or severity of any symptoms. All the included trials reported on radiologically visible changes to the numbers or sizes of lesions.

There were no trials reporting on freedom from seizures for one year, resumption of normal activities, reduction in ventricular size, or adverse events requiring withdrawal of anthelmintic drugs.

Risk of bias in included studies

Details of the methods used in each trial are available in the table 'Characteristics of included studies'.

Generation of allocation sequence

Viable lesions

Two trials described an adequate method of generating a truly random allocation sequence. Four trials did not report how they generated group allocation sequences (assessed as 'unclear'), but all were described as 'randomized'.

Non-viable lesions

Seven trials described an adequate method of generating a truly random allocation sequence. Two trials did not report how they generated group allocation sequences (assessed as 'unclear'), but all were described as 'randomized'.

Mixed viable and non-viable lesions

Three trials described an adequate method of generating a truly random allocation sequence. Four trials did not report how they generated group allocation sequences (assessed as 'unclear'), but all were described as 'randomized'.

Allocation concealment

Viable lesions

One trial reported an adequate method of ensuring allocation concealment. Five trials did not report enough information to allow allocation concealment to be assessed.

Non-viable lesions

Four trials reported an adequate method of ensuring allocation concealment. Five trials did not report enough information to allow allocation concealment to be assessed.

Mixed viable and non-viable lesions

Two trials reported an adequate method of ensuring allocation concealment. Five trials did not report enough information to allow allocation concealment to be assessed.

Blinding

Viable lesions

Three trials reported blinding of participants, personnel and outcomes assessors for all main outcomes. It was unclear whether blinding was done for the other three trials.

Non-viable lesions

Five trials reported blinding of participants, personnel and outcomes assessors for all main outcomes. It was unclear whether blinding was done for three trials. One trial did not use blinding.

Mixed viable and non-viable lesions

Four trials reported blinding of participants, personnel and outcomes assessors for all main outcomes. It was unclear whether blinding was done for three trials.

Addressing incomplete outcomes data

Viable lesions

Five trials either included 85% or over of the participants in the analysis, or included fewer than 85% of participants, but showed that participants who were not included were similar to those included. One trial did not meet this criteria.

Non-viable lesions

Six trials either included 85% or over of the participants in the analysis, or included fewer than 85% of participants, but showed that participants who were not included were similar to those included. Two trials did not meet this criteria, while in one trial this was unclear.

Mixed viable and non-viable lesions

Seven trials either included 85% or over of the participants in the analysis, or included fewer than 85% of participants, but showed that participants who were not included were similar to those included.

Effects of interventions

1. Albendazole versus placebo or no drug

1.1. Recurrence of seizures

Viable lesions

One small trial with adequate allocation concealment, including adults only, reported on recurrence of seizures by end of follow up, showing no significant effect of albendazole treatment (116 participants, Analysis 1.1).

Non-viable lesions

Four trials reported data on this outcome that could be included within meta-analysis. All four non-viable lesions included only children with one or two lesions. Albendazole showed a significant benefit (relative risk 0.49, 95% confidence interval (CI) 0.32 to 0.75; 329 participants, Analysis 1.1). One of the included trials (Gogia 2003) excluded seizures occurring during the first week of the trial, but is included in the analysis because its exclusion did not change the finding. In a sensitivity analysis, including only the three trials with adequate allocation concealment, this significant benefit remained (RR 0.53, 95% CI 0.31 to 0.88; 125 participants). One additional trial (103 participants, De Souza 2009) reported no significant differences in seizure recurrence between the albendazole and no anthelmintic groups, but did not present data.

Mixed viable and non-viable lesions

One trial, with unclear allocation concealment, reported on this outcome, showing a harmful effect of albendazole (RR 2.36, 95% CI 1.43 to 3.91; 298 participants, one trial, Analysis 1.1). Another trial, with adequate allocation concealment, presented data on the number of participants who remained free of seizures at 12 months, using Kaplan-Meier survival analysis, and found no significant difference between the albendazole and placebo groups (Carpio 2008).

One trial reported on the successful withdrawal of anticonvulsants during a two-year follow-up period (Garcia 2004); there was no significant difference between the albendazole and control groups (116 participants, Analysis 1.2).

1.2. Deaths and hospital admissions

Viable lesions

No trials reported on these outcomes.

Non-viable lesions

No trials reported on these outcomes.

Mixed viable and non-viable lesions

Two trials reported a total of nine deaths (Analysis 1.3). There was no significant difference between albendazole and treatment groups in the number of deaths overall (470 participants, two trials).

One trial (Das 2007) reported on hospital re-admissions after treatment (Analysis 1.4). Participants treated with albendazole had a higher risk of hospital admission during the periods up to three months (RR 2.53, 95% CI 1.54 to 4.17; 298 participants), three to six months (RR 5.07, 95% CI 2.17 to 11.82), and six to 12 months (RR 4.56, 95% CI 1.58 to 13.16). There was no significant difference between the albendazole and control groups during periods one to two years, two to three years, or three to four years.

1.3. Resolution of symptoms

Viable lesions

In one very small trial, fewer participants receiving albendazole had no resolution of symptoms ('symptom' not defined by the trial authors) at three months than in the control group (RR 0.25, 95% CI 0.07 to 0.93; 15 participants, Analysis 1.5).

Non-viable lesions

No trials in non-viable lesions reported on these outcomes.

Mixed viable and non-viable lesions

One trial reported on presence of symptoms of encephalopathy (headache, vomiting, and altered sensorium) during different time periods. The albendazole group had a higher risk of symptoms during the period up to three months (RR 3.04, 95% CI 1.77 to 5.21; 298 participants, Analysis 1.6), but there was no significant difference between the groups during other periods of time up to four years.

1.4. Persistence of radiological lesions

For the purposes of this review, persistence of lesions relates to the presence of cysts or lesions in any form, including calcified or nodular lesions.

Viable lesions

In trials including only adults with viable lesions, participants treated with albendazole compared with no anthelmintic had a lower risk of persistence of lesions at follow up (RR 0.56, 95% CI 0.45 to 0.70; 114 participants, two trials, Analysis 1.7)

Non-viable lesions

In trials including mainly children with non-viable lesions (one trial also included adults), there was no difference between the albendazole and no anthelmintic groups in persistence of lesions at follow up (570 participants, six trials, Analysis 1.7). A trial in adults and children (103 participants, De Souza 2009) reported no significant difference in cyst disappearance between the albendazole and no anthelmintic groups but did not present the data.

Mixed viable and non-viable lesions

In one trial including adults with both viable and non-viable lesions, there was no difference between the albendazole and no anthelmintic groups in persistence of lesions at follow up (298 participants, Analysis 1.7).

1.5. Adverse events during treatment

All types of lesion

There were no significant differences detected between the albendazole and no anthelmintic groups in the numbers of participants with headache during treatment in trials with viable lesions only (139 participants, two trials, Analysis 1.8), non-viable lesions only (83 participants, one trial, Analysis 1.8), or mixed viable and non-viable lesions (170 participants, one trial, Analysis 1.8). Overall, headache during treatment was more frequent in participants treated with albendazole than those not receiving

anthelmintics (RR 1.37, 95% CI 1.08 to 1.73; 392 participants, four trials, Analysis 1.8).

In a subgroup analysis by use of corticosteroids, there was a significant difference between the albendazole and no anthelmintic groups in headache during treatment when the albendazole group did not receive corticosteroids (RR 9.49, 95% CI 1.4 to 64.45; 106 participants, two trials, Analysis 1.9), but no significant difference in trials where participants in the albendazole group received corticosteroids.

In analyses not separating trials by types of lesion, there was a greater risk of adverse events with albendazole for dizziness during treatment (Analysis 1.10), and nausea, vomiting and abdominal pain (Analysis 1.11). There was no significant difference between the albendazole and no anthelmintic groups in occurrence of seizures during treatment (455 participants, five trials, Analysis 1.12)

2. Praziquantel versus placebo or no drug

One small trial made this comparison (15 participants, Sotelo 1988). The trial included participants with viable lesions, non-viable lesions, or both. It did not report on recurrence of seizures, deaths or hospital admissions.

2.1. Resolution of symptoms

There was no significant difference between praziquantel and no anthelmintic for continuing presence of symptoms at three months (15 participants, Analysis 2.1).

2.2. Radiological changes at follow up

There was a significant difference between praziquantel and no anthelmintic in persistence of lesions at follow up (RR 0.15, 95% CI 0.03 to 0.67, 15 participants, Analysis 2.2). More participants treated with praziquantel than no anthelmintic had a reduction in the number of lesions at three months follow up (RR 0.15, 95% CI 0.03 to 0.67; 15 participants, Analysis 2.3).

2.3. Adverse events during treatment

More participants treated with praziquantel compared with no anthelmintic reported any adverse event during treatment, although the difference was not significant (15 participants, Analysis 2.4).

3. Albendazole versus praziquantel

Three trials reported on this comparison (Sotelo 1988; Sotelo 1990; Del Brutto 1999). All three trials included only participants with viable lesions.

3.1. Recurrence of seizures

In one small trial, there was no significant difference in the risk of recurrence of seizures with albendazole treatment compared with praziquantel (19 participants, Analysis 3.1).

3.2. Resolution of symptoms

Fewer participants treated with albendazole compared with praziquantel still had symptoms of neurocysticercosis (types of symptoms not specified in the reports) three months after treatment (RR 0.58, 95% CI 0.36 to 0.92; 121 participants, two trials, Analysis 3.2).

3.3. Persistence of radiological lesions at follow up

There was a significant benefit of albendazole over praziquantel in the number of participants with persistence of lesions at follow up at three to six months (RR 0.64, 95% CI 0.45 to 0.91; 154 participants, three trials, Analysis 3.3).

Significantly fewer participants in the albendazole group had more lesions, or the same number of lesions, at follow up than before treatment (RR 0.41, 95% CI 0.19 to 0.92; 149 participants, three trials, Analysis 3.4).

3.4. Adverse events during treatment

There were no significant differences between albendazole and praziquantel in the number of adverse events during treatment (Analysis 3.5).

4. Albendazole combined with praziquantel versus albendazole alone

One trial, including only children with single non-viable lesions, reported on this comparison.

4.1. Recurrence of seizures

There was no significant difference between the groups in recurrence of seizures at six months (112 participants, Analysis 4.1).

4.2 Persistence of radiological lesions

Albendazole combined with praziquantel was associated with lower risk of persistence of lesions at six months compared with albendazole alone (RR 0.59, 95% CI 0.35 to 0.99; 103 participants, Analysis 4.2). At one month and three months there was no significant difference between the groups, but there was a trend towards benefit of albendazole combined with praziquantel.

4.3 Adverse events

Three children receiving albendazole combined with praziquantel and two children receiving albendazole alone developed headache on day three to four of treatment lasting for one or two days. None reported any gastrointestinal symptoms. There were no signs of raised intracranial pressure and none of the children required withdrawal of drugs.

5. Albendazole: longer versus shorter duration of treatment

Six trials reported on this comparison (Alarcon 1989; Sotelo 1990; Cruz 1995; Garcia 1997; Alarcon 2001; Singhi 2003). This included three trials where participants had only viable lesions (Alarcon 1989; Sotelo 1990; Alarcon 2001), one trial including non-viable lesions only (Singhi 2003), and two trials where participants had viable, non-viable or both types of lesion (Cruz 1995; Garcia 1997).

5.1. Recurrence of seizures and resolution of symptoms

Viable lesions

One trial (Alarcon 2001) assessed the mean number of seizures at 12 months after treatment. The results were highly skewed, but there was no apparent difference between groups treated for eight days and groups treated for three days (54 participants, 0.3 (+/- 0.5) compared with 0.5 (+/-1.0)).

One trial assessed the resolution of symptoms (not clearly defined in the trial report) three months after treatment. There was no

difference between groups treated for up to eight days and more than eight days in the number of participants whose symptoms had not resolved (49 participants, Analysis 5.1).

Non-viable lesions

No trials made this comparison.

Mixed viable and non-viable lesions

One trial assessed the resolution of symptoms (not clearly defined in the trial report) three months after treatment. There was no difference between groups treated for up to eight days and more than eight days in the number of participants whose symptoms had not resolved (53 participants, Analysis 5.1).

5.2. Persistence of radiological lesions

Viable lesions

There was no significant difference in persistence of lesions at final follow up between groups receiving albendazole for seven or eight days and longer than seven or eight days (103 participants, two trials, Analysis 5.2). There was also no significant difference between groups given albendazole for three days or eight days (54 participants, one trial).

Non-viable lesions

There was no significant difference in persistence of lesions at final follow up between groups receiving albendazole for seven or eight days and longer than seven or eight days (159 participants, two trials, Analysis 5.2).

Mixed viable and non-viable lesions

There was no significant difference in persistence of lesions at final follow up between groups receiving albendazole for seven or eight days and longer than seven or eight days (79 participants, two trials, Analysis 5.2).

5.3. Adverse events

All types of lesion

In analyses not separating trials by type of lesion, participants receiving shorter treatment durations reported fewer cases of nausea or other gastrointestinal symptoms than those receiving longer treatments (RR 0.54, 95% CI 0.30 to 0.97; 244 participants, four trials, Analysis 5.4).

6. Albendazole: with corticosteroids versus without corticosteroids

One trial, including participants with non-viable lesions only (Singhi 2004), made this comparison.

6.1 Recurrence of seizures

There was no significant difference between in recurrence of seizures during weeks one to 72 after treatment (72 participants, Analysis 6.1).

6.2 Radiological resolution of lesions

There was no significant difference between albendazole alone and albendazole with corticosteroids in the persistence of lesions at six months after treatment (72 participants, Analysis 6.2).

6.3 Adverse events

This trial did not report on adverse events.

DISCUSSION

Summary of main results

The results of trials comparing anthelmintic treatment with no anthelmintic are mixed and therefore difficult to interpret. Most trials assessed albendazole, which has largely taken over from praziquantel. We found only one small trial comparing praziquantel with no active treatment from which we could not come to any meaningful conclusions on its efficacy. Reduction in seizures with albendazole did not appear to correlate with radiological clearance of lesions. Findings for the three major outcomes categories of this review are described below.

Seizure recurrence

For seizure recurrence, most trials tended towards a benefit of albendazole, and this benefit was significant in the case of children with a single, non-viable lesion. This finding runs counter to most expert opinion which is of a view that treatment is unlikely to be beneficial for cases with non-viable lesions only. There was no significant benefit shown for people with viable lesions only, which seems counter-intuitive, but only one small trial reported on this outcome, hence a larger study is needed to ascertain the efficacy of albendazole in this group. One trial, including participants with both viable and non-viable lesions (Das 2007), showed a harmful effect of albendazole. This trial, which combined albendazole with steroids, also showed increased encephalopathy and admission to hospital with albendazole, and two deaths from encephalopathy.

Radiological clearance of lesions

For radiological clearance of lesions during the first 12 months, trials including people with viable lesions only showed a significant benefit of albendazole, while trials including only people with non-viable lesions, or a mixture of viable and non-viable lesions, showed no significant effect of albendazole. The majority of trials on viable lesions involved adults only, while those on non-viable lesions involved only children; the observed differences between trial results may also have been affected by the ages of the participants.

Our analysis showed no significant effect of duration of treatment on persistence of lesions at follow up. Assuming that presence of symptoms is associated with presence of lesions (Murthy 2006), these results suggest that a shorter duration of treatment is as effective as a longer course. Shorter courses were also associated with fewer cases of nausea or other gastrointestinal symptoms during treatment. One trial assessed albendazole in combination with praziquantel compared with albendazole alone; the findings suggested that the combination of two anthelmintics was better in the short term.

Adverse events

Participants treated with either albendazole or praziquantel experienced significantly more adverse events during treatment than those receiving no active treatment. Albendazole was associated with headache, dizziness, and nausea, vomiting and abdominal pain. There is some indirect (weak) evidence that corticosteroids used in conjunction with albendazole may protect against headache during treatment, as in trials using

corticosteroids there was no significant difference between albendazole and no active treatment in this outcome.

Overall completeness and applicability of evidence

We identified 21 relevant published trials. Most were published since the last update of this Cochrane Review (Salinas 1999). We also identified one relevant ongoing trial. All the trials were small; the largest enrolled 300 participants and the smallest enrolled 18. All trials, published and ongoing, were based in Central and South America and South-East Asia; there were no trials from Africa or China, where the disease is also endemic.

The trial participants varied, including children and adults and people with different numbers and types of lesions, although trials in children tended to include only non-viable lesions, while trials in adults mostly included only viable lesions. Together the trials included very few people with large numbers of lesions, or with lesions other than parenchymal cysts or lesions.

Treatment comparisons of the included trials were wide ranging, enabling analysis by type of drug (albendazole or praziquantel) and duration of treatment. We were also able to indirectly compare the frequencies of adverse events during treatment when anthelmintics were administered with or without corticosteroids.

