

Acupuncture for epilepsy (Review)

Cheuk DKL, Wong V



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Acupuncture for epilepsy (Review)

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[Intervention Review]

Acupuncture for epilepsy

Daniel KL Cheuk¹, Virginia Wong¹

¹Department of Pediatrics and Adolescent Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong SAR, China

Contact address: Daniel KL Cheuk, Department of Pediatrics and Adolescent Medicine, The University of Hong Kong, Queen Mary Hospital, Pokfulam Road, Hong Kong SAR, China. cheukkld@hkucc.hku.hk.

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ABSTRACT

Background

Seizures are poorly controlled in many people with epilepsy despite adequate current antiepileptic treatments. There is increasing interest in alternative therapies such as acupuncture; however, it remains unclear whether the existing evidence is rigorous enough to support the use of acupuncture. This is an update of a Cochrane review first published in 2006.

Objectives

To determine the effectiveness and safety of acupuncture in people with epilepsy.

Search strategy

We searched the Cochrane Epilepsy Group's Specialized Register (March 2008) and the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* Issue 1, 2008), MEDLINE, EMBASE, and other databases from inception to March 2008. Reference lists from relevant trials were reviewed. No language restrictions were imposed.

Selection criteria

Randomised controlled trials comparing acupuncture with placebo or sham treatment, antiepileptic drugs or no treatment; or comparing acupuncture plus other treatments with the same other treatments. involving people of any age with any type of epilepsy.

Data collection and analysis

Two review authors independently extracted trial data and assessed trial quality.

Main results

Eleven small trials with 914 participants, of generally poor methodological quality and with short follow up met the inclusion criteria. Ten trials were carried out in China and one in Norway.

Two trials found that more children treated with needle acupuncture plus Chinese herbs achieved 75% or greater reduction in seizure frequency (RR 1.52, 95% CI 1.12 to 2.05) and 50% or greater reduction in seizure duration (pooled RR 1.29, 95% CI 1.03 to 1.62) compared with Chinese herbs alone. However, after combining the results of four trials that compared the treatment group with a control group that could yield the net effect of needle acupuncture, we found that there was no significant difference between the treatment and the control groups in any reduction of seizure frequency (pooled RR 1.05, 95% CI 0.97 to 1.17). Compared to phenytoin, the pooled results from two trials showed that patients who received needle acupuncture appeared more likely to achieve

75% or greater reduction in seizure frequency (pooled RR 2.14, 95% CI 1.47 to 3.1). Compared to valproate, the pooled results from three trials showed catgut implantation at acupoints appeared more likely to result in 75% or greater reduction in seizure frequency (pooled RR 2.33, 95% CI 1.01 to 5.36).

Authors' conclusions

The current evidence does not support acupuncture as a treatment for epilepsy.

PLAIN LANGUAGE SUMMARY

Acupuncture for epilepsy

Patients with epilepsy are currently treated with antiepileptic drugs, but a significant number of people continue to have seizures and many experience adverse effects to the drugs. As a result there is increasing interest in alternative therapies and acupuncture is one of those. Eleven studies were included, however acupuncture has not yet been proven to be effective and safe for treating people with epilepsy.

BACKGROUND

Epilepsy is a common neurological disorder with an estimated annual incidence of 50 per 100,000 and a prevalence of 5 to 10 per 1000 in developed countries (Sander 1996). About two to three per cent of the general population will be given a diagnosis of epilepsy at some time in their lives (Hauser 1993), the majority of whom will go into remission. About 70% of patients with epilepsy become seizure free but up to 30% continue to have seizures despite treatment with adequate doses of antiepileptic drugs (AEDs), that is, become drug resistant. Hence there is a constant search for newer modes of treatment. Furthermore, the commonly used AEDs can have adverse effects such as causing gingival hyperplasia; gastrointestinal disturbances (nausea, vomiting); osteoporosis, osteomalacia, and bone marrow toxicity; hepatotoxicity; nephrotoxicity; neurological symptoms (ataxia, dizziness, diplopia, somnolence); cognitive, mood and behavioural disturbances; endocrine dysfunction; teratogenicity; as well as allergic reactions including skin rashes, toxic epidermal necrolysis or Steven Johnson syndrome (Holland 2001). Other treatments of epilepsy such as a ketogenic diet, use of a vagal nerve stimulator and epilepsy surgery have their own limitations and complications. As a result, many people are turning to alternative complementary therapy for treatment of their condition and acupuncture is one of the popular options.

Acupuncture is a procedure in which specific body areas, the meridian points, are pierced with fine needles for therapeutic purposes. It is one of the major modalities of treatment in traditional Chinese medicine. Its use can be traced back more than 2000 years

in China (Wu 1996). Apart from the traditional needle acupuncture various forms of acupuncture have been developed, including electroacupuncture, laser acupuncture, acupressure, and catgut implantation to acupoints. Being a relatively simple, inexpensive and safe treatment, acupuncture has been well accepted by inhabitants in China and people worldwide who are of Chinese origin. Acupuncture is widely used by many Chinese practitioners in various neurological disorders as an alternative treatment approach (Johansson 1993). It is also increasingly practiced in some Western countries (NIH 1998).

Acupuncture involves complex theories of regulation of the five elements (fire, earth, metal, water, and wood), yin and yang, Qi, and blood and body fluids. By stimulating various meridian points disharmony and dysregulation of organ systems is corrected to relieve symptoms and restore natural internal homeostasis (Maciocia 1989). Many studies in animals and humans have demonstrated that acupuncture can cause multiple biological responses (Wang 2001). These responses can occur both locally or close to the site of application (Jansen 1989) and at a distance, mediated mainly by sensory neurons to many structures within the central nervous system (Magnusson 1994). The result is activation of pathways affecting various physiological systems in the brain as well as in the periphery (Liu 2004; Middlekauff 2004; Sun 2001).

There are both anecdotal reports and animal studies that suggest acupuncture may inhibit seizures. In an experiment of penicillin-induced epilepsy in rats electroacupuncture was found to inhibit

seizures, possibly through decreasing neuronal and inducible nitric oxide synthase transcription in the hippocampus (Huang 1999; Yang 2000). Antagonism of GABA-A receptors was found to attenuate the antiepileptic effect of electroacupuncture, whilst electroacupuncture acted synergistically with the antagonists of non-N-methyl-D-aspartate (non-NMDA) receptors (Liu 1997). Electroacupuncture may theoretically have an effect on epilepsy by increasing the release of inhibitory neurotransmitters (Liu 1995; Wu 1992), such as serotonin, GABA, or opioid peptides. Beneficial effects on human epilepsy have been reported in uncontrolled studies (Shi 1987; Yang 1990). Reports on the effects of acupuncture on electroencephalographic recordings have, however, been conflicting (Chen 1983; Kloster 1999) and it is, therefore, unclear whether the existing evidence is scientifically rigorous enough to recommend acupuncture for routine use in people with epilepsy. We examined the efficacy and safety of acupuncture therapy in epilepsy in a systematic review of randomised controlled trials.

This is an update of a Cochrane review first published in 2006.

OBJECTIVES

To determine the effectiveness and safety of acupuncture in people with epilepsy.