Two comparisons reported by the included trials are not presented in the analysis because their comparisons did not fit into its structure. Gongora-Rivera 2006 compared only different doses of albendazole given for just one day; this was not presented as we had no other trials using albendazole for just one day, and hence no evidence that it was better than placebo. Sotelo 1990 compared praziquantel given for different durations; this comparison was not presented because we found no evidence that praziquantel was effective in treating neurocysticercosis.

Just over half of the included trials reported on the presence or severity of seizures, which are probably the most important outcomes to most patients. Three other trials reported on symptom severity or presence of symptoms, of which seizures would be the most common, and one trial reported separately on symptoms other than seizures. All the trials assessed and reported on the radiological presence or changes in the neurocysticerci, which may not be directly correlated with the presence or severity of seizures or other symptoms. Radiological outcomes are easy to assess, specific to neurocysticercosis, and perhaps clinically useful, as there is evidence that anti-epileptic drugs can usually be withdrawn following radiological clearance of lesions, and this may be a criteria for withdrawing anti-epileptic drugs in some patients and practices (Murthy 2006). However, in this review, children with a single non-viable lesion, and treated with albendazole compared with no anthelmintic, had a lowered risk of recurrence of seizures despite no difference in the radiological persistence of lesions.

Quality of the evidence

The risk of bias varied between trials, with the trials published most recently tending to be assessed as better for all indicators. Six trials reported an adequate method of allocation concealment; one trial including viable lesions only, four including non-viable lesions only, and two including both viable and non-viable lesions.

Potential biases in the review process

All of the included trials were small. In addition, unexplained heterogeneity was introduced by one relatively large, but poorly reported trial (Das 2007) with results mostly running in the opposite direction to those reported in other trials.

Agreements and disagreement with other studies and reviews

Our results slightly vary from other recent meta-analyses assessing albendazole compared with placebo or usual care, but the conclusions reached are similar.

A meta-analysis in children (four trials, 400 participants) with neurocysticercosis revealed a higher remission of seizures in those treated with albendazole compared to controls (RR 1.26, 95% CI 1.09 to 1.46). This agrees with our findings in children with non-viable lesions only. The authors also reviewed 10 observational studies and found conflicting results (Mazumdar 2007).

Del Brutto and colleagues (Del Brutto 2006) reported a meta-analysis of 11 randomized trials of patients with neurocysticercosis located in or adjacent to the cerebral parenchyma. Anthelmintic drug therapy was associated with complete resolution of viable lesions (44% versus 19%; P = 0.025) at follow up. Trials on non-viable lesions showed a trend toward lesion resolution favouring anthelmintic drugs (72% versus 63%; P = 0.38), but this was not significant. In patients with non-viable lesions, risk for seizure recurrence was lower after anthelmintic treatment (14% versus 37%; P < 0.001). The single trial evaluating the frequency of seizures in patients with non-viable lesions showed a 67% reduction in the rate of generalized seizures with treatment (P = 0.006).

As far as we know, there have been no other meta-analyses undertaken to compare different durations of treatment.

Ongoing trials are still using regimens of 10 days albendazole (Gilman 2007) despite evidence that shorter treatment durations may be as effective. These findings have implications relating to cost and patient choice and adherence in what may be an expensive disease to treat; a recent study in India reported that the total costs per patient of treating seizures associated with a single cysticerci in the brain may be equivalent to around half the per capita Gross National Product of the country (Murthy 2007).

Current consensus guidelines for the treatment of neurocysticercosis (Garcia 2002; Nogales-Gaete 2006) do not give any definitive advice on anthelmintic treatment for patients with five or fewer, or more than 100, viable lesions, or fewer than 100 non-viable lesions. This review presents evidence that albendazole treatment may reduce the recurrence of seizures in children with a single non-viable lesion, and reduce the persistence of lesions in neuroimaging in persons with small numbers of viable lesions**.** We did not find enough evidence to draw any conclusions on the safety and effectiveness of treatment for heavy parenchymal infection or extra-parenchymal (subarachnoid or ventricular) neurocysticercosis. There is also no current consensus on the use of corticosteroids when anthelmintics are used in cases of five or fewer viable cysts, or fewer than 100 non-viable lesions. This review presents evidence that corticosteroids may reduce the incidence of adverse events during treatment, even in people with only non-viable lesions or with small numbers of viable lesions.

AUTHORS' CONCLUSIONS

Implications for practice

For children with parenchymal neurocysticercosis, and with small numbers of non-viable neurocysticercosis lesions in the brain, albendazole treatment at the standard dose may reduce the risk of recurrence of seizures in the medium term (six to 18 months). However, it is still unclear whether and how different groups benefit from albendazole treatment. There is some evidence that parasite clearance may be speeded up in patients with viable lesions, but no evidence that this has any impact on seizure recurrence. Short courses of seven days or less are as effective as longer courses, although there is not enough evidence to say what the optimum duration of treatment is. Adverse events during treatment, including headache, dizziness, and gastrointestinal symptoms, are common. There is some indirect evidence that they may be reduced by giving corticosteroids with the albendazole and prescribing albendazole for the minimum effective duration, but this needs to be evaluated through randomized comparisons.

There is not enough evidence available to assess the effects of praziquantel treatment in any group, or albendazole treatment in people with moderate or heavy infections or extra-parenchymal cysts. It is not known whether people who are HIV positive will respond to treatment in the same way, as it is assumed that most participants in the included studies were HIV negative.

Implications for research

Further good quality, randomized controlled trials are needed to assess the effectiveness of albendazole treatment in different groups of patients, including adults and children, and people with different stages and numbers of lesions (less than five, five to 100 and more than 100). Some trials should include participants with heavy parenchymal infections, and those with any kind of extra-parenchymal infection. At least one trial should also include participants who are HIV positive, as HIV infection is common in Africa where neurocysticercosis is also common. Trials should carefully assess, record, and analyse the outcomes likely to be of most interest to the patient, including adverse events during treatment, recurrence of seizures, and successful withdrawal of anti-epileptic drugs.

Once it is clear which groups might benefit from albendazole treatment, trials should assess the optimal dosage and duration of albendazole treatment for different groups of people with different forms of neurocysticercosis. These should compare treatment of seven days duration with shorter durations, including treatment for as few as three days.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Alarcon 1989

Methods	Randomized controlled trial Duration: dates not supplied. Participants followed up for 4 months
Participants	Number: 23 enrolled; numbers of males and females not presented Inclusion criteria: adults and children aged > 13 years, with 1 to 3 parenchymal cysts > 10 mm without perilesional oedema, good general health and stable neurological disease Exclusion criteria: parenchymal cysts with ring enhancement and oedema surrounding the lesions, pregnant women Type of lesion: viable

Alarcon 1989 *(Continued)*

Interventions	Group 1. Albendazole: 15 mg/kg bodyweight for 3 days Group 2. Albendazole: 15 mg/kg bodyweight for 30 days Group 3. No albendazole
Outcomes	Included in the review: number of cysts and total diameter of cysts at baseline and 1 day, 30 days, and 3 months after treatment finishes. Adverse events
Notes	Location: Ecuador Source of funding: not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Quote: "randomly allocated" Decision: probably done, but unclear
Allocation concealment?	Unclear risk	Not described
Blinding? All outcomes	Unclear risk	Not described. Placebos were not used and different groups received follow-up scans at different times Decision: unclear, probably not done
Incomplete outcome data addressed? All outcomes	Low risk	23 randomized and follow-up data available for all (100%)
Free of selective reporting?	Low risk	No evidence of selective reporting; outcomes reported individually for all participants
Free of other bias?	Low risk	No evidence of other bias

Alarcon 2001

Methods	Randomized controlled trial Duration: participants recruited between January 1989 and December 1996, and followed up for 12 months
Participants	Number: 95 enrolled, data available for 83 (36 male, 47 female) Inclusion criteria: adults with neurological signs and symptoms and 1 to 6 non-enhancing parenchymal cysts without perilesional oedema Exclusion criteria: ring or nodular cysts, oedema surrounding the lesions, subarachnoid or intraventricular cysts, hydrocephalus, previous treatment with albendazole or praziquantel, pregnant women, intracranial hypertension Type of lesion: viable
Interventions	Group 1. Albendazole: 15 mg per kg bodyweight for 3 days Group 2. Albendazole: 15 mg per kg bodyweight for 8 days Group 3. No albendazole

Alarcon 2001 *(Continued)*

Outcomes	Included in the review: number of cysts at baseline, 3 months, and 6 months; persistence of cysts at 3 months and 12 months; number of seizures per year at baseline and 12 months; adverse events associated with treatment
Notes	Location: Ecuador Source of funding: not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Method not described, but trial described as 'randomized' Decision: unclear, but probably done
Allocation concealment?	Unclear risk	Not described Decision: unclear
Blinding? All outcomes	Low risk	Quote: "Evaluation of the number of cysts on CT at baseline and at follow-up was performed by a single neuroradiologist blinded to the treatment allocation"
Incomplete outcome data addressed? All outcomes	Low risk	95 participants randomized; 8 excluded before starting treatment, 4 lost to follow up (87% included in the analysis)
Free of selective reporting?	Low risk	No evidence of selective reporting
Free of other bias?	Low risk	No evidence of other bias

Baranwal 1998

Methods	Randomized controlled trial Duration: dates not supplied. Participants followed up for 24 months.
Participants	Number: 63 enrolled, 57 included in analysis (33 male, 24 female) Inclusion criteria: children aged 2 years to 12 years with a single small enhancing lesion in brain parenchyma plus seizures for less than 3 months Exclusion criteria: neurologic deficit or suspected tuberculosis Type of lesion: non-viable
Interventions	Group 1. Albendazole: 15 mg per kg bodyweight for 28 days, plus 1 to 2 mg prednisolone per day for 5 days Group 2. Placebo, plus 1 to 2 mg prednisolone per day for 5 days
Outcomes	Included in the review: recurrence of seizures at 3 months after treatment; persistence of lesion at 1 month and 3 months; recurrence of seizures 8 months after tapering anticonvulsants after 18 to 24 months seizure-free following treatment Not included in the review: calcification of lesion at 3 months; lesion diameter at baseline and 1 month

Baranwal 1998 *(Continued)*

Notes	Location: India Source of funding: not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	Quote: "...numbered in a random sequence using a random number table" Decision: done
Allocation concealment?	Low risk	Quote: "Envelopes containing albendazole or placebo capsules for the full course of therapy were prepared in advance and numbered in a random sequence" Decision: done
Blinding? All outcomes	Low risk	Quote: "All persons involved in the study i.e. patient, clinical investigator and neuroradiologist were blind to the random allocation. Results were decoded after completion of 6 months of study to identify the groups" Decision: done
Incomplete outcome data addressed? All outcomes	Low risk	63 randomized, 6 lost to follow up (90% included in the analysis)
Free of selective reporting?	Low risk	No evidence of selective reporting
Free of other bias?	Low risk	No evidence of other bias

Carpio 2008

Methods	Randomized controlled trial Duration: dates not supplied. Participants followed up for 12 months Inclusion of randomized participants in the analysis: 161/178 = 90% (in addition, 7 died)
Participants	Number: 178 enrolled, 97 male, 77 female; 4 with missing data on sex Inclusion criteria: any age or gender with new onset symptoms associated with neurocysticercosis within 2 months prior to recruitment, and neurocysticercosis cysts an axial CT or MRI imaging of the brain. Could include 1 or more active parenchymal cysts, degenerative or transitional parenchymal cysts, or cysts with a extra-parenchymal location. Exclusion criteria: having only calcified cysts, pregnancy, papilloedema, active tuberculosis, syphilis, ocular cysticercosis, active gastric ulcers or any progressive or life-threatening disorder Type of lesion: viable or non-viable cysts, or a combination of the two
Interventions	Group 1: For participants weighing more than 50 kg, 400 mg of albendazole every 12 hours for 8 days. For participants weighing less than 50 kg, including children, 15 mg per kg bodyweight per day for 8 days. Participants weighing over 50 kg also received 75 mg prednisolone daily for 8 days, then 50 mg per day for 1 week, then 25 mg per day for 1 week. Participants weighing less than 50 kg received 1.5 mg per kg bodyweight prednisone for 8 days, then 1 mg per kg for 1 week, then 0.5 mg for 1 week.

Carpio 2008 *(Continued)*

	Group 2: Placebo with an identical appearance to albendazole, plus prednisolone as for Group 1
Outcomes	Included in the review: freedom from seizures for 12 months following treatment; mean time seizure-free following treatment; freedom from cysts 1 month, 6 months and 12 months following treatment; reduction in the number of cysts 1 month, 6 months and 12 months following treatment; deaths due to cysticercosis; all-cause deaths; adverse events during treatment, and during the first month following treatment
Notes	Location: Ecuador Source of funding: NINDS grant R01-NS39403. Glaxo/SKB and Acromax Co supplied the active drug and placebo

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	Quote: "Patients were allocated to treatment group according to a stratified block randomisation schedule. Two strata were considered: centre (sex centres) and location of the cyst (parenchymal versus extraparenchymal). Permuted blocks of size 4 and 6 were used to balance the treatment allocation within each stratum" Decision: done
Allocation concealment?	Low risk	Quote: "The randomisation lists were kept in electronic form on a computer accessible only to the statistician" Decision: done
Blinding? All outcomes	Low risk	Quotes: "All other research staff were blinded to the treatment arm"... "double-blind, placebo controlled trial" Decision: done
Incomplete outcome data addressed? All outcomes	Low risk	Of 178 participants, 161 (90%) were followed up and included in the analysis. In addition, 7 died.
Free of selective reporting?	Low risk	No evidence of selective reporting
Free of other bias?	Low risk	No evidence of other bias

Cruz 1995

Methods	Randomized controlled trial Duration: dates not specified. Participants followed up for 4 months.
Participants	Number: 61 enrolled, 53 included in the analysis (33 male, 20 female) Inclusion criteria: adults with cystic or encephalitic forms of cerebral cysticercosis - any developmental stage of the parasite, localization parenchymous, subarachnoid, or ventricular Exclusion criteria: patients in a coma or generally poor condition Type of lesion: mixed viable, non-viable, and both viable and non-viable

Cruz 1995 *(Continued)*

Interventions	Group 1. Albendazole: 800 mg per day for 8 days Group 2. Albendazole: 800 mg per day for 15 days Group 3. Albendazole: 800 mg per day for 30 days
Outcomes	Included in the review: persistence of cysts at 3 months; number of cysts at baseline and 3 months; symptom change at 3 months; adverse events
Notes	Location: Ecuador Source of funding: partially funded by SmithKline Beecham Pharmaceuticals

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Quote: "...were randomised to one of 3 different treatment groups" Decision: unclear, probably done
Allocation concealment?	Unclear risk	Not described Decision: unclear
Blinding? All outcomes	Unclear risk	Not described. Participants were treated for different durations, without the use of placebos. Decision: unclear, probably not done
Incomplete outcome data addressed? All outcomes	Low risk	Of 61 participants randomized, 53 completed 3 months follow up (87%)
Free of selective reporting?	Low risk	No evidence of selected reporting
Free of other bias?	Low risk	No evidence of other bias

Das 2007

Methods	Randomized controlled trial Duration: between January 1997 and January 2005
Participants	Number: 300 enrolled (178 male, 122 female) Inclusion criteria: adults presenting with recent-onset seizures, with CT and MRI scan results strongly suggestive of neurocysticercosis and at least 2 lesions with ring enhancement, of which at least 1 was in the vesicular stage, and antibodies against neurocysticercosis detected by ELISA on at least 3 occasions Exclusion criteria: primary seizure disorder, family history of seizure, pre-existing focal neurological deficit, or any metabolic or hereditary disease Type of lesion: mixed viable and non-viable
Interventions	Group 1. 15 mg per kg bodyweight albendazole daily for 14 days, plus 2 mg dexamethasone orally at 8-hour intervals for 14 days, plus anti-epileptic drugs at appropriate doses. Dexamethasone tapered off over time.