The following hypotheses were investigated.

- (1) Acupuncture can increase the probability of becoming seizure free.
- (2) Acupuncture can reduce the frequency and duration of seizures.
- (3) Acupuncture can improve quality of life.
- (4) Acupuncture is associated with adverse effects.

METHODS

Criteria for considering studies for this review

Types of studies

- (1) Randomised controlled clinical trials using truly random or quasi-random allocation of treatment were included in the review.
- (2) Studies comparing acupuncture with at least one control group that used no treatment, placebo treatment, sham treatment or AED were included.
- (3) Studies were single or double blind or unblinded.
- (4) Parallel group or crossover designs were included.

Types of participants

People with an epilepsy syndrome of any type (Commission 1989), who were of any age and of either gender.

Types of interventions

Trials evaluating all forms of acupuncture therapy including acupuncture, laser acupuncture, electroacupuncture or catgut implantation at acupoints were to be included in the review regardless of times of treatment and length of treatment period. Both traditional acupuncture in classical meridian points and contemporary acupuncture in non-meridian or trigger points were included regardless of the source or methods of stimulation (for example hand, needle, laser, electrical stimulation, or catgut implantation). Acupuncture could be given alone or as an add-on to antiepileptic drugs (AEDs).

The control interventions considered included placebo acupuncture, sham acupuncture or AEDs. Placebo acupuncture refers to a needle attached to the skin surface (not penetrating the skin but at the same acupoints) (Furlan 1999). Sham acupuncture refers to a needle placed in an area close to, but not in, acupuncture points (Furlan 1999) or subliminal skin electrostimulation via electrodes attached to the skin (SCSSS 1999).

The treatment comparisons investigated in this review are listed below.

- (1) Acupuncture alone compared to no treatment.
- (2) Acupuncture alone compared with placebo or sham treatment or antiepileptic medication.
- (3) Acupuncture in addition to baseline antiepileptic medication compared with baseline antiepileptic medication alone.
- (4) Acupuncture in addition to baseline antiepileptic medication compared with placebo or sham treatment in addition to baseline antiepileptic medication.

Trials that only compared different forms of acupuncture were excluded since we did not intend to investigate whether one type of acupuncture was more effective than another. Trials that compared acupuncture in addition to herbal medicines or other alternative therapies with antiepileptic drug treatment were also excluded since such trial cannot resolve which component of the combination, i.e., acupuncture or herbs, is more effective than control treatment.

Types of outcome measures

Primary outcomes

- (1) Seizure freedom.
- (2) Satisfactory seizure control: 50% or greater reduction in seizure frequency.
- (3) Absolute or percentage reduction in seizure frequency and duration.

(4) Improved quality of life if assessed by validated, reliable scales.

Secondary outcomes

(1) Incidence of adverse or harmful effects:

- (a) sedation;
 - (b) cognitive side-effects;
 - (c) allergic reactions - skin rashes, Steven Johnson syndrome.
- (2) Withdrawals due to side effects or due to lack of efficacy.

Search methods for identification of studies

We searched the Cochrane Epilepsy Group's Specialized Register (March 2008). This register contains reports of trials identified from regular searches of the Cochrane Central Register of Controlled Trials (CENTRAL) and MEDLINE. Relevant reports are also identified by handsearching selected journals and conference proceedings. A more detailed description of this activity is given in the 'Specialized Register' section of the [Cochrane Epilepsy Group](#) module.

In addition, we searched MEDLINE on Ovid (1966 to 2008), EMBASE (1980 to 2008), CINAHL (1982 to 2008), AMED (the Allied and Complementary Medicine Database, 1985 to 2008), TCMLARS (Traditional Chinese Medical Literature Analysis and Retrieval System, 1984 to 2008) and the China Biological Medicine Database (CBM-disc, 1979 to 2008). The latter two are databases of Chinese biomedical research literature. We also searched the Chinese Acupuncture Trials Register and the National Institute of Health Clinical Trials Database.

We searched the reference lists of all relevant papers for further studies. In addition, we contacted colleagues and experts in the field to ascertain any unpublished or ongoing studies. There were no language restrictions either in the search or inclusion of studies. However, multiple publications reporting the same groups of patients or subsets were to be excluded.

Data collection and analysis

Two review authors (Daniel Ka Leung Cheuk and Virginia Wong) independently assessed trials for inclusion, extracted trial data and assessed trial quality. Any disagreement between the two review authors was resolved by mutual discussion.

Extraction of trial data

We extracted the following data, if available.

- (1) Study methods:
 - (a) design (for example parallel or crossover design);
 - (b) randomisation method (including list generation);
 - (c) method of allocation concealment;
 - (d) blinding method;

(e) stratification factors.

(2) Participants:

- (a) inclusion and exclusion criteria;
- (b) number (total and per group);
- (c) age and sex distribution;
- (d) seizure type and epilepsy syndrome;
- (e) duration of epilepsy;
- (f) etiology of epilepsy;
- (g) presence of neurological signs;
- (h) number and types of AEDs taken.

(3) Intervention and control:

- (a) type of acupuncture;
- (b) details of treatment regime including duration of treatment;
- (c) type of control;
- (d) details of control treatment including drug dosage;
- (e) washout period if crossover design.

(4) Follow-up data:

- (a) duration of follow up;
- (b) dates of treatment withdrawal and reasons for treatment withdrawal;
- (c) withdrawal rates.

(5) Outcome data:

as described above.

(6) Analysis data:

- (a) methods of analysis (intention-to-treat and per protocol analysis);
- (b) comparability of groups at baseline (yes or no);
- (c) statistical techniques.

Quality assessment

We used the Jadad validated quality scale ([Jadad 1996](#)) to rate the quality of the studies.

Data analysis

Relative risks with 95% confidence intervals (CI) were used for binary outcomes. Weighted mean differences with 95% CI were used for continuous outcomes. All analyses included all participants in the treatment groups to which they were allocated (that is intention-to-treat analyses).

We assessed the clinical heterogeneity by comparing the distribution of important participant factors between trials (age, gender, seizure type, duration of epilepsy, number of AEDs taken at time of randomisation) and trial factors (randomisation concealment, blinding, losses to follow up). Statistical heterogeneity was assessed by the I^2 test where a value greater than 50% would be considered to indicate significant heterogeneity.

Where the interventions were the same, or similar enough, and if there was no important clinical heterogeneity we planned to syn-

these results in a meta-analysis. If no significant statistical heterogeneity was present, the data would be synthesised using a fixed-effect model, otherwise a random-effects analysis was planned.

We planned to assess the impact of important patient characteristics including seizure type, duration and etiology of epilepsy and presence of neurological signs upon outcome, although insufficient data were available to do so. We also planned to undertake sensitivity analyses including: (i) all studies; (ii) only those using adequate methods of allocation concealment, such as sealed opaque envelopes or telephone randomisation.

RESULTS

Description of studies

See: [Characteristics of included studies](#); [Characteristics of excluded studies](#).