Das 2007 *(Continued)*

	Group 2. Placebo plus anti-epileptic drugs
Outcomes	Included in the review: seizures, hospital admissions, and resolution of lesions at 3 months, 6 months, 1 year, 2 years, 3 year and 4 years
Notes	Location: India Source of funding: Burdwan Medical College and Hospital

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Quote: "The patients were randomly allocated into two groups" Decision: unclear, probably done
Allocation concealment?	Unclear risk	Not described Decision: unclear
Blinding? All outcomes	Unclear risk	Placebos used, but blinding not described for investigators and medical staff Decision: unclear
Incomplete outcome data addressed? All outcomes	Low risk	300 randomized, 2 died within 3 months, 298 followed up for 5 years (100% follow up)
Free of selective reporting?	Low risk	No evidence of selective reporting
Free of other bias?	Low risk	No evidence of other bias

De Souza 2009

Methods	Randomized controlled trial Duration: participants enrolled between May 2002 and October 2003 and followed up for up to 64 months (mean 31 months)
Participants	Number: 123 enrolled, 103 included in the analysis (59 male, 44 female) Inclusion criteria: all patients presenting with new onset focal or generalized seizures with MRI-confirmed solitary cysticercal lesion in the brain parenchyma Exclusion criteria: past history of epilepsy, received albendazole or praziquantel in the past, evidence of other lesions on CT or MRI, significant neurological deficits, raised intracranial pressure or seizures refractory to acute treatment Types of lesion: non-viable
Interventions	Group 1: Anti-epileptic drugs only Group 2: Anti-epileptic drugs plus albendazole 15 mg per kg bodyweight per day for 28 days

De Souza 2009 *(Continued)*

Outcomes	Included in the review: time to becoming seizure-free; total number of seizures from onset of illness until the last visit; duration of anti-epileptic drug therapy; number of months seizure free at the last visit; number of months taken off anti-epileptic drugs at last visit; disappearance of calcification of cysts Not included in the review: types of seizure; mean cyst area; perilesional oedema
Notes	Location: India Source of funding: Indian Council for Medical Research

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	Quote: "The patients were randomised to two groups by means of a random number table" Decision: done
Allocation concealment?	Unclear risk	Not described Decision: unclear
Blinding? All outcomes	Unclear risk	Not described. Placebos not used Decision: unclear, probably not done
Incomplete outcome data addressed? All outcomes	Low risk	Of 123 participants recruited, 103 (84%) had a minimum follow up of 12 months, and so were included. It was stated that the demographic profile, seizure type and MRI findings in the 20 excluded participants did not differ from those included.
Free of selective reporting?	Low risk	No evidence of selective reporting
Free of other bias?	Low risk	No evidence of other bias

Del Brutto 1999

Methods	Randomized controlled trial Duration: dates not specified
Participants	Number: 20 enrolled (8 male, 12 female) Inclusion criteria: adults with less than 20 parenchymal brain cysts with no evidence of surrounding inflammation Exclusion criteria: mixed forms of the disease Type of lesion: viable
Interventions	Group 1. Albendazole: 15 mg per kg for 7 days plus prednisolone 1 mg per kg bodyweight per day, until a few days after the end of the trial Group 2. Praziquantel: 100 mg per kg bodyweight for 1 day, plus 2 mg doses of intravenous dexamethasone administered 6 and 8 hours after the last dose of praziquantel

Del Brutto 1999 *(Continued)*

Outcomes	Included in the review: number of cysts at baseline and 3 months; persistence of cysts at 3 months; persistence of seizures at 6 to 12 months; adverse events associated with treatment Not included in the review: improvement in motor deficit at 6 to 12 months
Notes	Location: Ecuador Source of funding: not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	Quote: "...patients were randomly allocated (from a table of random numbers) to one of two treatment groups" Decision: done
Allocation concealment?	Unclear risk	Not described Decision: unclear
Blinding? All outcomes	Low risk	Quote: "All CT studies were independently reviewed by two experienced radiologists, blinded to the therapy used..." Decision: done
Incomplete outcome data addressed? All outcomes	Low risk	20 participants randomized, all 20 followed up to 6 months (100%)
Free of selective reporting?	Low risk	No evidence of selective reporting
Free of other bias?	Low risk	No evidence of other bias

Garcia 1997

Methods	Randomized controlled trial Duration: dates not supplied. Participants followed up for 12 months.
Participants	Number: 55 enrolled (32 male, 23 female) Inclusion criteria: adults with live cysts or nodular enhancing lesions, with or without contrast enhancement, in any part of the brain. Positive immunoblot Exclusion criteria: pregnant or lactating women Type of lesion: viable or mixed (41), non-viable (9)
Interventions	Group 1. Albendazole: 400 mg daily for 14 days plus dexamethasone 1.5 mg 3 times daily for 5 days and 0.5 mg 3 times daily for 5 days then 0.5 mg 3 times daily for 2 days Group 2. Albendazole: 400 mg daily for 7 days plus dexamethasone 1.5 mg 3 times daily for 5 days and 0.5 mg 3 times daily for 5 days then 0.5 mg 3 times daily for 2 days
Outcomes	Included in the review:

Garcia 1997 *(Continued)*

	Number of cysts at baseline, 3 months and 1 year; persistence of cysts at 3 months; gastrointestinal symptoms during treatment
Notes	Location: Peru Source of funding: funded in part by grants number 1-U01 A135894-01 from the National Institutes for Health; and from SmithKline Beecham Pharmaceuticals, London, UK

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	Quote: "Patients were blindly assigned to one of two treatment groups using a previously assigned randomization schedule" Decision: done
Allocation concealment?	Unclear risk	Quote: "Patients were blindly assigned to one of two treatment groups using a previously assigned randomization schedule" Decision: unclear, but probably done
Blinding? All outcomes	Unclear risk	Quote: "CT scans were read by an experienced reader, blinded to the therapy used" Decision: done
Incomplete outcome data addressed? All outcomes	Low risk	55 participants randomized, 50 included in the analysis (91%)
Free of selective reporting?	Low risk	No evidence of selective reporting
Free of other bias?	Low risk	No evidence of other bias

Garcia 2004

Methods	Randomized controlled trial Duration: recruitment between January 1997 and March 1999. Follow up for 6 months.
Participants	Number: 120 enrolled (61 male, 59 female) Inclusion criteria: adults with fewer than 20 viable parenchymal cysts plus 1 or more seizures in the previous 6 months Exclusion criteria: primary generalized seizures, history of antiparasitic treatment, evidence on CT of other diseases, moderate or severe intracranial hypertension, status epilepticus, focal neurological deficits, unstable vital signs, impending risk of death, or pregnancy. Type of lesion: viable
Interventions	Group 1. Albendazole: 400 mg every 12 hours and 2 mg dexamethasone every 8 hours for 10 days Group 2. Placebos
Outcomes	Included in the review: recurrence of seizures during months 2 to 30; partial seizures in month 1, months 2 to 12 and months 13 to 30, and following tapering of anti-epileptic drugs; seizures with gen-

Garcia 2004 *(Continued)*

	eralization in month 1, months 2 to 12 and months 13 to 30, and following tapering of anti-epileptic drugs; number of cysts at baseline and 6 months; persistence of seizures at 6 months; adverse events associated with treatment
Notes	Location: Peru Source of funding: not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	Random assignment in blocks of 6 according to a pre-established list taken from a random-numbers table
Allocation concealment?	Low risk	Randomization performed from remote site by a statistician not otherwise involved in the study. All drugs and placebos were administered by the study personnel, who received them in sealed, opaque, sequentially numbered envelopes
Blinding? All outcomes	Low risk	Blinded all study participants and personnel
Incomplete outcome data addressed? All outcomes	Low risk	120 randomized, 116 received study medication, 2 were excluded from the analysis, 14 lost to follow up (100/120 = 83%). The reasons for all withdrawals were clearly documented.
Free of selective reporting?	Low risk	No evidence of selective reporting
Free of other bias?	Low risk	No evidence of other bias

Gogia 2003

Methods	Randomized controlled trial Duration: recruitment March to July 2000
Participants	Number: 72 enrolled (38 male, 34 female) Inclusion criteria: children aged 18 months to 12 years with ring-enhancing lesions in brain parenchyma, plus seizures without a history of epilepsy Exclusion criteria: tuberculosis, known epilepsy on anti-epileptic medication, chronic central nervous system disorders. CT scans showing disc, nodular or calcific lesions. Type of lesion: non-viable
Interventions	Group 1. Prednisolone: 2 mg per kg for 3 days followed by albendazole 15 mg per kg bodyweight for 28 days Group 2. Prednisolone: 2 mg per kg for 3 days followed by placebo for 28 days
Outcomes	Included in the review: persistence of lesions at 6 months; recurrence of seizures at 6 months Not included in the review: calcification of lesions at 6 months; nodular lesions at 6 months
Notes	Location: India

Gogia 2003 *(Continued)*

	Source of funding: not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	Quote: "The enrolled children were randomized using a random number table" Decision: done
Allocation concealment?	Low risk	Quote: "...coded as drug A or drug B..." "The drugs were dispensed in coded envelopes" Decision: done
Blinding? All outcomes	Low risk	Quote: "The drugs were dispensed in coded envelopes. The investigators and the patients were thus blinded to which drug was being given to which patient. The radiologist responsible for reading the X-rays was also blinded to the drug therapy" Decision: done
Incomplete outcome data addressed? All outcomes	Low risk	72 participants were randomized; all 72 were followed up for seizure recurrence at 6 months (100%)
Free of selective reporting?	Low risk	No evidence of selective reporting
Free of other bias?	Low risk	No evidence of other bias

Gongora-Rivera 2006

Methods	Randomized controlled trial Duration: between November 1999 and January 2001
Participants	Number: 36 enrolled (14 male, 22 female) Inclusion criteria: adults with subarachnoid and intraventricular cysticercosis Exclusion criteria: concurrent disease that contraindicated corticosteroid, albendazole allergy, previous cysticidal or surgical treatment for neurocysticercosis in the previous 3 months, pregnant or lactating women, neurological diseases affecting function, unable to attend for regular follow up, Karnofsky score ≤ 50 points Type of lesion: degenerating, viable, or mixed
Interventions	Group 1. Intravenous dexamethasone: 8 mg every 8 hours for 4 days followed by 15 mg per kg albendazole for 1 day Group 2. Intravenous dexamethasone: 8 mg every 8 hours for 4 days followed by 30 mg per kg albendazole for 1 day
Outcomes	Included in the review: symptom severity score at baseline and 7 days; adverse events associated with treatment Not included in the review: reduction in cyst volume at 90 days

Gongora-Rivera 2006 *(Continued)*

Notes	Location: Mexico Source of funding: not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	Quote: "...a computer-generated randomization plan" Decision: done
Allocation concealment?	Low risk	Quote: "The code of the two different albendazole doses was available in sealed envelopes and was not opened until the trial completion"
Blinding? All outcomes	Low risk	Quote: "For blinding the pharmaceutical laboratory...provided according to a computer-generated randomization plan, tablets containing 200 mg or 400 mg albendazole with identical appearance. Neither the patient nor the study staff were aware of treatment assignment" Decision: done
Incomplete outcome data addressed? All outcomes	Low risk	Inclusion of randomized participants in the analysis: 36 randomized, 5 did not compete the study (86%). An intention-to-treat analysis was also undertaken with similar results obtained.
Free of selective reporting?	Low risk	No evidence of selective reporting
Free of other bias?	Low risk	No evidence of other bias

Kalra 2003

Methods	Randomized controlled trial Duration: dates not specified. Participants followed up for 6 months.
Participants	Number: 123 enrolled (65 male, 58 female) Inclusion criteria: children aged 1 to 14 years with seizures plus 1 or 2 ring-enhancing lesions, excluding intraventricular cysts Exclusion criteria: suspected tuberculosis, intraocular cysts, multiple lesions, disk or calcified lesions, intraventricular cysts, or hydrocephalus Type of lesion: non-viable
Interventions	Group 1. Dexamethasone: 0.15 mg per kg bodyweight per day for 5 days plus 15 mg per kg albendazole for 28 days starting on day 3 Group 2. No dexamethasone or albendazole
Outcomes	Included in review: persistence of lesions at 3 months; complete or partial resolution or calcification of lesions at 3 months; seizure recurrence at 3 and 6 months
Notes	Location: India Source of funding: not stated

Kalra 2003 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	Quote: "A simple randomization scheme was used for allocation of patients to the treated or control groups" Decision: done
Allocation concealment?	Low risk	Quote: "Random assignment code was concealed up to the time of allocation in sealed envelopes labelled with a unique patient number" Decision: done
Blinding? All outcomes	High risk	Quote: "Evaluation of CT lesions...was performed by a single radiologist blinded to the treatment assignment and to the clinic outcome" Blinding of participants was not described, and placebos were not used. Abstract refers to an "open trial". Decision: partially done, for radiological outcomes only
Incomplete outcome data addressed? All outcomes	High risk	123 participants randomized, 30 lost to follow up at 3 months (93/123 = 76%). No discussion of the difference between participants available for follow up and those lost to follow up.
Free of selective reporting?	Low risk	No evidence of selective reporting
Free of other bias?	Low risk	No evidence of other bias

Kaur 2009

Methods	Randomized controlled trial Duration: participants enrolled January to December 2007 and followed up for 6 months
Participants	Number: 112 enrolled (69 male, 43 female), 103 included in the analysis Inclusion criteria: children aged 1 to 13 years with focal or generalized seizures for less than 3 months, no neuro deficits on clinical examination, and characteristic neuroimaging findings of single, small (< 20 mm) well-defined lesion with peripheral (ring) or uniform (disc) contrast enhancement with or without surrounding oedema, with minimal or no mass effect, without any midline shift Exclusion criteria: multiple lesions, extra parenchymal neurocysticercosis, focal neurologic deficit, suspected tuberculosis, any active systemic disease, or history of prior antiparasitic treatment Category of lesion: degenerating
Interventions	Group 1: Albendazole 15 mg per kg bodyweight per day for 7 days, oral prednisolone 2 mg per kg per day for 5 days, plus 75 mg per kg praziquantel for 1 day Group 2: Albendazole 15 mg per kg bodyweight per day for 7 days, oral prednisolone 2 mg per kg per day for 5 days, plus 75 mg per kg placebo for 1 day
Outcomes	Included in the review: complete resolution of lesion at 1, 3, and 6 months, recurrence of seizures within 6 months, adverse effects of therapy

Kaur 2009 *(Continued)*

Notes	Location: India Source of funding: not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Quote: "All children were randomized and allocated to either of these two groups using a table of random numbers" Decision: done
Allocation concealment?	Low risk	Quote: "Identical looking sachets in strengths of 50, 100, and 200 mg of praziquantel and placebo were prepared...these sachets were coded as group A and B. The code was kept secret and opened only after completion of the study" Decision: done
Blinding? All outcomes	Low risk	Quote: "All persons involved in the study including the patient, the clinical investigator and the neuroradiologist were blinded to the random allocation" Decision: done
Incomplete outcome data addressed? All outcomes	Low risk	112 children were enrolled, 9 did not report for follow up, so 103 included in the main analysis (92%)
Free of selective reporting?	Low risk	No evidence of selective reporting
Free of other bias?	Low risk	No evidence of other bias

Padma 1994

Methods	Randomized controlled trial Duration: dates not specified. Participants followed up for 3 months
Participants	Number: 75 enrolled (52 male, 23 female) Inclusion criteria: adults and children aged 3.5 to 50 years with epilepsy, parenchymal single small enhancing lesions Exclusion criteria: neurological deficit on examination Type of lesion: non-viable
Interventions	Group 1. Albendazole: 15 mg per kg per day for 7 days Group 2. Placebo
Outcomes	Included in the review: complete resolution, partial resolution, and no resolution of lesion at 1 week, 1 month and 3 months
Notes	Location: India Source of funding: not stated

Padma 1994 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Quote: "Patients were randomly allocated to placebo or albendazole therapy" Decision: unclear, probably done
Allocation concealment?	Unclear risk	Not described Decision: unclear
Blinding? All outcomes	Low risk	Quote: "CTs were assessed by a neuroradiologist who was not aware of the treatment received by the patient" Placebos were used for participants Decision: done
Incomplete outcome data addressed? All outcomes	Low risk	75 participants randomized, follow-up data at 3 months available for 68 (91%)
Free of selective reporting?	Low risk	No evidence of selective reporting
Free of other bias?	Low risk	No evidence of other bias

Padma 1995

Methods	Randomized controlled trial Duration: dates not specified. Participants followed up for 3 months.
Participants	Number: 29 enrolled (22 male, 7 female) Inclusion criteria: adults and children aged 8 to 50 with multiple cystic lesions suggestive of neurocysticercosis plus neurological signs Exclusion criteria: calcified lesions only Type of lesion: degenerating, viable or mixed (possible to follow the radiological clearance of individual lesions by type)
Interventions	Group 1. Albendazole: 15 mg per kg per day for 7 days Group 2. Placebo
Outcomes	Included in the review: change in number of lesions at 1 and 3 months; persistence of lesions at 1 week, 1 month, and 3 months Not included in the review: change in oedema at 1 and 3 months
Notes	Location: India Source of funding: not stated

Risk of bias

Padma 1995 *(Continued)*

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Quote: "We undertook a randomized, double-blind, placebo-controlled study" Decision: unclear, probably done
Allocation concealment?	Unclear risk	Not described Decision: unclear
Blinding? All outcomes	Low risk	Quote: "...double-blind, placebo-controlled study"... "Placebo tablets of similar appearance"..."The CTS scans were assessed...by a neuroradiologist who was not aware of the treatment given" Decision: done
Incomplete outcome data addressed? All outcomes	Low risk	29 randomized, 29 included in the analysis (100%)
Free of selective reporting?	Low risk	No evidence of selective reporting
Free of other bias?	Low risk	No evidence of selective reporting

Singhi 2000

Methods	Randomized controlled trial Duration: recruitment from 1994 to 1998. Participants followed up for 6 months.
Participants	Number: 176 included in the analysis, male/female ratio not presented Inclusion criteria: children up to the age of 14 with a single small ring-enhancing lesion in brain parenchyma Exclusion criteria: none stated Type of lesion: non-viable
Interventions	Group 1. Albendazole: 15 mg per kg bodyweight for 28 days plus prednisolone at 2 mg per kg per day for 5 days Group 2. No albendazole or prednisolone
Outcomes	Included in the review: persistence of lesions at month 3 to 6 Not included in the review: lesion size decreased, increased, or remained the same at 3 to 6 months
Notes	Location: India Source of funding: not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Unclear risk	Quote: "Children..were chosen at random to receive either albendazole therapy or no specific anticysticeral therapy"..."randomly allocated children"

Singhi 2000 *(Continued)*

		Decision: unclear, probably done
Allocation concealment?	Unclear risk	No described Decision: unclear
Blinding? All outcomes	Unclear risk	Not described. Placebos not used. Decision: unclear, probably not done.
Incomplete outcome data addressed? All outcomes	Unclear risk	Not clear how many participants enrolled and randomized, outcomes data presented for 176
Free of selective reporting?	Low risk	No evidence of selective reporting
Free of other bias?	Low risk	No evidence of other bias

Singhi 2003

Methods	Randomized controlled trial Duration: recruitment from June 1999 to June 2000. Participants were followed up for 12 months.
Participants	Number: 147 randomized, 122 included in the analysis (68 male, 54 female) Inclusion criteria: children with seizures for less than 3 months and up to 3 small enhancing lesions in parenchyma Exclusion criteria: raised intracranial pressure, focal neurological deficit, neurodevelopmental delay, any chronic systemic disease, other lesions on imaging, evidence of tuberculosis Type of lesion: non-viable
Interventions	Group 1. Oral prednisolone: 2 mg per kg once daily for 5 days plus 15 mg per kg per day albendazole for 4 weeks starting 2 days after prednisolone started Group 2. Oral prednisolone: 2 mg per kg once daily for 5 days plus 15 mg per kg per day albendazole for 1 week starting 2 days after prednisolone started
Outcomes	Included in the review: persistence of lesions at 1 month; recurrence of seizures within 12 months; epigastric discomfort with treatment Not included in the review: lesion size reduced at 6 months
Notes	Location: India Source of funding: not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	Quote: "...they were randomized according to random number tables..." Decision: done
Allocation concealment?	Unclear risk	Not described

Singhi 2003 *(Continued)*

		Decision: unclear
Blinding? All outcomes	Low risk	Quote: "None of the persons involved in the study (i.e. patient, investigators and neuroradiologist) was aware of this random allocation. The code was opened only after completion of the study" Decision: done
Incomplete outcome data addressed? All outcomes	High risk	147 randomized, 25 excluded due to poor compliance with treatment or inadequate follow up (83% included in the analysis). No discussion of the differences between participants included in the analysis and those excluded.
Free of selective reporting?	Low risk	No evidence of selective reporting
Free of other bias?	Low risk	No evidence of other bias

Singhi 2004

Methods	Randomized controlled trial Duration: dates not specified
Participants	Number: 133 enrolled, 110 included in the analysis (66 male, 44 female) Inclusion criteria: children aged 1 to 14 years with seizures for less than 3 months and a single small enhancing lesion in parenchyma Exclusion criteria: history of generalized seizures, neurologic deficit, multiple lesions on CT, or suspected tuberculosis Type of lesion: non-viable
Interventions	Group 1. Prednisolone: 2 mg per kg per day for 3 weeks tapering off in the 4th week Group 2. Albendazole: 15 mg per kg per day for 4 weeks Group 3. Albendazole: 15 mg per kg per day for 4 weeks plus prednisolone 2 mg per kg per day
Outcomes	Included in the review: persistence of lesion at 3 and 6 months; recurrence of seizures between weeks 1 and 72, and after withdrawing from antiepilepsy drugs Not included in the review: partial resolution of lesion at 3 and 6 months; disappearance of perilesional oedema at 3 and 6 months
Notes	Location: India Source of funding: not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Adequate sequence generation?	Low risk	Quote: "The children were randomly assigned...using random number tables" Decision: done
Allocation concealment?	Unclear risk	Not described Decision: unclear

Singhi 2004 *(Continued)*

Blinding? All outcomes	Unclear risk	Quote: "All CT scans were assessed by a neuroradiologist who was blinded to treatment assignment and to clinical outcome" Blinding not described for participants Decision: unclear, partially done for radiological outcomes
Incomplete outcome data addressed? All outcomes	Low risk	133 participants were randomized, 23 lost to follow up (85% included in the analysis)
Free of selective reporting?	Low risk	No evidence of selective reporting
Free of other bias?	Low risk	No evidence of other bias

Sotelo 1988

Methods	Randomized controlled trial Duration: dates not specified. Participants were followed up for 4 months.
Participants	Number: 25 enrolled (16 male, 9 female) Inclusion criteria: adults with parenchymal brain cysticercosis Exclusion criteria: none stated Type of lesion: viable
Interventions	Group 1. Albendazole: 15 mg per kg per day for 1 month (no steroids) Group 2. Praziquantel: 50 mg per kg per day for 2 weeks (no steroids) Group 3. Steroids and symptomatic treatment only
Outcomes	Included in the review: persistence of cysts at 3 to 4 months; number of cysts at baseline and 3 to 4 months; resolution of symptoms at 3 to 4 months; adverse events associated with treatment
Notes	Location: Mexico Source of funding: not stated

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	Quote: "Patients were randomly allocated in three groups..." Decision: unclear, probably done
Allocation concealment?	Unclear risk	Not described Decision: unclear
Blinding? All outcomes	Unclear risk	Not described. Placebos not used. Decision: unclear, probably not done

Sotelo 1988 *(Continued)*

Incomplete outcome data addressed? All outcomes	Low risk	25 participants enrolled and randomized, 25 included in the analysis (100%)
Free of selective reporting?	Low risk	No evidence of selective reporting
Free of other bias?	Low risk	No evidence of other bias

Sotelo 1990

Methods	Randomized controlled trial Duration: dates not stated. Participants followed up for 3 months
Participants	Number: 114 enrolled (67 male, 47 female) Inclusion criteria: adults and children aged 7 to 72 years with parenchymal brain cysts without CT evidence of surrounding inflammation Exclusion criteria: any parenchymal cysticerci surrounded by oedema or showing enhancement after contrast medium administration Type of lesion: viable
Interventions	Group 1. Praziquantel: 50 mg per kg bodyweight for 15 days Group 2. Praziquantel: 50 mg per kg bodyweight for 8 days Group 3. Albendazole: 15 mg per kg bodyweight for 30 days Group 4. Albendazole: 15 mg per kg bodyweight for 8 days
Outcomes	Included in the review: mean number of cysts before and 3 months after treatment; persistence of lesions after 3 months; over 50% lesions disappeared after 3 months; no resolution after 3 months; adverse events associated with treatment, adverse events severe enough to need steroids; persistence of symptoms after 3 months; improvement in signs and symptoms after 3 months
Notes	Location: Mexico Source of funding: supported by the Secretaria de Salud de Mexico

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Adequate sequence generation?	Unclear risk	Quote: "...patients were randomly allocated to one of four treatment groups" Decision: unclear, probably done
Allocation concealment?	Unclear risk	Not described Decision: unclear
Blinding? All outcomes	Unclear risk	Quote: "Evaluation of all CT studies was done at the end of the trial by two groups of clinicians and radiologists who were not aware of the treatment group to which the patients had been allocated" Blinding not described for participants, and placebos not used Decision: unclear, partially done for radiological outcomes

Sotelo 1990 *(Continued)*

Incomplete outcome data addressed? All outcomes	Low risk	114 participants were enrolled and randomized, follow-up data were available for all 114 (100%)
Free of selective reporting?	Low risk	No evidence of selective reporting
Free of other bias?	Low risk	No evidence of other bias

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

Study	Reason for exclusion
Antoniuk 1991	Groups not allocated on a random basis, but according to clinical differences
Bustos 2006	No control group
Carpio 1995	Quasi-randomized
Lopez-Gomez 2001	Comparisons did not meet the inclusion criteria
Marquez-Caraveo 2004	No control group
Medina 1993	Unclear whether groups were randomized; unable to contact the author for clarification
Proano 2006	No control group
Sanchetee 1994	No control group
Thussu 2008	Quasi-randomized

Characteristics of studies awaiting assessment *[ordered by study ID]*

Cruz 1991

Methods	Randomized or quasi-randomized controlled trial Duration: dates not supplied. Participants followed up for 3 months
Participants	Number: 100 enrolled (45 male, 55 female) Inclusion criteria: adults with diagnosed cerebral cysticercosis - any developmental stage of the parasite, localization parenchymous, subarachnoid, or ventricular Exclusion criteria: none stated Type of lesion: embryonal, encephalitic, cystic, calcified, or mixed
Interventions	Group 1. Praziquantel: 50 mg/kg bodyweight daily for 15 days plus 750 mg intravenous dexamethasone over 3 days followed by oral prednisolone every 3 days until day 45 Group 2. Albendazole: 15 mg/ kg for 30 days plus 750 mg intravenous dexamethasone over 3 days followed by oral prednisolone every 3 days until day 45

Cruz 1991 *(Continued)*

Outcomes	Persistence of encephalitic lesions at 3 months; persistence of cysts at 3 months; No change, slight improvement, marked improvement, and freedom from headache at 3 months; no change, slight improvement, marked improvement, and freedom from seizures at 3 months; no change, slight improvement, marked improvement, and freedom from raised intracranial pressure at 3 months; no change, slight improvement, marked improvement, and freedom from miscellaneous signs at 3 months
Notes	Location: Ecuador Source of funding: partially funded by SmithKline Beecham Pharmaceuticals

Pretell 2000

Methods	Controlled clinical trial Duration: dates not stated, 3 months follow up
Participants	Number: 26 (16 males, 10 females) Inclusion criteria: single enhancing lesion in the brain parenchyma Exclusion criteria: pregnancy, other intracranial pathology
Interventions	Group 1: Praziquantel 3 doses (25 mg/ kg) at 2-hour intervals for 1 day Group 2: No antiparasitic therapy
Outcomes	Adverse effects of treatment, radiological resolution of lesions
Notes	Location: Peru Source of funding: the Food and Drug Administration; the Fogarty Foundation/NIH; NIAID/NIH (USA)

Takayanagui 1992

Methods	Controlled clinical trial Duration: dates not stated, follow up for 6 months
Participants	Number: 59 Inclusion criteria: parenchymal non-enhancing cystic lesions Exclusion criteria: lesions with enhancement, encephalitic cysticercosis, intraventricular cysts
Interventions	Group 1: Praziquantel daily doses 50 mg/kg for 21 days Group 2: Albendazole daily doses 20 mg/ kg for 21 days Group 3: No antihelmintic
Outcomes	Number of cysts before and 6 months after treatment, adverse events
Notes	Location: Brazil Source of funding: not stated

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

Gilman 2007

Trial name or title	Randomized study of albendazole in patients with epilepsy due to neurocysticercosis
Methods	Randomized controlled trial
Participants	Number expected: 120 Inclusion criteria: presence of taenia solium infection as demonstrated by serology and head CT, at least 2 spontaneous seizures within the last 6 months, age 16 to 65 Exclusion criteria: more than 20 cysts, prior therapy for cysticercosis, focal neurological or motor deficits, cranial nerve lesions, history of epilepsy for over 5 years, CT head evidence of: arteriovenous malformations, trauma, cerebral infarcts, haemorrhages, focal disease not attributable to cysticercosis, moderate or severe intracranial hypertension, status epilepticus
Interventions	Intervention: Albendazole and dexamethasone for 10 days Control: Placebo for 10 days
Outcomes	Recurrence and number of seizures. Persistence and number of cysts. Participants are followed on day 15 and 30, then every 3 months for 3 years.
Starting date	May 2000
Contact information	Robert H Gilman, John Hopkins University, USA
Study ID	NCT00004403
Notes	Location: USA Registration number: NCT00004403 Source of funding: FDA Office of Orphan Products Development

DATA AND ANALYSES

Comparison 1. Albendazole vs placebo or no drug

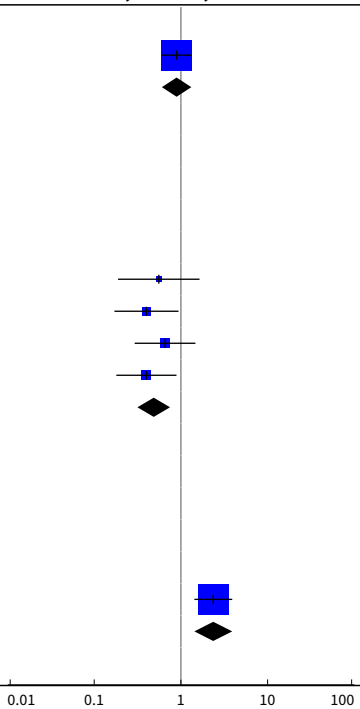
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Recurrence of seizures at trial's final follow-up time	6		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 Viable lesions	1	116	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.60, 1.32]
1.2 Non-viable lesions	4	329	Risk Ratio (M-H, Random, 95% CI)	0.49 [0.32, 0.75]
1.3 Mixed viable and non-viable lesions	1	298	Risk Ratio (M-H, Random, 95% CI)	2.36 [1.43, 3.91]

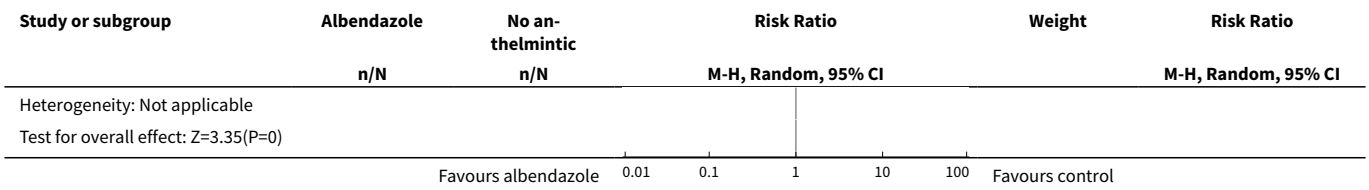
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2 No successful withdrawal of anti-convulsant drugs at follow up	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2.1 Viable lesions	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 All-cause death	2	470	Risk Ratio (M-H, Fixed, 95% CI)	0.83 [0.24, 2.85]
4 Hospital admission, by follow-up period	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
4.1 Start to 3 months	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.2 3 to 6 months	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.3 6 to 12 months	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.4 1 to 2 years	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.5 2 to 3 years	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.6 3 to 4 years	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Symptoms not resolved after 3 months	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
6 Symptoms of encephalopathy (headache, vomiting, or altered sensorium), by period of follow up	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
6.1 Start to 3 months	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.2 3 to 6 months	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.3 6 to 12 months	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.4 1 to 2 years	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.5 2 to 3 years	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.6 3 to 4 years	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Persistence of lesions at trial's final follow-up time (up to 12 months)	9		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
7.1 Viable lesions	2	192	Risk Ratio (M-H, Fixed, 95% CI)	0.56 [0.45, 0.70]
7.2 Non-viable lesions	6	570	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.86, 1.11]
7.3 Mixed viable and non-viable lesions	1	298	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.97, 1.06]
8 Headache during treatment	4	392	Risk Ratio (M-H, Fixed, 95% CI)	1.37 [1.08, 1.73]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.1 Viable lesions	2	139	Risk Ratio (M-H, Fixed, 95% CI)	2.96 [0.49, 17.77]
8.2 Non-viable lesions	1	83	Risk Ratio (M-H, Fixed, 95% CI)	15.82 [0.98, 255.96]
8.3 Mixed viable and non-viable lesions	1	170	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [0.92, 1.42]
9 Headache during treatment - by corticosteroid use	4		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
9.1 Corticosteroids given with albendazole	2	286	Risk Ratio (M-H, Fixed, 95% CI)	1.16 [0.93, 1.44]
9.2 No corticosteroids given	2	106	Risk Ratio (M-H, Fixed, 95% CI)	9.49 [1.40, 64.45]
10 Dizziness during treatment	3	222	Risk Ratio (M-H, Fixed, 95% CI)	3.77 [1.42, 9.97]
11 Nausea, vomiting, or abdominal pain during treatment	4	392	Risk Ratio (M-H, Fixed, 95% CI)	1.40 [1.01, 1.94]
12 Seizures during treatment	5	455	Risk Ratio (M-H, Fixed, 95% CI)	1.62 [0.79, 3.31]

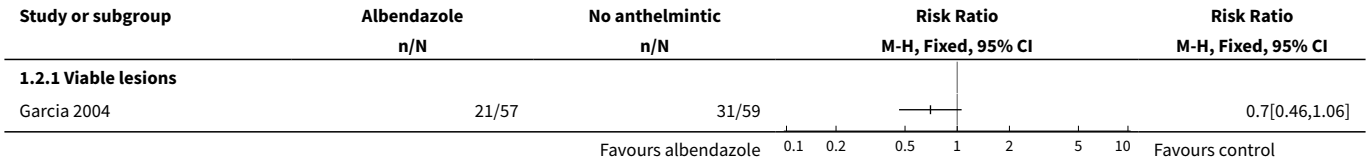
Analysis 1.1. Comparison 1 Albendazole vs placebo or no drug, Outcome 1 Recurrence of seizures at trial's final follow-up time.