Fourteen randomised controlled trials were identified by the search strategy, eleven of which met the inclusion criteria (Deng 2001; Kloster 1999; Leng 2000; Ma 2001; Peng 2003; Shi 2001; Xiong 2003; Yu 1999; Zhang 2006; Zhou 2000; Zhuang 2006). The reasons for exclusion of the remaining three studies (Deng 2001b; Kuang 1996; Xu 2004) are listed in the Characteristics of excluded studies. Details of the eleven included studies are given in the table 'Characteristics of included studies' and are summarised below.

One of the included trials was published in two papers (Kloster 1999; Stavem 2000), each focusing on different sets of outcomes. That trial was performed in Norway and published in English while the remaining ten trials were performed in China and published in Chinese (Deng 2001; Leng 2000; Ma 2001; Peng 2003; Shi 2001; Xiong 2003; Yu 1999; Zhang 2006; Zhou 2000; Zhuang 2006); they were translated for this review. The eleven trials included a total of 914 people with epilepsy. One trial included only adults (Kloster 1999), four trials included only children (Ma 2001; Peng 2003; Shi 2001; Xiong 2003), and the remaining six trials included both adults and children (Deng 2001; Leng 2000; Yu 1999; Zhang 2006; Zhou 2000; Zhuang 2006). Three trials included patients with both partial and generalised epilepsy (Kloster 1999; Yu 1999; Zhou 2000), while seven trials included only patients with generalised epilepsy (Deng 2001; Leng 2000; Ma 2001; Peng 2003; Xiong 2003; Zhang 2006; Zhuang 2006) and one trial included only patients with childhood absence epilepsy (Shi 2001). The duration of epilepsy was highly variable in the included trials, ranging from three days to over 30 years. The baseline seizure frequency varied from once every four to six months to many times a day. Etiologies of epilepsy in the patients were reported in three trials only, which encompassed a wide variety in two trials (Ma 2001; Xiong 2003) and only childhood absence in one trial (Shi 2001). Neurological signs were not mentioned

in any of the trials. One trial reported that patients were taking a mean number of two antiepileptic drugs before entering the trial (Kloster 1999) and one trial excluded patients who are currently using AED (Peng 2003). One trial just summarised what kind of drugs patients were taking without mentioning the average number of AEDs that patients required before entering the trial (Xiong 2003). Two trials just mentioned that some patients were taking AEDs without giving details (Ma 2001; Yu 1999). The remaining 6 trials did not mention anything about the drug history of the subjects (Leng 2000; Zhou 2000; Deng 2001; Shi 2001; Zhang 2006; Zhuang 2006).

The type of acupuncture used in the included trials varied. Traditional needle acupuncture was used in the five trials (Ma 2001; Shi 2001; Xiong 2003; Yu 1999; Zhou 2000); and catgut implantation into acupoints was used in four trials (Deng 2001; Leng 2000; Peng 2003; Zhuang 2006). One trial included two treatment groups, using catgut implantation in one group and needle acupuncture plus valproate in another (Zhang 2006). One trial combined traditional needle acupuncture and electroacupuncture in the treatment group (Kloster 1999). The acupoints chosen in the included trials were highly variable. While acupoints chosen were fixed and universally applied to all patients in five trials (Leng 2000; Peng 2003; Shi 2001; Xiong 2003; Yu 1999), the remaining six trials (Deng 2001; Kloster 1999; Ma 2001; Zhang 2006; Zhou 2000; Zhuang 2006) allowed some flexibility in the use of additional acupoints on top of the protocol acupoints set for all patients.

All eleven included trials used a parallel groups, randomised control design. One trial had two intervention groups (catgut implantation in acupoints, and needle acupuncture plus valproate) and one control group (valproate alone) (Zhang 2006). One trial (Xiong 2003) employed two control groups (carbamazepine in one control group and Chinese herbs in the other), while the other ten trials used only one control group. The controls chosen were sham acupuncture in one trial (Kloster 1999), Chinese herbal tablet in one trial (Ma 2001), phenytoin in two trials (Yu 1999; Zhou 2000), and valproate in six trials (Deng 2001; Leng 2000; Peng 2003; Shi 2001; Zhang 2006; Zhuang 2006). Duration of follow up ranged from 12 weeks to 12 months.

Only three trials used seizure freedom as an outcome measure (Leng 2000; Peng 2003; Shi 2001). Most of the trials reported the number of patients with good (75% or over), moderate (50 to 74%) or mild (25 to 49%) reduction in seizure frequency and some trials reported good (75% or over) or moderate (50 to 74%) reduction in seizure duration as major outcomes. Two trials reported seizure score as an outcome measures (Zhang 2006; Zhuang 2006), but the score was not clearly defined. One trial (Kloster 1999) used the percentage reduction in seizure frequency; percentage increase in seizure-free weeks; and the numbers of patients who had their seizure frequency improved, remain static or worsened as outcome measures. This trial also reported the quality of life of the patients as the major outcome in another paper (Stavem 2000).

Three trials reported electroencephalogram (EEG) improvements before and after treatment (Deng 2001; Ma 2001; Xiong 2003), while one trial reported between-group difference in EEG (Kloster 1999).

Risk of bias in included studies

Included studies were of poor methodological quality in general. The trials were all quite small, recruiting only 34 to 129 patients in each trial (18 to 86 patients in the treatment group and 16 to 65 patients in control groups), thus limiting the statistical power. In addition, all trials did not report a sample size calculation, which is essential for ensuring adequate sample size and statistical power. Although all trials mentioned that the patients were randomly allocated to the intervention and control groups, the method of randomisation was not adequately described and allocation concealment was not mentioned in any trial. Ten of the eleven trials included did not blind the participants, the trial investigators or the outcome assessors (Deng 2001; Leng 2000; Ma 2001; Peng 2003; Shi 2001; Xiong 2003; Yu 1999; Zhang 2006; Zhou 2000; Zhuang 2006). Furthermore, comparability of the intervention and control groups was questionable in all trials. Most of the trials (Deng 2001; Leng 2000; Peng 2003; Shi 2001; Xiong 2003; Yu 1999; Zhang 2006; Zhuang 2006) did not provide data on important baseline characteristics of the intervention and control groups to judge the comparability of the two groups. While the remaining three trials (Kloster 1999; Ma 2001; Zhou 2000) claimed that the two groups were comparable at baseline the data they provided suggested otherwise, since one group seemed to have more frequent seizures than the other. Some of the trials did not define outcomes clearly. For example, the "seizure score" used in two trials (Zhang 2006; Zhuang 2006) was not well defined. Furthermore, the acupuncture treatment in some of the trials included were not standardised. Some trials relied on the discretion of the clinician in choosing acupoints (Deng 2001; Kloster 1999; Ma 2001; Zhang 2006; Zhou 2000; Zhuang 2006) and some trials the number of courses of acupuncture or the interval between courses were variable (Deng 2001; Yu 1999). The control treatment was also not standardised for some trials. In one trial, whether valproate or carbamazepine was used in the control patients depended on the clinician's judgement and preference (Deng 2001). In another trial, the dose of phenytoin used was variable (Zhou 2000).