Study or subgroup	Albendazole n/N	No anthelmintic n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 Viable lesions					
Garcia 2004	25/57	29/59		100%	0.89[0.6,1.32]
Subtotal (95% CI)	**57**	**59**		**100%**	**0.89[0.6,1.32]**
Total events: 25 (Albendazole), 29 (No anthelmintic)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.57(P=0.57)					
1.1.2 Non-viable lesions					
Gogia 2003	4/32	9/40		16.02%	0.56[0.19,1.64]
Kalra 2003	6/45	15/45		25.86%	0.4[0.17,0.94]
Baranwal 1998	7/31	11/32		28.69%	0.66[0.29,1.47]
Singhi 2004	9/72	10/32		29.43%	0.4[0.18,0.89]
Subtotal (95% CI)	**180**	**149**		**100%**	**0.49[0.32,0.75]**
Total events: 26 (Albendazole), 45 (No anthelmintic)					
Heterogeneity: Tau^2=0; Chi^2=1.02, df=3(P=0.8); I^2=0%					
Test for overall effect: Z=3.26(P=0)					
1.1.3 Mixed viable and non-viable lesions					
Das 2007	42/148	18/150		100%	2.36[1.43,3.91]
Subtotal (95% CI)	**148**	**150**		**100%**	**2.36[1.43,3.91]**
Total events: 42 (Albendazole), 18 (No anthelmintic)					

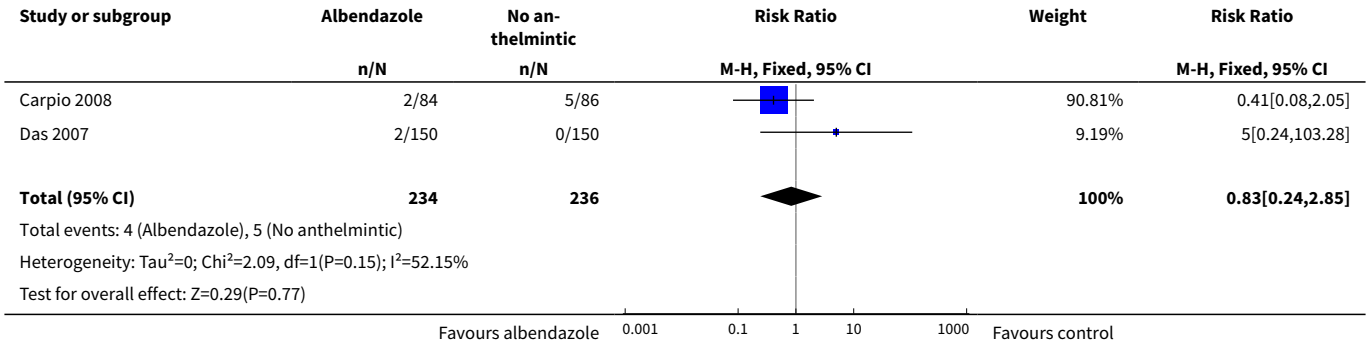




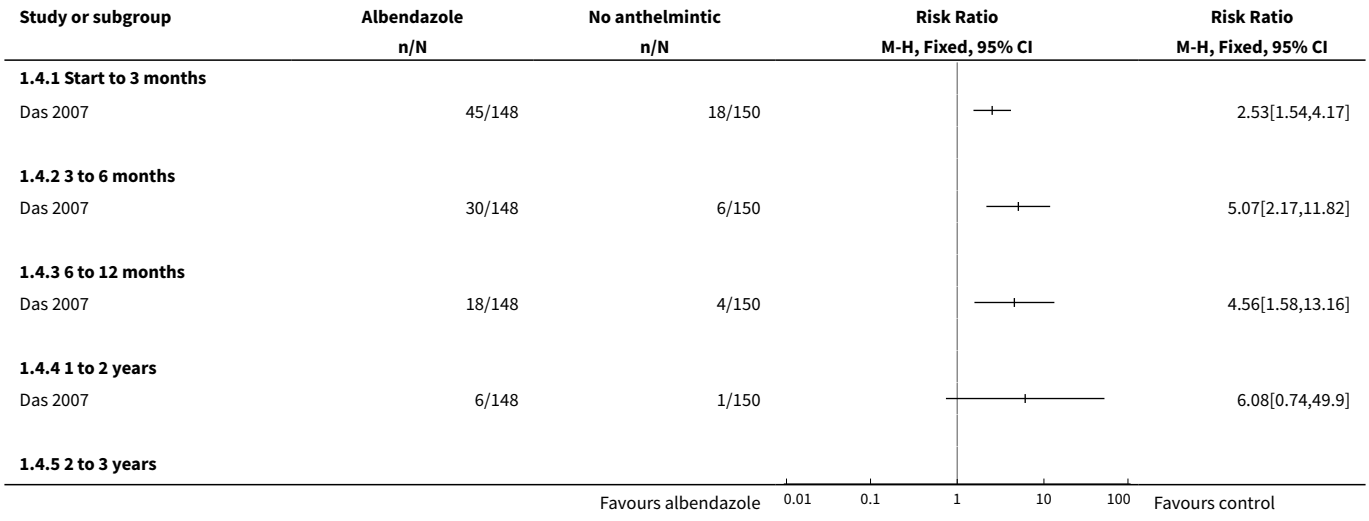
Analysis 1.2. Comparison 1 Albendazole vs placebo or no drug, Outcome 2 No successful withdrawal of anticonvulsant drugs at follow up.

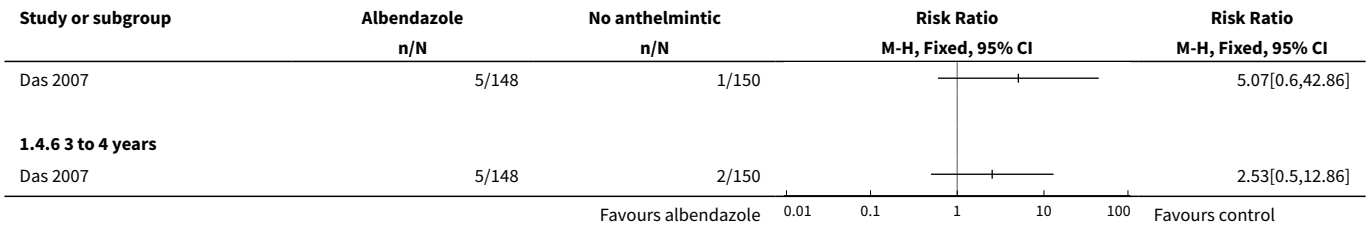


Analysis 1.3. Comparison 1 Albendazole vs placebo or no drug, Outcome 3 All-cause death.

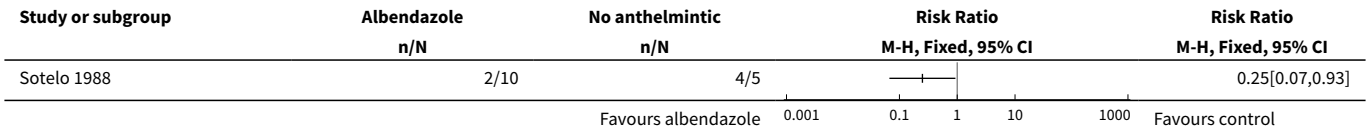


Analysis 1.4. Comparison 1 Albendazole vs placebo or no drug, Outcome 4 Hospital admission, by follow-up period.

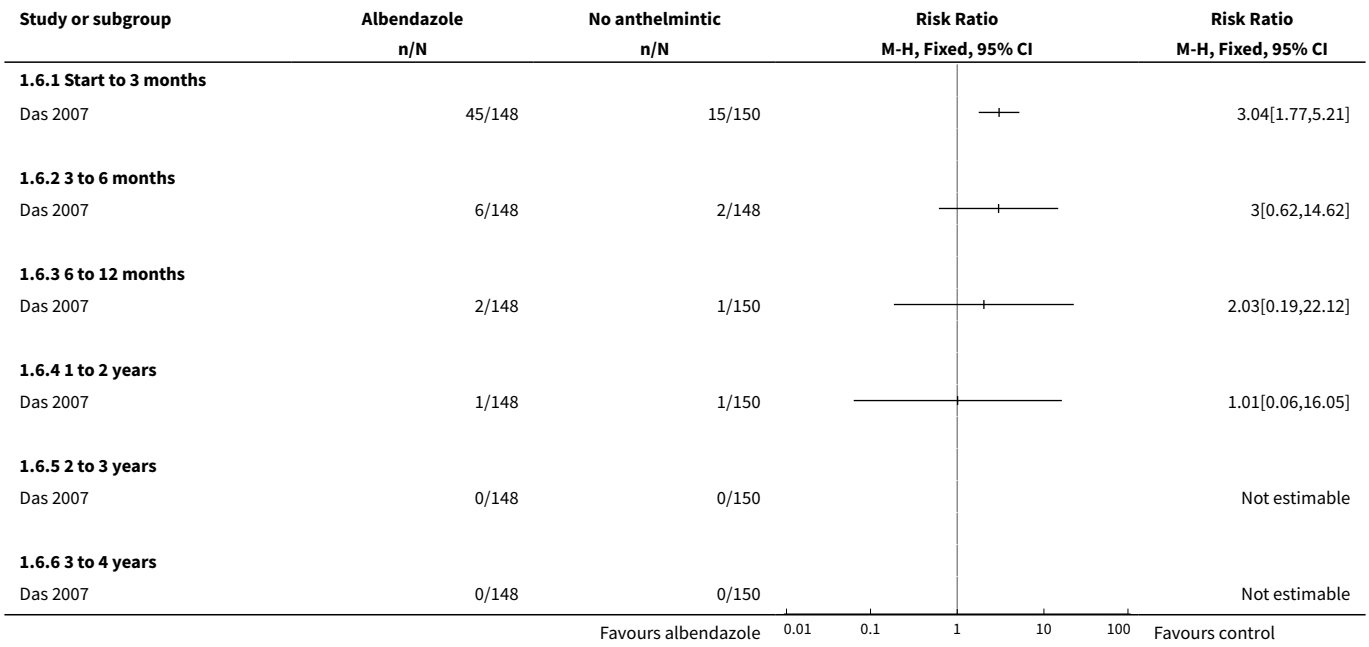




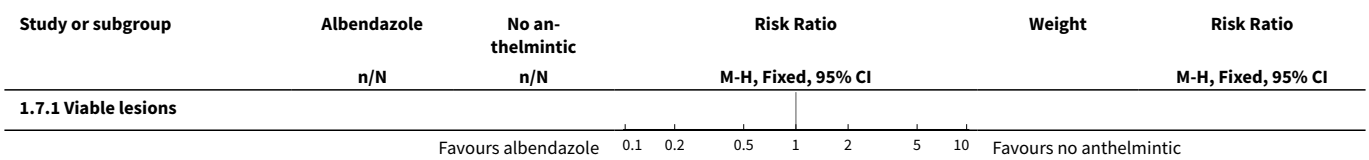
Analysis 1.5. Comparison 1 Albendazole vs placebo or no drug, Outcome 5 Symptoms not resolved after 3 months.

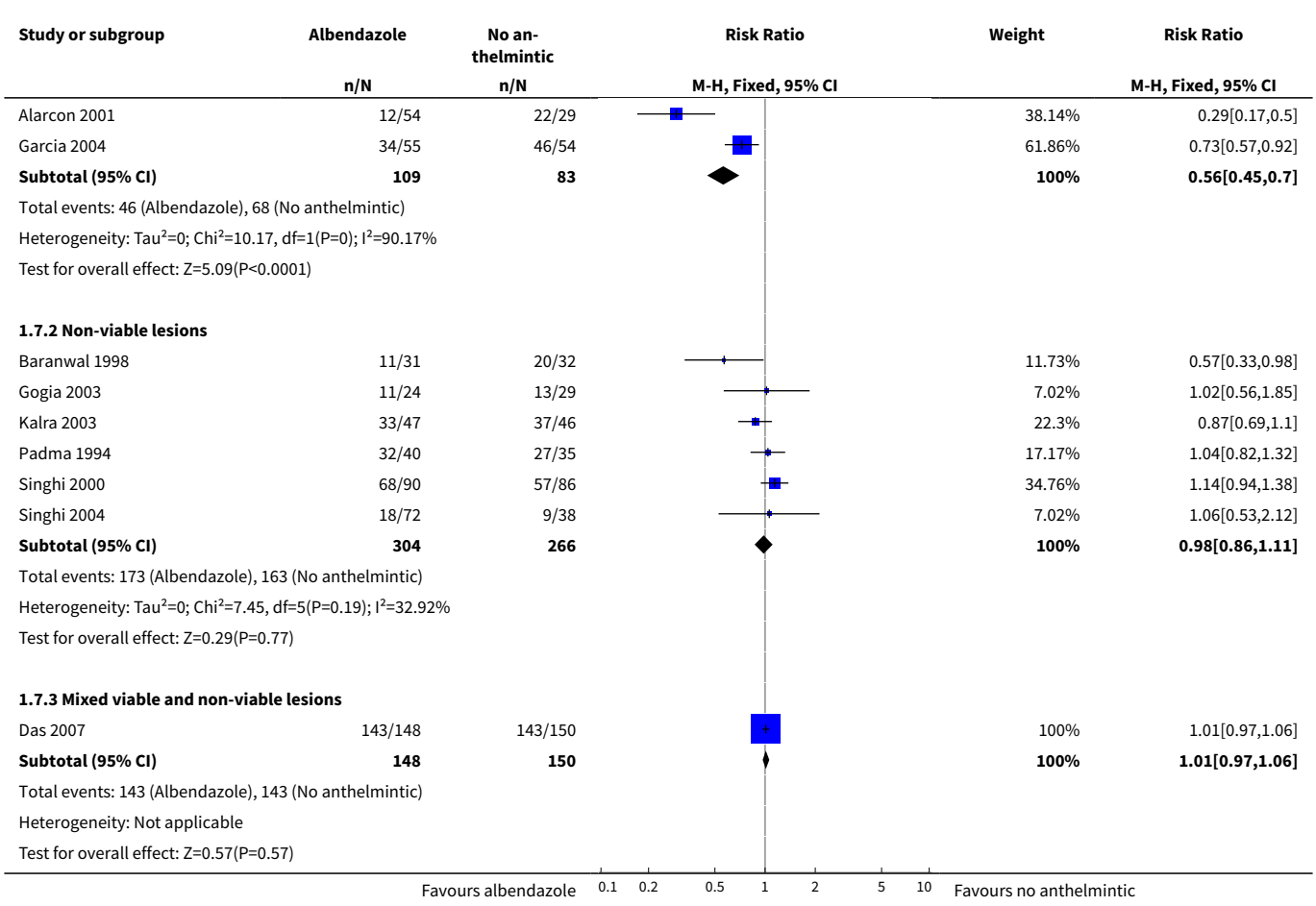


Analysis 1.6. Comparison 1 Albendazole vs placebo or no drug, Outcome 6 Symptoms of encephalopathy (headache, vomiting, or altered sensorium), by period of follow up.

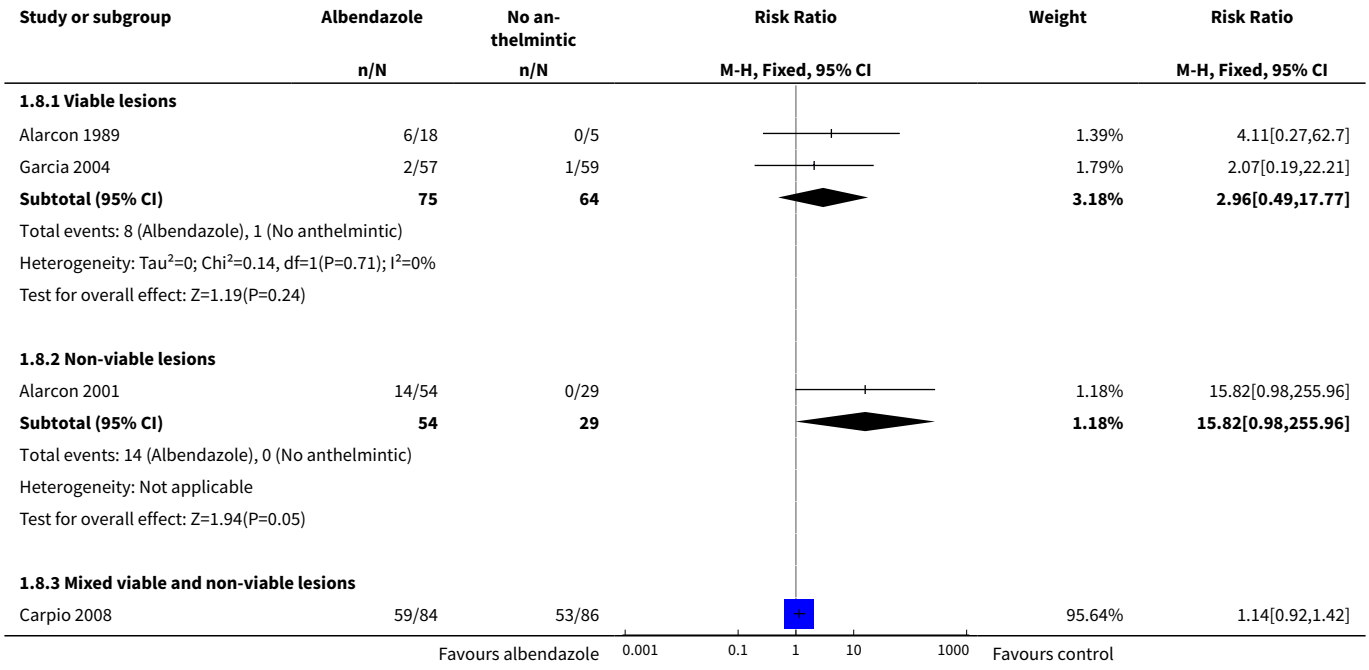


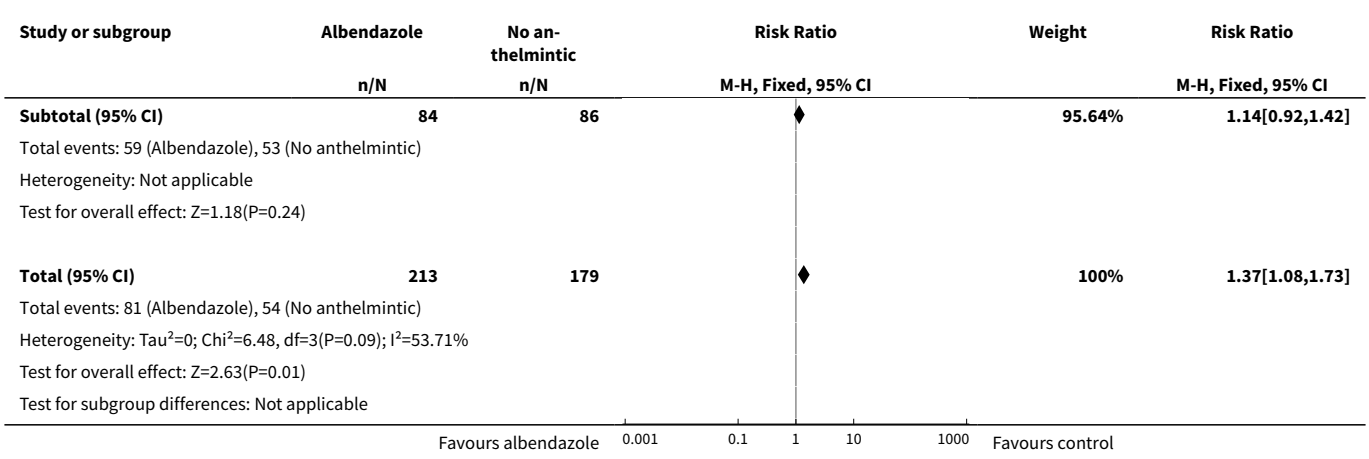
Analysis 1.7. Comparison 1 Albendazole vs placebo or no drug, Outcome 7 Persistence of lesions at trial's final follow-up time (up to 12 months).



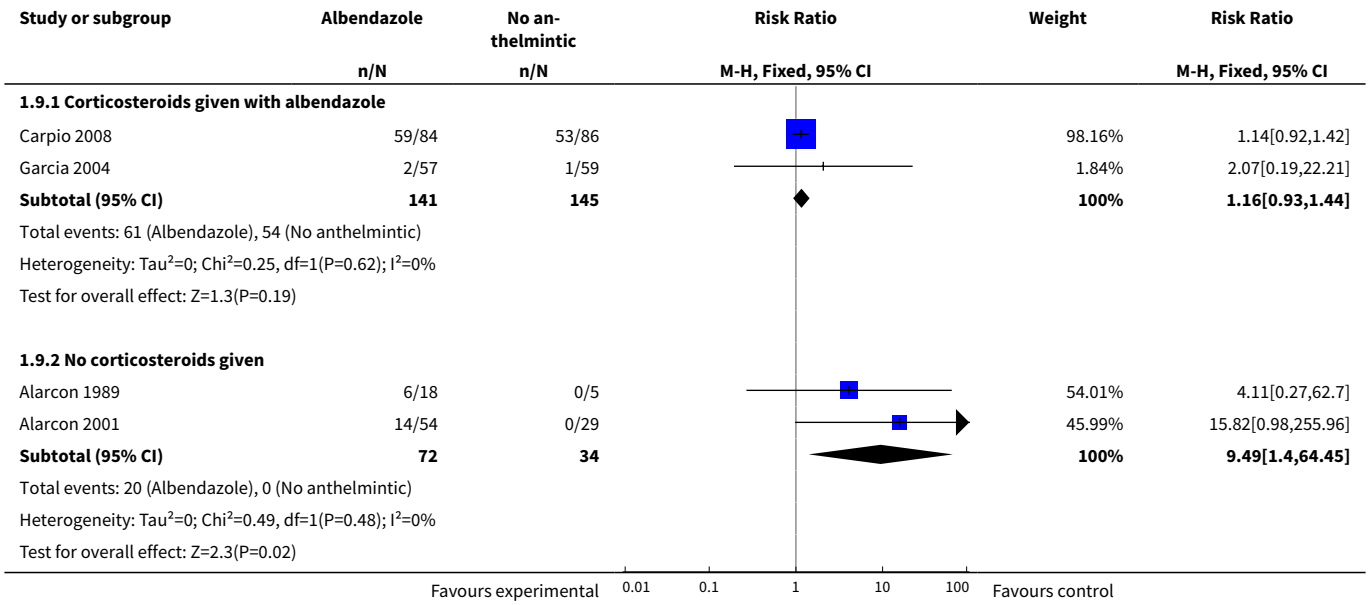


Analysis 1.8. Comparison 1 Albendazole vs placebo or no drug, Outcome 8 Headache during treatment.

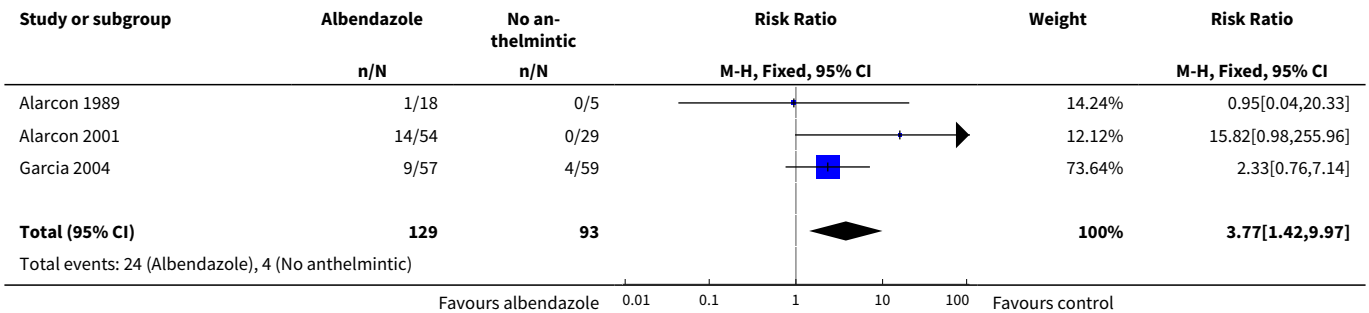


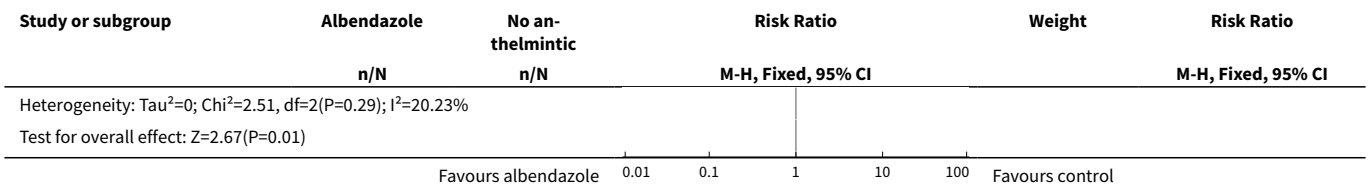


Analysis 1.9. Comparison 1 Albendazole vs placebo or no drug, Outcome 9 Headache during treatment - by corticosteroid use.

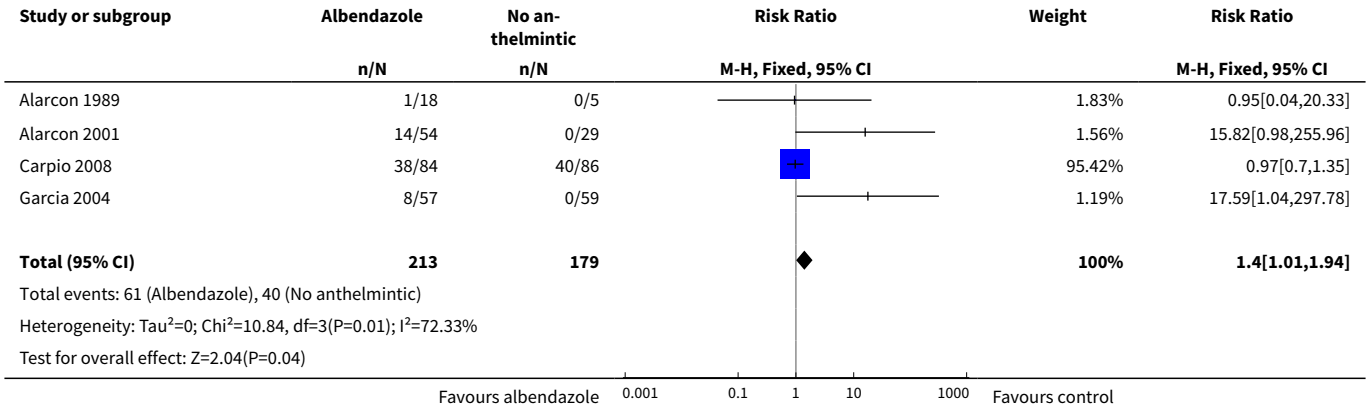


Analysis 1.10. Comparison 1 Albendazole vs placebo or no drug, Outcome 10 Dizziness during treatment.

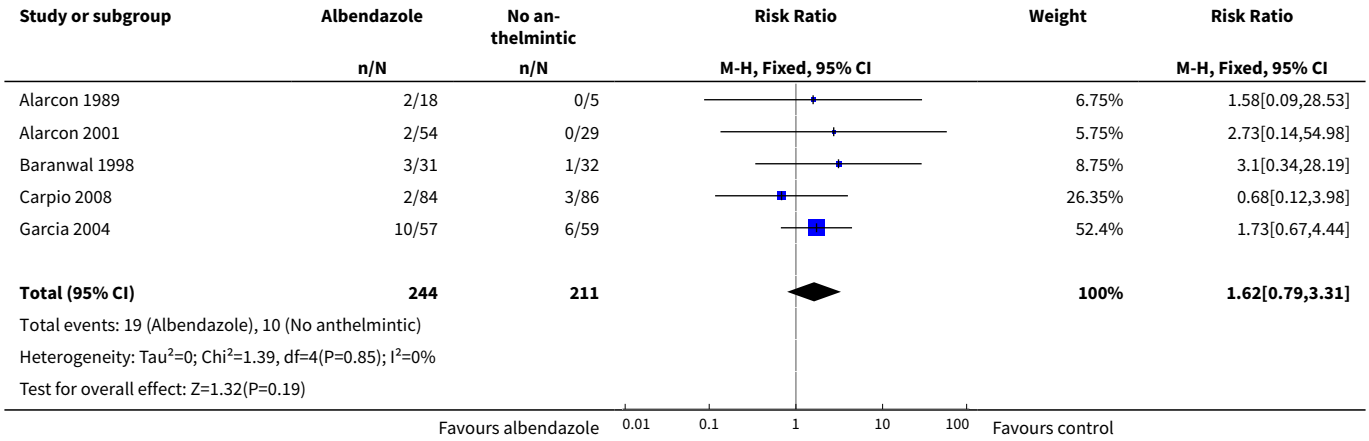




Analysis 1.11. Comparison 1 Albendazole vs placebo or no drug, Outcome 11 Nausea, vomiting, or abdominal pain during treatment.



Analysis 1.12. Comparison 1 Albendazole vs placebo or no drug, Outcome 12 Seizures during treatment.



Comparison 2. Praziquantel vs placebo or no drug

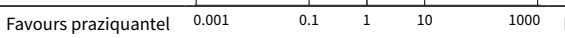
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Symptoms not resolved after 3 months	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2 Persistence of lesions at follow up	1	15	Risk Ratio (M-H, Fixed, 95% CI)	0.35 [0.14, 0.85]
3 No reduction in number of lesions at 3 months	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
4 Any adverse events during treatment	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Analysis 2.1. Comparison 2 Praziquantel vs placebo or no drug, Outcome 1 Symptoms not resolved after 3 months.

Study or subgroup	Praziquantel n/N	No anthelmintic n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Sotelo 1988	3/10	4/5		0.38[0.13,1.06]

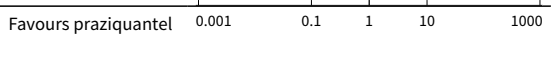
Analysis 2.2. Comparison 2 Praziquantel vs placebo or no drug, Outcome 2 Persistence of lesions at follow up.

Study or subgroup	Praziquantel n/N	No anthelmintic n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Sotelo 1988	3/10	5/5		100%	0.35[0.14,0.85]
Total (95% CI)	**10**	**5**		**100%**	**0.35[0.14,0.85]**
Total events: 3 (Praziquantel), 5 (No anthelmintic)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.31(P=0.02)					



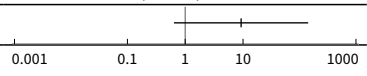
Analysis 2.3. Comparison 2 Praziquantel vs placebo or no drug, Outcome 3 No reduction in number of lesions at 3 months.

Study or subgroup	Praziquantel n/N	No anthelmintic n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Sotelo 1988	1/10	5/5		0.15[0.03,0.67]



Analysis 2.4. Comparison 2 Praziquantel vs placebo or no drug, Outcome 4 Any adverse events during treatment.

Study or subgroup	Praziquantel n/N	No anthelmintic n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Sotelo 1988	8/10	0/5		9.27[0.64,134.31]

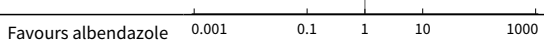


Comparison 3. Albendazole vs praziquantel

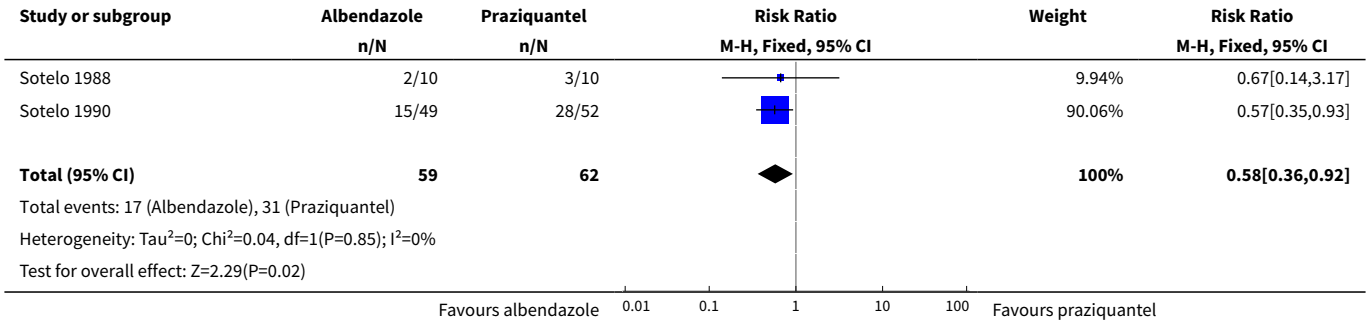
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Recurrence of seizures at follow up	1	19	Risk Ratio (M-H, Fixed, 95% CI)	0.18 [0.01, 3.35]
2 Symptoms not resolved after 3 months	2	121	Risk Ratio (M-H, Fixed, 95% CI)	0.58 [0.36, 0.92]
3 Persistence of lesions at follow up	3	154	Risk Ratio (M-H, Fixed, 95% CI)	0.64 [0.45, 0.91]
4 No reduction in number of lesions at 3 months	3	149	Risk Ratio (M-H, Fixed, 95% CI)	0.41 [0.19, 0.92]
5 Adverse events	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 Headache or vomiting or both	1	20	Risk Ratio (M-H, Fixed, 95% CI)	0.6 [0.19, 1.86]
5.2 Seizures during treatment	1	20	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.02, 7.32]
5.3 Any adverse event	2	134	Risk Ratio (M-H, Fixed, 95% CI)	1.12 [0.94, 1.32]

Analysis 3.1. Comparison 3 Albendazole vs praziquantel, Outcome 1 Recurrence of seizures at follow up.