All trials used intention-to-treat analysis. A follow up of at least three months was used. There were no dropouts in ten trials (Deng 2001; Leng 2000; Ma 2001; Peng 2003; Shi 2001; Xiong 2003; Yu 1999; Zhang 2006; Zhou 2000; Zhuang 2006) and dropouts were accounted for in the remaining trial (Kloster 1999), as dropouts were mentioned to be due to lack of efficacy requiring changes of AED. Appropriate statistical techniques were used. However, the overall Jadad score was not satisfactory. Only one trial had a score of four points (Kloster 1999) while the remaining ten trials were given only two points out of a maximum of five (Deng 2001; Leng

2000; Ma 2001; Peng 2003; Shi 2001; Xiong 2003; Yu 1999; Zhang 2006; Zhou 2000; Zhuang 2006).

Effects of interventions

Needle acupuncture plus Chinese herbs compared to Chinese herbs alone

Two trials compared needle acupuncture plus Chinese herbs with Chinese herbs alone (Ma 2001; Xiong 2003). Although the Chinese herbs used were different in the two studies they were the same in the treatment and control groups in each study. Therefore, unless significant interaction between the effects of acupuncture and the particular type of Chinese herbs was present, it is expected that the comparison of outcomes between the treatment and control groups represented the net effect of acupuncture. Where the outcomes described were comparable the results were combined in meta-analysis. We found that apart from using different acupoints and different control herbs there was no significant clinical heterogeneity between the two trials. Both trials included only paediatric patients with generalised epilepsy of widely differing durations. There was also no significant statistical heterogeneity in the various outcomes reported and hence the results were combined in meta-analyses by the fixed-effect model.

None of the trials reported our pre-determined primary outcome of seizure freedom but we had complete data on the outcome of 50% or more reduction in seizure frequency. Both trials showed a mild positive effect of acupuncture in achieving 50% or greater reduction in seizure frequency (pooled RR 1.13, 95% CI 0.97 to 1.31), though not reaching statistical significance (P value 0.13). When we looked at the number of patients with 75% or greater reduction in seizure frequency, we found a statistically significant difference between the treatment and control groups (pooled RR 1.52, 95% CI 1.12 to 2.05) favouring acupuncture treatment. The treatment group were also more likely to have 50% or greater reduction in seizure duration (pooled RR 1.29, 95% CI 1.03 to 1.62).

Neither of the two trials reported the absolute or percentage reduction in seizure frequency or duration, or quality of life changes. However, they reported the positive changes in EEG in different ways. One trial (Ma 2001) showed a trend for improvement in EEG background and epileptic discharges in the treatment group using an EEG scoring system, while the other trial (Xiong 2003) showed a greater frequency of EEG normalisation in the treatment group. Nevertheless, both changes did not reach statistical significance.

Needle acupuncture plus valproate compared to valproate alone

One trial compared needle acupuncture plus valproate with valproate alone (Zhang 2006). This trial reported more patients in the treatment group achieved 50% or greater reduction in seizure frequency (RR 1.9, 95% CI 1.07 to 3.38). Percentage of patients who achieved seizure freedom was not mentioned and the seizure score after treatment was not significantly different between the two groups.

Needle acupuncture compared to sham acupuncture

Only one trial used sham acupuncture as control treatment (Kloster 1999). This trial did not report seizure freedom or number of patients with 50% or greater reduction in seizure frequency, but reported the percentage reduction in seizure frequency and percentage increase in seizure-free weeks. However, the authors did not report the standard deviations of the means and therefore no statistical reanalysis was performed. The percentage reduction in seizure frequency was reported to be higher in the treatment group (45%) compared to the control group (20%), but not reaching statistical significance (P value 0.38). In addition, the percentage increase in seizure-free weeks was higher in the control group compared to the treatment group (50% versus 100%) but without a statistical test on the difference. Six out of 18 patients in the treatment group compared to five out of 16 in the control group had fewer seizures on follow up, which was not significantly different (RR 1.07, 95% CI 0.4 to 1.83). Similarly, the numbers of patients without an increase in seizures on follow up were not different between the treatment and the control groups (RR 0.98, 95% CI 0.58 to 1.66).

This trial also reported the quality of life of the patients on follow up at 12 weeks after treatment, using the QOLIE-89 questionnaire (Stavem 2000). There were no statistically significant differences between the treatment and control groups in either the raw score or the T-score. The authors also did not find any significant differences between the treatment and the control groups in any of the 17 subscores of the various items in the questionnaire.

Needle acupuncture compared to control treatment

Since the above four trials (Kloster 1999; Ma 2001; Xiong 2003; Zhang 2006) compared the treatment group with a control group in a way that could yield the net effect of needle acupuncture, we tried to combine the results of the four trials on the common outcome, that is any degree of reduction in seizure frequency. We found that there was no significant difference between the treatment and the control groups in this respect (pooled RR 1.05, 95% CI 0.97 to 1.17).

Needle acupuncture compared to phenytoin

Two trials compared needle acupuncture with phenytoin (Yu 1999; Zhou 2000). The acupuncture regimen and acupoints chosen were different in these two trials. Otherwise the trials appeared

similar. There were more patients in the treatment group who achieved 75% or greater reduction in seizure frequency (pooled RR 2.14, 95% CI 1.47 to 3.1). The study by Zhou also reported more patients in the treatment group who achieved 25% or greater reduction in seizure frequency (RR 1.61, 95% CI 1.2 to 2.17), and lower seizure frequency after treatment (mean difference 25.1 per year, 95% CI 14.24 to 35.96 per year).

Needle acupuncture compared to valproate

One trial compared needle acupuncture with valproate (Shi 2001). This trial reported more patients in the treatment group who achieved 50% or greater reduction in seizure frequency (RR 1.44, 95% CI 1.05 to 1.98). However, the percentage of patients who achieved seizure freedom was not significantly different between the two groups.

Catgut implantation at acupoints plus valproate or carbamazepine compared to valproate or carbamazepine alone

One trial compared catgut implantation at acupoints plus valproate or carbamazepine with valproate or carbamazepine alone (Deng 2001). Which drug was used in the treatment group depended on the discretion of the clinician and the dose of AED used in the treatment group was just half that used in the control group. This trial reported more patients in the treatment group who achieved 75% or greater reduction in seizure frequency (RR 1.42, 95% CI 1.07 to 1.88). Seizure freedom was not mentioned and there was no statistically significant difference between the two groups with respect to other endpoints.

Catgut implantation at acupoints compared to valproate

Four trials compared catgut implantation at acupoints with valproate (Leng 2000; Peng 2003; Zhang 2006; Zhuang 2006). The trial by Peng only included pediatric patients while the other three trials included patients from all age groups. The acupuncture regimens were the same in the trials by Zhang and Zhuang, while the trials by Leng and Peng each used different regimens. The trials by Zhang and Zhuang had a similar sets of outcomes including seizure score, but seizure freedom was not reported. On the other hand, the trials by Leng and Peng reported seizure freedom but seizure score was not used. The pooled results from the three trials (Peng 2003; Zhang 2006; Zhuang 2006) that reported 75% or greater reduction in seizure frequency showed that the treatment group was better than the control group with borderline statistical significance (pooled RR 2.33, 95% CI 1.01 to 5.36). The pooled results of two trials (Zhang 2006; Zhuang 2006) also showed the treatment group had more patients with 25% or greater reduction in seizure frequency (pooled RR 1.17, 95% CI 1.04 to 1.33).