Study or subgroup	Albendazole n/N	Praziquantel n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Del Brutto 1999	0/10	2/9		100%	0.18[0.01,3.35]
Total (95% CI)	**10**	**9**		**100%**	**0.18[0.01,3.35]**
Total events: 0 (Albendazole), 2 (Praziquantel)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.15(P=0.25)					

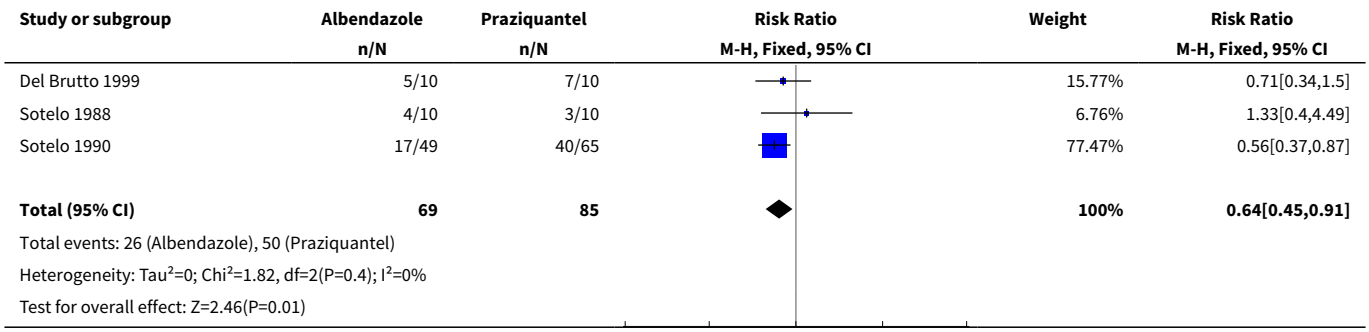


Analysis 3.2. Comparison 3 Albendazole vs praziquantel, Outcome 2 Symptoms not resolved after 3 months.



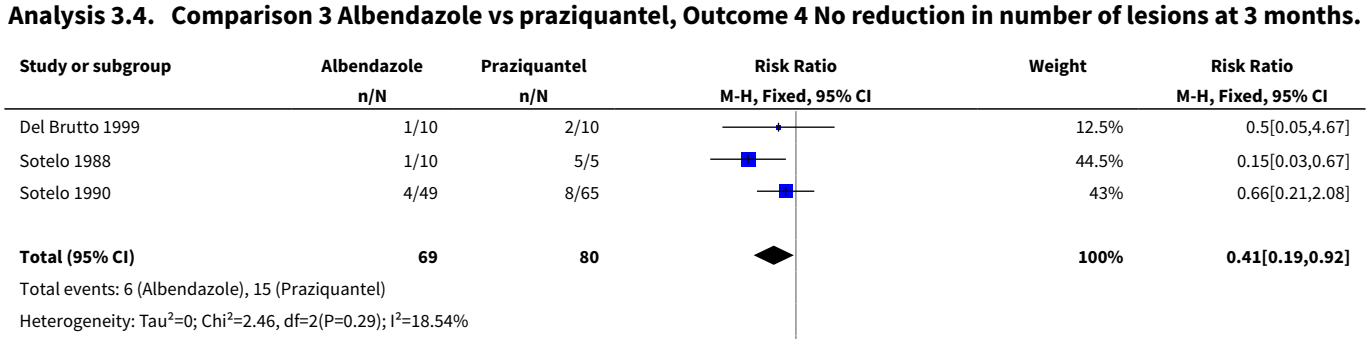
Study or subgroup	Albendazole n/N	Praziquantel n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Sotelo 1988	2/10	3/10		9.94%	0.67[0.14,3.17]
Sotelo 1990	15/49	28/52		90.06%	0.57[0.35,0.93]
Total (95% CI)	**59**	**62**		**100%**	**0.58[0.36,0.92]**
Total events: 17 (Albendazole), 31 (Praziquantel)					
Heterogeneity: Tau^2=0; Chi^2=0.04, df=1(P=0.85); I^2=0%					
Test for overall effect: Z=2.29(P=0.02)					

Analysis 3.3. Comparison 3 Albendazole vs praziquantel, Outcome 3 Persistence of lesions at follow up.



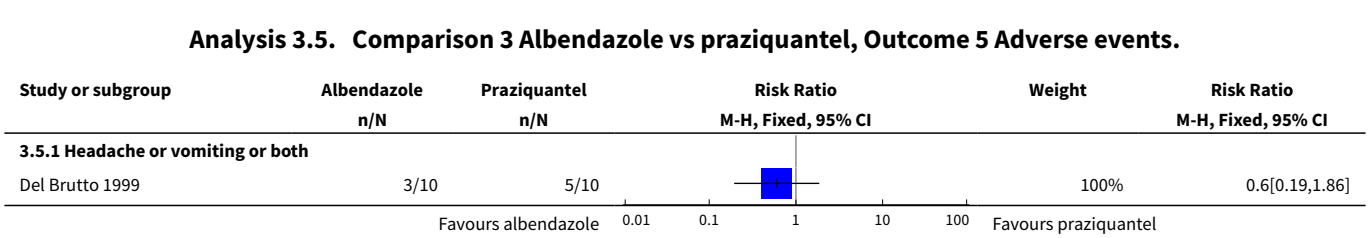
Study or subgroup	Albendazole n/N	Praziquantel n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Del Brutto 1999	5/10	7/10		15.77%	0.71[0.34,1.5]
Sotelo 1988	4/10	3/10		6.76%	1.33[0.4,4.49]
Sotelo 1990	17/49	40/65		77.47%	0.56[0.37,0.87]
Total (95% CI)	**69**	**85**		**100%**	**0.64[0.45,0.91]**
Total events: 26 (Albendazole), 50 (Praziquantel)					
Heterogeneity: Tau^2=0; Chi^2=1.82, df=2(P=0.4); I^2=0%					
Test for overall effect: Z=2.46(P=0.01)					

Analysis 3.4. Comparison 3 Albendazole vs praziquantel, Outcome 4 No reduction in number of lesions at 3 months.

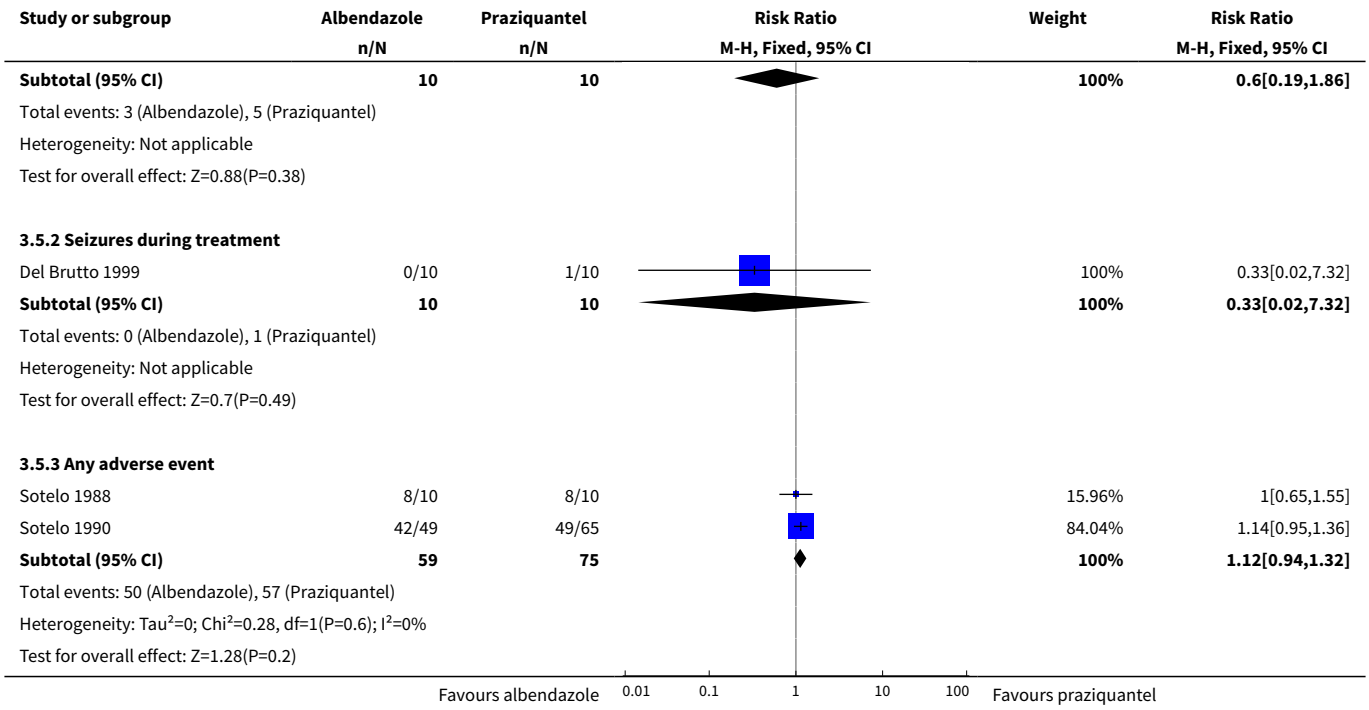


Study or subgroup	Albendazole n/N	Praziquantel n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Del Brutto 1999	1/10	2/10		12.5%	0.5[0.05,4.67]
Sotelo 1988	1/10	5/5		44.5%	0.15[0.03,0.67]
Sotelo 1990	4/49	8/65		43%	0.66[0.21,2.08]
Total (95% CI)	**69**	**80**		**100%**	**0.41[0.19,0.92]**
Total events: 6 (Albendazole), 15 (Praziquantel)					
Heterogeneity: Tau^2=0; Chi^2=2.46, df=2(P=0.29); I^2=18.54%					
Test for overall effect: Z=2.16(P=0.03)					

Analysis 3.5. Comparison 3 Albendazole vs praziquantel, Outcome 5 Adverse events.



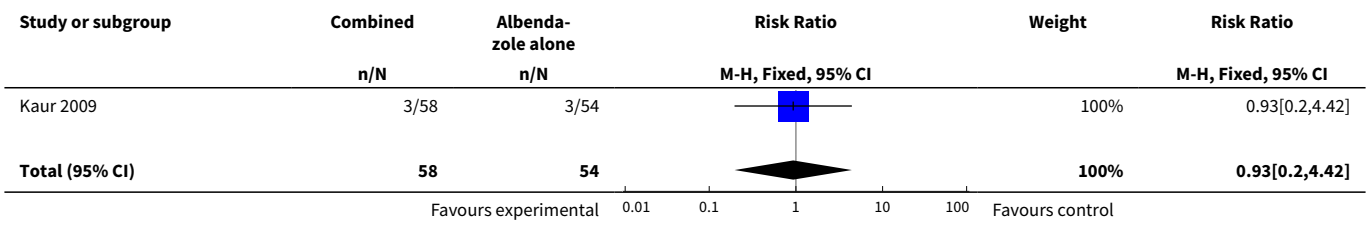
Study or subgroup	Albendazole n/N	Praziquantel n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
3.5.1 Headache or vomiting or both					
Del Brutto 1999	3/10	5/10		100%	0.6[0.19,1.86]

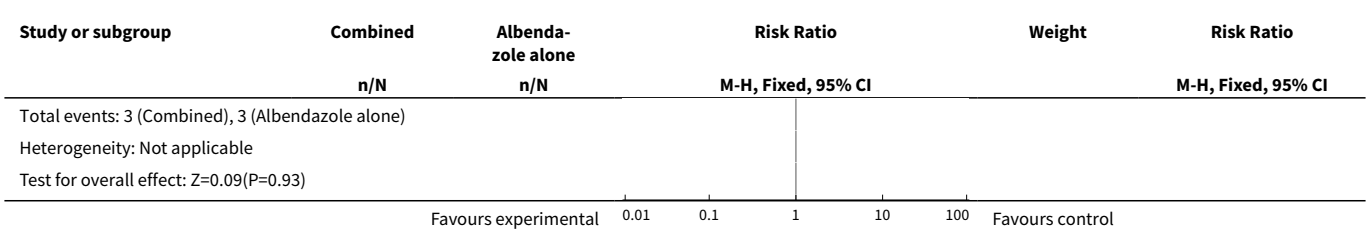


Comparison 4. Albendazole combined with praziquantel vs albendazole alone

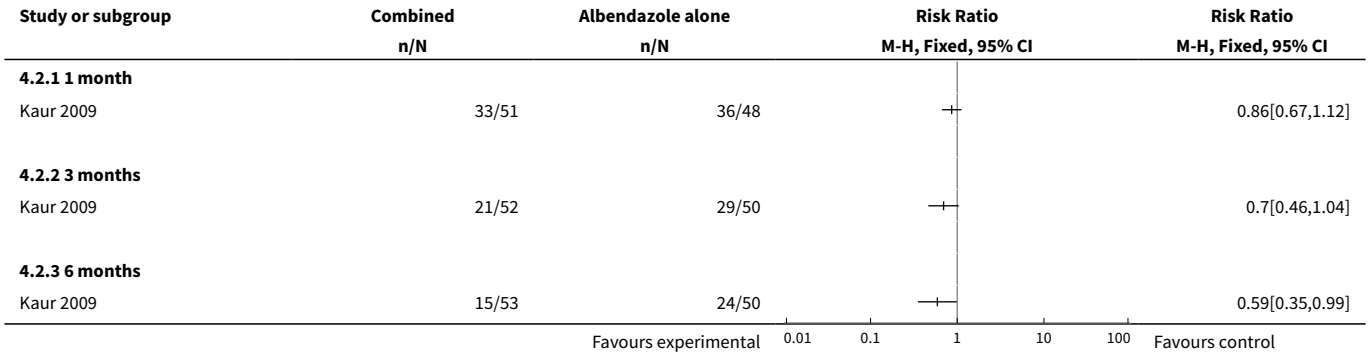
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Recurrence of seizures within 6 months	1	112	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.20, 4.42]
2 Persistence of lesions, by follow-up period	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2.1 1 month	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 3 months	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.3 6 months	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 4.1. Comparison 4 Albendazole combined with praziquantel vs albendazole alone, Outcome 1 Recurrence of seizures within 6 months.





Analysis 4.2. Comparison 4 Albendazole combined with praziquantel vs albendazole alone, Outcome 2 Persistence of lesions, by follow-up period.



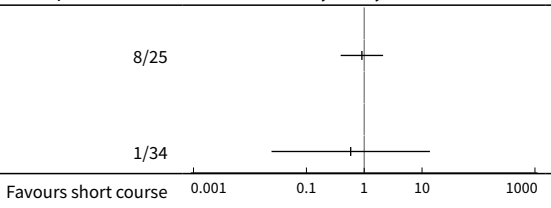
Comparison 5. Albendazole: longer vs shorter duration of treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Symptoms not resolved after 3 months: 8 days vs more than 8 days	2		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1 Viable lesions	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Mixed viable and non-viable lesions	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Persistence of lesions at longest length of follow up: 7 or 8 days vs. more than 7 to 8 days	5		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 Viable lesions	2	103	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.52, 1.76]
2.2 Non-viable lesions	2	159	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.64, 1.50]
2.3 Mixed viable and non-viable lesions	2	79	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.53, 1.36]
3 No reduction in number of lesions at 3 months follow up, by length of treatment comparison	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 8 days vs > 8 days	2	102	Risk Ratio (M-H, Fixed, 95% CI)	0.69 [0.17, 2.74]
4 Adverse events	5		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Headache during treatment	2	72	Risk Ratio (M-H, Fixed, 95% CI)	1.22 [0.58, 2.58]
4.2 Seizures during treatment	2	72	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.15, 6.59]
4.3 Nausea or gastrointestinal symptoms	4	244	Risk Ratio (M-H, Fixed, 95% CI)	0.54 [0.30, 0.97]
4.4 Any adverse event	1	49	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.75, 1.19]
5 Persistence of lesions (viable lesions only): 3 days vs 8 days	1	54	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.37, 2.71]

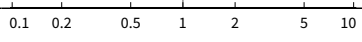
Analysis 5.1. Comparison 5 Albendazole: longer vs shorter duration of treatment, Outcome 1 Symptoms not resolved after 3 months: 8 days vs more than 8 days.