There was no statistically significant difference between the two groups with respect to other endpoints.

Adverse effects of acupuncture

No adverse effects were reported by any of the trials included. Based on other trials and previous observational studies of acupuncture in patients with epilepsy and a variety of other conditions, adverse effects of acupuncture were uncommon. They included infections from poor aseptic techniques and inappropriate needle placement rarely causing damage to surrounding structures.

Among the included trials, only five dropouts were reported in one trial (Kloster 1999), three in the treatment group and two in the control group. There were no dropouts in the remaining ten trials. The dropouts in the trial by Kloster were due to lack of efficacy requiring changes in antiepileptic medications. Therefore, one of the important potential adverse effects of acupuncture is that patients might be deprived of the beneficial effects of proven AED treatments.

Subgroup analysis

Since none of the trials contained stratified data and individual raw data were not available, although requests were made to the authors of the included studies, we could not perform subgroup analyses to assess the impact of acupuncture on epilepsies of different etiologies, durations or frequencies.

Sensitivity analysis

Since no trial had high quality with adequate concealment of randomisation, the planned sensitivity analysis was not performed.

DISCUSSION

Based on the current systematic review, no firm conclusions can be drawn regarding the effect of acupuncture on epilepsy. Although there were eleven randomised controlled trials identified, they were heterogeneous with respect to the treatment and comparison groups used and the number of patients recruited in each trial was small. The trials included were also heterogeneous with respect to the age of patients, underlying epilepsy types, and outcomes chosen; and they were of poor methodological quality, as evidenced by the lack of descriptions of randomisation methods, concealment of randomisation, or attempts of blinding in most trials. The reliability of randomisation is questionable in all trials since the treatment and the control groups might not be comparable at baseline. The treatment and control groups had at least one potentially important baseline difference in three trials, and important baseline characteristics were not mentioned in most of the other trials. The follow-up period used in the trials was also quite

short, just one year at most. Whether acupuncture is effective in the long term certainly needs further investigation. Although needle acupuncture and catgut implantation at acupoints appeared better than control treatment in some endpoints, they were not effective in most other endpoints, and the selective effectiveness were based on trials of poor methodological qualities. On the other hand, the trial with the highest quality (Kloster 1999) concluded that acupuncture was not effective in reducing seizure frequency, increasing seizure-free weeks or improving quality of life in any aspect. However, its small sample size might have limited the statistical power to detect a small difference. Since this trial focused on adults only, whether acupuncture has different effects on different age groups warrants further investigation.

Some of the trials included compared acupuncture with AED treatments only, without concurrent placebo or sham control group. We cannot tell whether acupuncture is effective per se in these trials. The drugs used in the control group might not be appropriate for all patients, as the patients might have been resistant to those treatments already. The dosage of the AED used in the control group might also be inadequate. Sometimes the AED used might aggravate seizures in some patients, resulting in apparent effectiveness of acupuncture which in fact is not effective. Furthermore, we cannot reliably determine which AED acupuncture might be superior to, as the control treatment was not standardised in some trials. Similarly, which acupuncture regimen is effective in which type of patients cannot be reliably determined, as the treatment regimen was individualised in some of the trials. As the current study only included trials on needle acupuncture, electroacupuncture and catgut implantation at acupoints, whether other forms of acupuncture such as laser acupuncture or acupressure is effective for treating epilepsy is uncertain.

Although no adverse effects were found in the trials included, we cannot assure the safety of acupuncture in epilepsy patients since the small sample sizes might have limited the power of detecting rare adverse effects. Although existing literature on acupuncture in epilepsy patients and patients with a variety of other conditions have supported that it is a relatively safe treatment modality, which obviates the side-effects of antiepileptic drugs, acupuncture is not without risks. Infections and inappropriate needle placement causing inadvertent damage do occur occasionally. Acupuncture should, therefore, be performed by a well-trained therapist who is experienced, understands the theories behind it, and takes the necessary precautions.

AUTHORS' CONCLUSIONS

Implications for practice

Although numerous observational human studies and experimental animal studies have suggested potential benefits of acupuncture for treating epilepsy, there is a paucity of high quality clin-

ical evidence. The current evidence does not support the use of acupuncture as a treatment for epilepsy.

Implications for research

There are few randomised controlled trials assessing acupuncture for epilepsy, especially using control groups that allow estimation of the net effect of acupuncture. The existing trials are of small size and low methodological quality. Further high quality studies of larger sample size and with appropriate standardised control groups are needed to assess the effectiveness of acupuncture in treating epilepsy. The randomisation method used should be rigorous and concealed. Although blinding of the therapist applying acupuncture is difficult, blinding of the patients, the other care providers and outcome assessors should be attempted in order to minimise performance and assessment biases. Since epilepsy is a highly heterogeneous disease with different etiologies and severity, acupuncture is likely to have different effects, if any, on different subgroups of patients. Future clinical trials should, therefore, be focused on a particular subgroup, or include a very large sample size to delineate the effect of acupuncture on different types of patients. The effectiveness of different forms of acupuncture at different acupoints using different regimen should also be investigated systematically in a standardised way. Since epilepsy in children and adults have many important differences, both pediatric and adult clinical trials are needed before the results can be safely generalised to all age groups. Since epilepsy is a chronic disease which is well known to wax and wane, with or without treatment, a longer follow-up period with serial measurements of outcomes is also highly recommended to determine the genuine effectiveness of acupuncture and its long-term effects.

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REFERENCES

References to studies included in this review

Deng 2001 *{published data only}*

Deng Yuanjiang, Wang Jingjing, Lin Yaping, Liu Weiyang, Wang Lihwa. Clinical Observation on treatment of epilepsy general tonic-clonic attack with catgut implantation at acupoint plus antiepileptic Western medicine of small dose. *Chinese Acupuncture and Moxibustion* 2001;21(5):271–3.

Kloster 1999 *{published data only}*

Kloster R, Lasso PG, Lossius R, Nakken KO, Dahl R, Zui-Ling X,

et al. The effect of acupuncture in chronic intractable epilepsy. *Seizure* 1999;8(3):170–4.

Leng 2000 *{published data only}*

Leng YuLing, Pan QingRong, Chen XueNong, Yang TingFei. Epilepsy treated by point thread embedding. Report of 86 cases. *Journal of External Therapy of Traditional Chinese Medicine* 2000;9(4):16.