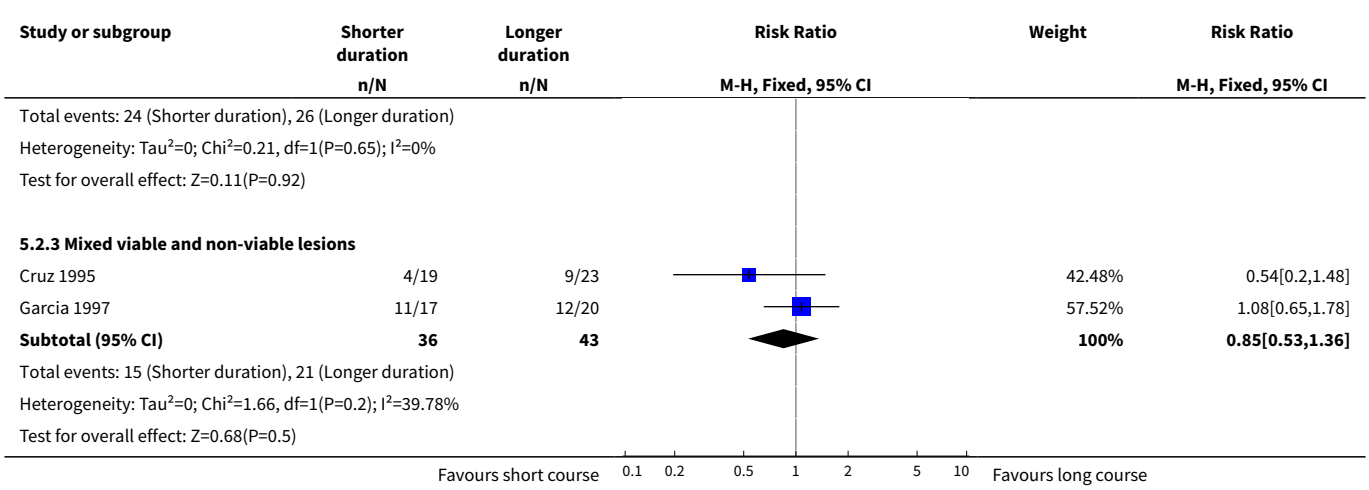
Study or subgroup	Shorter duration n/N	Longer duration n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
5.1.1 Viable lesions				
Sotelo 1990	7/24	8/25		0.91[0.39,2.12]
5.1.2 Mixed viable and non-viable lesions				
Cruz 1995	0/19	1/34		0.58[0.02,13.66]



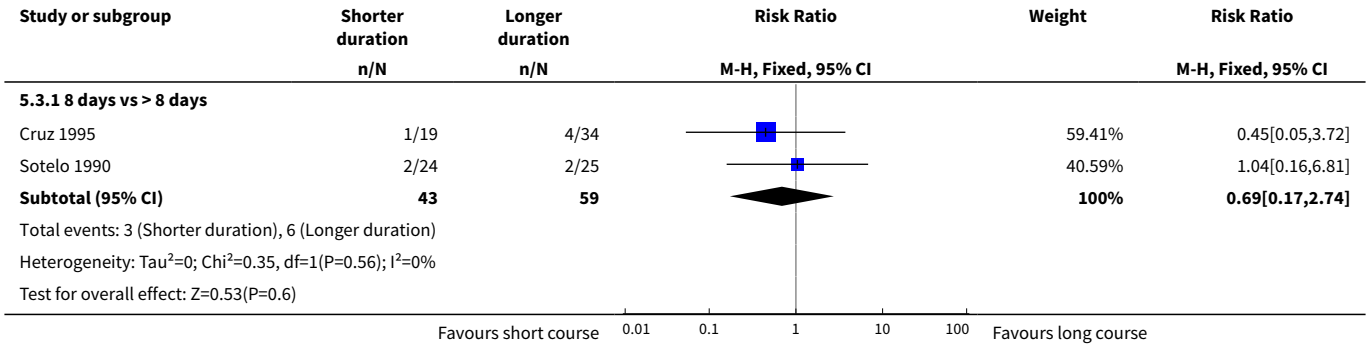
Analysis 5.2. Comparison 5 Albendazole: longer vs shorter duration of treatment, Outcome 2 Persistence of lesions at longest length of follow up: 7 or 8 days vs. more than 7 to 8 days.

Study or subgroup	Shorter duration n/N	Longer duration n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
5.2.1 Viable lesions					
Alarcon 2001	6/27	6/27		40.5%	1[0.37,2.71]
Sotelo 1990	8/24	9/25		59.5%	0.93[0.43,2]
Subtotal (95% CI)	**51**	**52**		**100%**	**0.96[0.52,1.76]**
Total events: 14 (Shorter duration), 15 (Longer duration)					
Heterogeneity: Tau^2=0; Chi^2=0.01, df=1(P=0.9); I^2=0%					
Test for overall effect: Z=0.14(P=0.89)					
5.2.2 Non-viable lesions					
Garcia 1997	11/17	12/20		43.66%	1.08[0.65,1.78]
Singhi 2003	13/62	14/60		56.34%	0.9[0.46,1.75]
Subtotal (95% CI)	**79**	**80**		**100%**	**0.98[0.64,1.5]**

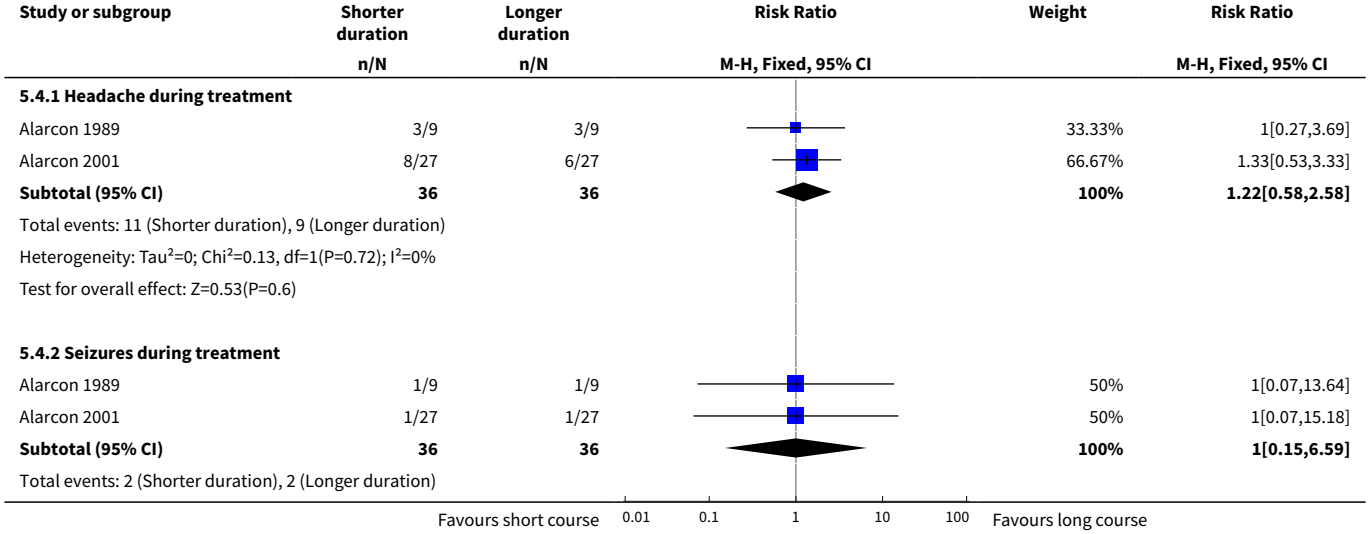


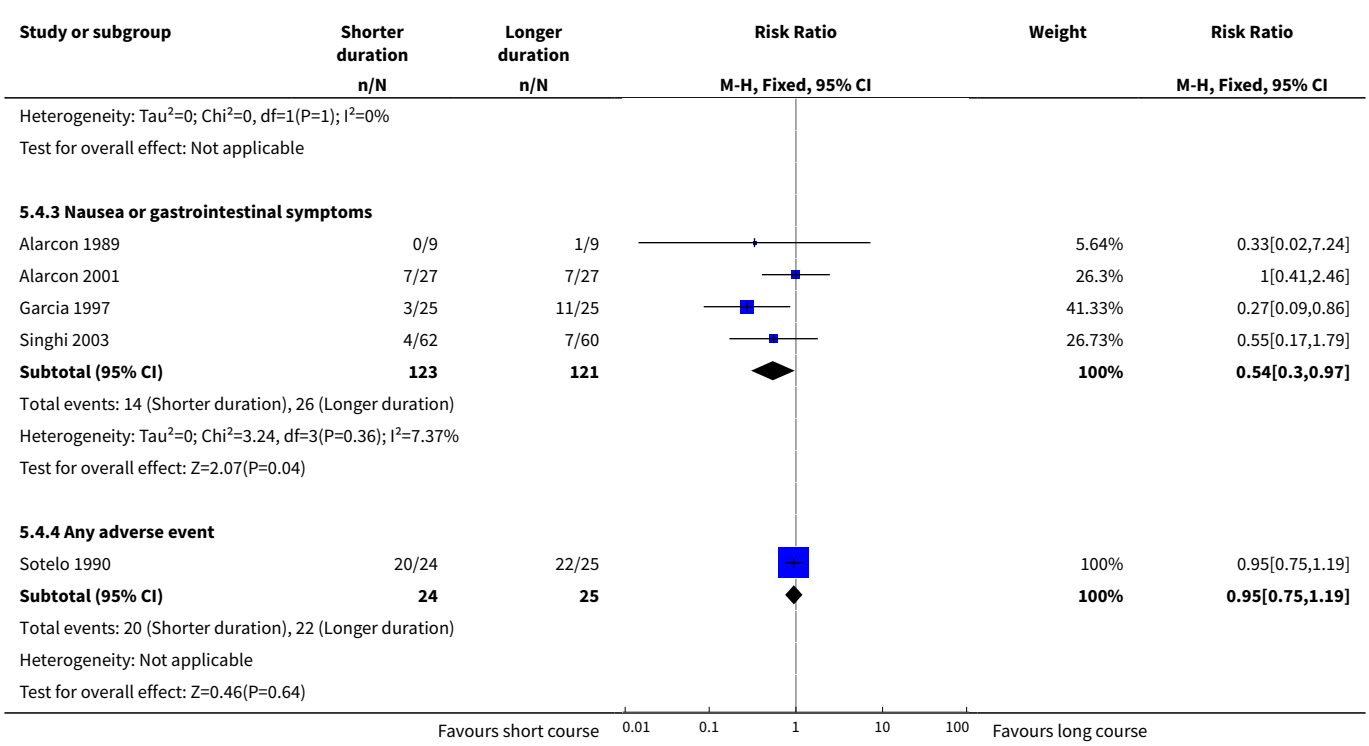


Analysis 5.3. Comparison 5 Albendazole: longer vs shorter duration of treatment, Outcome 3 No reduction in number of lesions at 3 months follow up, by length of treatment comparison.

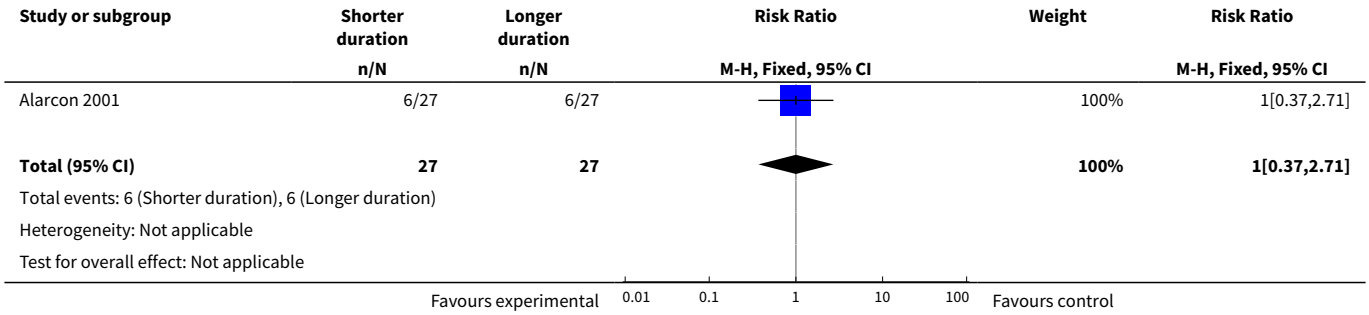


Analysis 5.4. Comparison 5 Albendazole: longer vs shorter duration of treatment, Outcome 4 Adverse events.





Analysis 5.5. Comparison 5 Albendazole: longer vs shorter duration of treatment, Outcome 5 Persistence of lesions (viable lesions only): 3 days vs 8 days.

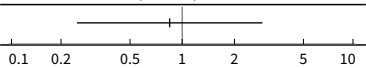


Comparison 6. Albendazole: with corticosteroids vs without corticosteroids

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Recurrence of seizures between weeks 1 and 72	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2 Persistence of lesions at 6 months	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

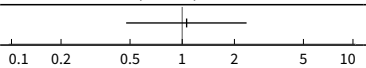
Analysis 6.1. Comparison 6 Albendazole: with corticosteroids vs without corticosteroids, Outcome 1 Recurrence of seizures between weeks 1 and 72.

Study or subgroup	Corticosteroids n/N	No corticosteroids n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Singhi 2004	4/35	5/37		0.85[0.25,2.9]



Analysis 6.2. Comparison 6 Albendazole: with corticosteroids vs without corticosteroids, Outcome 2 Persistence of lesions at 6 months.

Study or subgroup	Corticosteroids n/N	No corticosteroids n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Singhi 2004	9/35	9/37		1.06[0.47,2.35]



APPENDICES

Appendix 1. Search methods: detailed search strategies

Search set	CIDG SR[a]	CENTRAL	MEDLINE[b]	EMBASE[b]	LILACS[b]
1	Taenia solium	NEUROCYSTICERCOSIS	Taenia solium	Taenia solium	Taenia solium
2	cysticercosis	Taenia solium	cysticercosis	neurocysticercosis	neurocysticercosis
3	neurocysticercosis	1 or 2	neurocysticercosis	BRAIN CYSTICERCOSIS	1 or 2
4	—	—	1 or 2 or 3	1 or 2 or 3	albendazole
5	—	—	albendazole	albendazole	praziquantel
6	—	—	praziquantel	praziquantel	metrifonate
7	—	—	pyquiton	metrifonate	4 or 5 or 6
8	—	—	metrifonate	5 or 6 or 7	3 and 7
9	—	—	5 or 6 or 7 or 8	3 and 8	—
10	—	—	4 and 9	Limit 9 to human	—
11	—	—	Limit 10 to human	—	—

[a]Cochrane Infectious Diseases Group Specialized Register.
[b]Search terms used in combination with the search strategy for retrieving trials developed by The Cochrane Collaboration (Lefebvre 2008); upper case: MeSH or EMTREE heading; lower case: free text term.

Appendix 2. Trial description: lesion type

Lesion type	No. trials	Trial
Viable, non-enhancing, or without surrounding oedema, or, if mixed, at least one viable lesion per participant	7	Alarcon 1989; Sotelo 1990; Garcia 1997; Del Brutto 1999; Alarcon 2001; Garcia 2004
Non-viable, enhancing or with surrounding oedema	9	Padma 1994; Baranwal 1998; Singhi 2000; Gogia 2003; Kalra 2003; Singhi 2003; Singhi 2004; De Souza 2009; Kaur 2009
Any stage of lesion(s) or types of lesion not described	7	Sotelo 1988; Cruz 1995; Padma 1995; Garcia 1997; Gongora-Rivera 2006; Carpio 2008; Das 2007

WHAT'S NEW

Date	Event	Description
15 February 2010	Amended	corrected search dates in abstract
1 September 2009	New citation required and conclusions have changed	This review replaces an earlier Cochrane Review 'Drugs for treating neurocysticercosis (tapeworm infection of the brain)' (Salinas 1999), which was withdrawn from *The Cochrane Library* in 2005 due to the availability of new trial evidence. A new team of authors worked on this review. The criteria for inclusion of trials has changed.

HISTORY

Protocol first published: Issue 4, 2006
Review first published: Issue 2, 1996

Date	Event	Description
5 May 2009	New search has been performed	Search updated; see 'Search methods for identification of studies'.

CONTRIBUTIONS OF AUTHORS

The selection of trials for inclusion, assessment of methodological quality, and data extraction was undertaken as indicated in the methods of the review. The analyses were undertaken mainly by Katharine Abba, in consultation with the other two authors. All three authors contributed to the discussion and conclusions of the review.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- Liverpool School of Tropical Medicine, UK.
- Apollo Hospital, Chennai, India.

External sources

- Department for International Development, UK.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

An additional outcome was added: 'resolution of symptoms' as this was an important outcome presented in reports of some of the included trials. An additional category was also added as a control group intervention in the inclusion criteria: 'another dose or duration of anthelmintic', as it became apparent that these comparisons would be important.

INDEX TERMS

Medical Subject Headings (MeSH)

Adrenal Cortex Hormones [therapeutic use]; Albendazole [therapeutic use]; Anticestodal Agents [*therapeutic use]; Brain Diseases [*drug therapy] [parasitology]; Neurocysticercosis [*drug therapy]; Praziquantel [therapeutic use]; Randomized Controlled Trials as Topic; Trichlorfon [therapeutic use]

MeSH check words

Adult; Child; Humans