Ma 2001 *{published data only}*

Ma Rong, Zhang XiLian, Liu Yuzhen, Li XinMin, Yang

- ChangQuan, Xiong Jie. Clinical observation on treatment of tonic attack of infantile epilepsy with acupuncture plus Xi Feng capsule. *Journal of Traditional Chinese Medicine* 2001;**42**(5): 276–8.
- Peng 2003** {published data only}
Peng Yao Shu. Clinical study on treatment of infantile primary epilepsy with acupoint catgut-implantation therapy. *World Journal of Acupuncture-Moxibustion* 2003;**13**(1):38–41.
- Shi 2001** {published data only}
Shi JiangFeng. Absence seizures of epilepsy treated by scalp acupuncture combined with hydro-acupuncture at renying point. Report of 45 cases. *Shaanxi Journal of Chinese Traditional Medicine* 2001;**22**(1):43–4.
- Xiong 2003** {published data only}
Xiong Xie, Zhang GuoZhong, Huang WeiYa, Sun JiaQiang. Clinical observation of acupuncture and Chinese medicine for treatment of epilepsy in children. *Chinese Journal of Information on Traditional Chinese Medicine* 2003;**10**(7):62–3.
- Yu 1999** {published data only}
Yu DeShou, Ping XingMui, Zhao XianLiang. Epilepsy treated by acupuncture with growing fluid and extinguishing wind. Report of 30 cases. *Jiangsu Journal of Traditional Chinese Medicine* 1999;**20**(11):37.
- Zhang 2006** {published data only}
Zhang Jing, Li Yuzhu, Zhuang Lixing. Clinical observation on catgut implantation at acupoint for treatment of generalised tonic-clonic epilepsy. Report of 90 cases. *Journal of Clinical Acupuncture and Moxibustion* 2006;**22**(6):8–10.
- Zhou 2000** {published data only}
Zhou You Long. Epilepsy treated by acupuncture with complementation with Yin and Yang. Report of 60 cases. *Journal of Traditional Chinese Medicine* 2000;**41**(7):441.
- Zhuang 2006** {published data only}
Zhuang Lixing, Zhang Jing, Li Yuzhu. Clinical observation on catgut implantation at acupoint for treatment of general paroxysmal epilepsy. *Chinese Acupuncture and Moxibustion* 2006;**26**(9):611–3.
- References to studies excluded from this review**
- Deng 2001b** {published data only}
Deng YuanJiang, Huang ZhengZheng, Lin YaPeng, Liu JieYing, Huang LiHwa. Clinical observation on 88 cases of epilepsy with general tonicoclonic attack treated with medicated thread implantation at acupoint. *Journal of Traditional Chinese Medicine* 2001;**42**(7):406–8.
- Kuang 1996** {published data only}
Kuang KingRong, Zhou DeLin, Yu XiaoLi. Clinical observation on 40 cases of epilepsy treated with acupuncture and Chinese herbs. *Jiangxi Journal of Traditional Chinese Medicine* 1996;**27**(6):47.
- Xu 2004** {published data only}
Xu JieHong, Lie XinSheng, Lie DongLan. Acupuncture combined with herbal seizure tablet for treatment of epilepsy in children. Report of 64 cases. *Journal of Traditional Chinese Medicine* 2004;**45**(5):349.
- Chen 1983**
Chen K, Chen G, Feng X. Observation of immediate effect of acupuncture on electroencephalograms in epileptic patients. *Journal of Traditional Chinese Medicine* 1983;**3**:121–4.
- Commission 1989**
Commission on Classification and Terminology of the International League Against Epilepsy. Proposal for revised classification of epilepsies and epileptic syndromes. *Epilepsia* 1989;**30**:389–99.
- Furlan 1999**
Furlan AD, van Tulder MW, Cherkov DC, Tsukayama H, Lao L, et al. Acupuncture and dry-needling for low back pain. *Cochrane Database of Systematic Reviews* 1999, Issue 1. [Art. No.: CD001351. DOI: 10.1002/14651858.CD001351.pub2]
- Hauser 1993**
Hauser WA, Annegers JF, Kurland LT. Incidence of epilepsy and unprovoked seizures in Rochester, Minnesota: 1935–1984. *Epilepsia* 1993;**34**:453–68.
- Holland 2001**
Holland KD. Efficacy, pharmacology, and adverse effects of antiepileptic drugs. *Neurologic Clinics* 2001;**19**(2):313–45.
- Huang 1999**
Huang ZN, Yang R, Chen G, Cheng JS. Effect of electroacupuncture and 7-NI on penicillin-induced epilepsy and their relation with intrahippocampal NO changes. *Sheng Li Xue Bao* 1999;**51**(5):508–14.
- Jadad 1996**
Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary?. *Controlled Clinical Trials* 1996;**17**(1):1–12.
- Jansen 1989**
Jansen G, Lundberg T, Kjartansson S, Samuelson UE. Acupuncture and sensory neuropeptides increase cutaneous blood flow in rats. *Neuroscience Letters* 1989;**97**:305–9.
- Johansson 1993**
Johansson K, Lindgren I, Widner H, Wiklund I, Johansson BB. Can sensory stimulation improve the functional outcome in stroke patients?. *Neurology* 1993;**43**:2189–92.
- Kloster 1999**
Kloster R, Lasso PG, Lossius R, Nakken KO, Dahl R, Zui-Ling X, et al. The effect of acupuncture in chronic intractable epilepsy. *Seizure* 1999;**8**(3):170–4.
- Liu 1995**
Liu J, Cheng J. Changes of amino acids release in rat's hippocampus during kainic acid induced epilepsy and acupuncture. *Zhen Ci Yan Jiu* 1995;**20**(3):50–4.
- Liu 1997**
Liu J, Cheng JS. Hippocampal non-NMDA and GABA-A receptors in benzylpenicillin-induced epilepsy and electro-acupuncture antiepilepsy. *Zhongguo Yao Li Xue Bao* 1997;**18**(2):189–91.
- Liu 2004**
Liu JH, Yan J, Yi SX, Chang XR, Lin YP, Hu JM. Effects of electroacupuncture on gastric myoelectric activity and substance P

- in the dorsal vagal complex of rats. *Neuroscience Letters* 2004;**356**(2):99–102.
- Maciocia 1989**
Maciocia G. *Foundations of Chinese Medicine: A comprehensive Text for Acupuncturists and Herbalists*. Edinburgh: Churchill Livingstone, 1989.
- Magnusson 1994**
Magnusson M, Johansson K, Johansson BB. Sensory stimulation promotes normalization of postural control after stroke. *Stroke* 1994;**25**:1176–80.
- Middlekauff 2004**
Middlekauff HR, Shah JB, Yu JL, Hui K. Acupuncture effects on autonomic responses to cold pressor and handgrip exercise in healthy humans. *Clinical Autonomic Research: official journal of the Clinical Autonomic Research Society* 2004;**14**(2):113–8.
- NIH 1998**
NIH Consensus Conference. Acupuncture. *JAMA* 1998;**280**(17):1518–24.
- Sander 1996**
Sander JWAS, Shorvon SD. Epidemiology of the epilepsies. *Journal of Neurology, Neurosurgery, and Psychiatry* 1996;**61**(5):433–43.
- SCSSS 1999**
Swedish Collaboration on Sensory Stimulation in Stroke. Sensory stimulation after stroke: a randomized controlled trial. *Cerebrovascular Diseases* 1999;**9** (Suppl 1):1–28.
- Shi 1987**
Shi Z, Gong B, Jia Y, Hua Z. The efficacy of electroacupuncture on 98 cases of epilepsy. *Journal of Traditional Chinese Medicine* 1987;**7**:21–2.
- Stavem 2000**
Stavem K, Kloster R, Rossberg E, Larsson PLG, Dahlc R, Kinge E, et al. Acupuncture in intractable epilepsy: lack of effect on health-related quality of life. *Seizure* 2000;**9**(6):422–6.
- Sun 2001**
Sun HL, Li XM. Clinical study on treatment of cerebral apoplexy with penetration needling of scalp acupoints [tou xue tou ci zhi liao nao zu zhong lin chuang yan jiu]. *Chinese Acupuncture and Moxibustion* 2001;**21**(5):275–8.
- Wang 2001**
Wang G, Jiang N, He Z. Effects of scalp acupuncture on plasma ET-1, MDA and NO contents in the patient of cerebral infarction. *Chinese Acupuncture and Moxibustion* 2001;**21**(4):241–2.
- Wu 1992**
Wu D. Mechanism of acupuncture in suppressing epileptic seizures. *Journal of Traditional Chinese Medicine* 1992;**12**:187–92.
- Wu 1996**
Wu JN. A short history of acupuncture. *Journal of Alternative and Complementary Medicine* 1996;**2**(1):19–21.
- Yang 1990**
Yang J. Treatment of status epilepticus with acupuncture. *Journal of Traditional Chinese Medicine* 1990;**10**:101–2.
- Yang 2000**
Yang R, Huang ZN, Cheng JS. Anticonvulsion effect of acupuncture might be related to the decrease of neuronal and inducible nitric oxide synthases. *Acupuncture Electrotherapy Research* 2000;**25**(3–4):137–43.
- * Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Deng 2001

Methods	RCT Simple randomisation No blinding	
Participants	Treatment group (males): 64 (30) Control: 65 (28). Age Treatment group: mean 21.75 (SD 12.03) years; Control group: mean 22.43 (SD 13.25) years. Inclusion: generalised tonic-clonic epilepsy Exclusion: nil Seizure type: generalised tonic-clonic epilepsy Duration of epilepsy Treatment group: mean 7.36 +/- 7.03 years; Control group: mean 7.85 +/- 8.02 years. Baseline seizure frequency: not available Number of AEDs taken: not available	
Interventions	Treatment group: catgut implantation at 3-4 of 7 acupoints, every 25-30 days, for 4-5 times, plus carbamazepine or valproate at half doses + aminobutyric acid 500 mg 2-3 times/day + Vitamin B6 20-30 mg 2-3 times/day + cinnarizine 25-50 mg 2-3 times/day Control group: carbamazepine 100-200 mg 2-3 times/day or valproate 200 mg 2-3 times/day + aminobutyric acid 500 mg 2-3 times/day + Vitamin B6 20-30 mg 2-3 times/day + cinnarizine 25-50 mg 2-3 times/day Duration of treatment: 1 year Duration of FU: 1 year	
Outcomes	92% or greater reduction in seizure frequency: Treatment group: 18; Control group: 11 75% or greater reduction in seizure frequency: Treatment group: 46; Control group: 33 50% or greater reduction in seizure frequency: Treatment group: 60; Control group: 56 25% or greater reduction in seizure frequency: Treatment group: 63; Control group: 63 EEG abnormality after treatment: Mild abnormality: Treatment group: 31; Control group: 22; Moderate abnormality: Treatment group: 17; Control group: 28; Severe abnormality: Treatment group: 3; Control group: 7	
Notes	Jadad score: 2 Comparability of the groups at baseline was uncertain since there was no data on etiology of epilepsy, current AED treatments, and frequency of seizures. No dropouts Duration of FU: 1 year	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Kloster 1999

Methods	RCT Block randomisation Double blind	
Participants	Treatment group (males): 18 (9) Control group: 16 (7). Age Treatment group: mean 37.7 (SD 12.8) years; Control group: mean 37.4 (SD 15) years. Inclusion: chronic intractable epilepsy, adult > 18 years, duration > 2 years, verified diagnosis of epilepsy, partial or generalised, ≥ 1 seizures/week. Exclusion: non-epileptic seizures +/- epilepsy, inability to cooperate, progressive cerebral illness; seizure type: partial or generalised - primary generalised (1 case, 5 controls), partial with generalisation (17 cases, 11 controls). Duration of epilepsy Treatment group: mean 27.6 +/- 14.3 years; Control group: mean 26.4 +/- 12.1 years. Baseline seizure frequency Treatment group: 3.5/week; Control: 2/week. Number of AEDs taken Treatment: mean 2 +/- 0.8; Control: mean 2.3 +/- 0.8.	
Interventions	Treatment group: needle acupuncture, at LR3, L14, GV20, plus ≥ 1 acupoints chosen according to Traditional Chinese Medicine diagnosis, Suzhou Hwato acupuncture needles with diameter 0.3 mm, length 25-55 mm; stimulation given until patient felt needle sensation; needles inserted to varying depths and angles, stimulated by manual rotation or electrically, 3 Hz, 3-20 mA depending on patient's endurance, using standard TENS apparatus. Control group: sham acupuncture, with bilateral needling of 3 points: S1 (2.5cun lateral to umbilicus), S2 (3cun above midpoint of patella), S3 (1cun distal to midpoint between LI15 and TE14), sterilised Suzhou Hwato acupuncture needles diameter 0.25mm, length 13mm, to a depth < 5mm; minimal manual stimulation, no electrical stimulation. Both: 30min/session, 3 sessions/week for 7.5 weeks with 4 days break in the middle.	
Outcomes	Percentage reduction of seizure frequency and duration: Treatment group: 45%; Control group: 20%. Change in seizure frequency after treatment Treatment group: fewer seizures (6), unchanged (5), more seizures (4); Control group: fewer seizures (5), unchanged (5), more seizures (4). Percentage increase in number of seizure-free weeks Treatment group: 50%; Control group: 100%. EEG after treatment: no difference between treatment and control groups. QOL: no difference between treatment and control groups in any item of the QOLIE-89 questionnaire.	
Notes	Jadad score: 4. The two groups had different baseline seizure frequency and percentage of patients with primary generalised epilepsy. Dropouts due to lack of efficacy, requiring changes of AED Treatment group: 3; Control: 2. Duration of follow up: 12 weeks.	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Leng 2000

Methods	RCT Simple randomisation No blinding
Participants	Treatment group (males): 86 (67) Control group: 32 (21) Age Treatment group: mean 29.7 (range 3-43) years; Control group: mean 28 (range 17-45) years. Inclusion: generalised epilepsy Exclusion: nil Seizure type: generalised epilepsy Duration of epilepsy Treatment group: 3 days to 4 years; Control group: 7 days to 3 years. Baseline seizure frequency: not available Number of AEDs taken: not available
Interventions	Treatment group: catgut implantation at 9 acupoints monthly Control group: Na valproate 100 mg BD Duration of treatment: 6 months
Outcomes	Seizure freedom: Treatment group: 6; Control group: 2 50% or greater reduction in seizure frequency: Treatment group: 86; Control group: 30
Notes	Jadad score: 2 Comparability of groups at baseline was uncertain since there was no data on etiology of epilepsy, current AED treatments, and frequency of seizures. No dropouts Duration of follow up: 1 year

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Ma 2001

Methods	RCT Simple randomisation No blinding
Participants	Treatment group (boys): 30 (23); Control group: 30 (18). Age: Treatment group: < 5 years (4), 5-10 years (6), 10-16 years (20); Control group: < 5 years (2), 5-10 years (9), 10-16 years (19). Inclusion: generalised epilepsy, < 16 years. Duration of epilepsy: Treatment group: < 1 year (10), 1-5 years (12), 5-10 years (5), 10-15 years (3); Control group: < 1 year (13), 1-5 (10), 5-10 years (5), 10-15 years (2). Baseline seizure frequency Treatment group: > 1/day (12), 1-6/week (7), 1-3/month (6), 1/1-2 months (2), 1/2-4 months (1), 1/4-6 months (2); Control group: > 1/day (5), 1-6/week (3), 1-3/month (9), 1/1-2 months (4), 1/2-4 months (6), 1/4-6 months (3).

Ma 2001 (Continued)

	Etiology of epilepsy: antenatal problems (7), caesarian section (10), forceps delivery (4), birth asphyxia (9), history of febrile convulsion (15), history of trauma (11), history of brain disorder (9), mental retardation (3), history of intoxication (8), history of phobia (4), family history of epilepsy (2), prematurity (1), history of hypocalcemic seizure (1).
Interventions	Treatment group: acupuncture + mixed Chinese herbal capsule (Xi Feng capsule). Acupuncture at 6 points for 30 minutes, daily for 8 days then rest for 2 days then begin another course. Additional acupuncture at 1 or 2 acupoints depending on TCM diagnosis. Xi Feng capsule to be taken 3 times at age-dependent dosage: < 1 year (1 tab), 1-3 years (2 tabs), 4-16 years (age-1 tabs, max 8 tabs). Control group: Xi feng capsule alone Duration of treatment: 6 months
Outcomes	50% or greater reduction in seizure frequency Treatment group: 27(90%); Control group: 24(80%). Reduction in duration of seizures Treatment group: 9 >75%, 15 50-74%, 6 < 50%; Control group: 4 > 75%, 14 50-74%, 12 < 50%. Improvement in EEG Treatment group: 15 had ≥ 4 points reduction, 9 had 2-3 points reduction, 2 had < 2 points reduction; Control group: 9 had ≥ 4 points reduction, 14 had 2-3 points reduction, 3 had < 2 points reduction. Marking of EEG background: normal (0), borderline abnormal (1), mild generalised abnormality (2), moderate generalised abnormality (3), severe generalised abnormality (4). Marking of epileptic discharge: nil (0), occasional (2), modest (4), quite frequent (6), very frequent (8).
Notes	Jadad score: 2. The treatment group had more frequent seizures. No dropouts. Duration of follow up: 6 months.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Peng 2003

Methods	RCT Simple randomisation No blinding
Participants	Treatment group (males): 32 (20) Control group: 31 (17) Age Treatment group: mean 11.25 (range 6-16) years; Control group: mean 12.13 (range 6-15) years. Inclusion: patients with primary epilepsy aged 6-16 years not being treated with Western medicines Exclusion: patients with secondary epilepsy and patients being treated with antiepileptics were excluded. Seizure type: generalised epilepsy Duration of epilepsy Treatment group: mean 6.53 (range 4-13) years; Control group: mean 5.69 (range 3-11) years. Baseline seizure frequency: not available

Peng 2003 (Continued)

	Number of AEDs taken: 0
Interventions	Treatment group: catgut implantation in 6 acupoints (GV1, CV15, bilateral BL15 and bilateral ST36) every 20 days for 3 times Control group: Na valproate 5-10 mg/kg/day divided into 3 doses Duration of treatment: 60 days
Outcomes	Seizure freedom: Treatment group: 8; Control group: 0 75% or greater reduction in seizure frequency: Treatment group: 20; Control group: 16 50% or greater reduction in seizure frequency: Treatment group: 28; Control group: 28
Notes	Jadad score: 2 Comparability of groups at baseline was uncertain since there was no data on frequency of seizures at baseline No dropouts Duration of follow up: 6 months

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Shi 2001

Methods	RCT Simple randomisation No blinding
Participants	Treatment group (males): 45 (20) Control group: 35 (16) Age Treatment group: mean 9 (range 5-14) years; Control group: mean 10 (range 6-13) years. Inclusion: childhood absence epilepsy Exclusion: nil Seizure type: childhood absence epilepsy Duration of epilepsy Treatment group: 10 months to 4 years; Control group: 6 months to 5 years. Baseline seizure frequency: not available Number of AEDs taken: not available
Interventions	Treatment group: acupuncture at 6 acupoints (including injection of diazepam to 2 acupoints) alternate day Control group: Na valproate 200 mg tds + piracetam 800 mg tds Duration of treatment: 80 days
Outcomes	Seizure freedom: Treatment group: 14; Control group: 6 50% or greater reduction in seizure frequency: Treatment group: 37; Control group: 20

Shi 2001 (Continued)

Notes	<p>Jadad score: 2 Comparability of groups at baseline was uncertain since there was no data on etiology of epilepsy, current AED treatments, and frequency of seizures No dropouts Duration of follow up: 1 year</p>	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Xiong 2003

Methods	<p>RCT Simple randomisation No blinding</p>	
Participants	<p>Treatment group: 30 Control group 1: 30 Control group 2: 30 Overall 64 boys Age: 1-4 years (14), 4-10 years (52), 10-17 years (24) Inclusion: generalised epilepsy, < 18 years Duration of epilepsy: < 1 year (18), 1-3 years (45), 3-6 years (10), 6-10 years (7). Etiology: history of febrile convulsion (28), trauma (19), intoxication (13), forceps delivery (3), positive family history (7), perinatal asphyxia (2), brain disease (1). AEDs used: carbamazepine (19), valproate (22), Chinese herbs (25), other drugs (5), drug naive (19).</p>	
Interventions	<p>Treatment group: acupuncture + Chinese herb mixtures. Acupuncture at 10 points for 30 minutes, daily for 10 days then rest for 2 days then begin another course. Chinese herb mixture to be taken twice daily at age-dependent dosage: < 3 years (50-100 ml), 3-9 years (100-200 ml), 9-17 years (200-500 ml); Control group 1: Chinese herb mixture alone; Control group 2: carbamazepine alone, dosage according to age.</p>	
Outcomes	<p>50% or greater reduction in seizure frequency Treatment group: 27(90%); Control 1: 24(80%); Control 2: 22(73%). Reduction in duration of seizures Treatment: 10 > 75%, 15 50-74%, 5 < 50%; Control 1: 4 > 75%, 14 50-74%, 12 < 50%; Control 2: 5 > 75%, 13 50-74%, 12 < 50%. Improvement in EEG Treatment group: 4 normal before treatment, 25 abnormal before treatment, 14 normal after treatment, 16 abnormal after treatment; Control 1: 4 normal before treatment, 26 abnormal before treatment, 9 normal after treatment, 21 abnormal after treatment; Control 2: 6 normal before treatment, 24 abnormal before treatment, 7 normal after treatment, 23 abnormal after treatment.</p>	
Notes	<p>Jadad score: 2. No data available on comparability of the treatment and the control groups at baseline. No dropouts. Duration of follow up: 6 months.</p>	

Xiong 2003 (Continued)

<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Yu 1999

Methods	RCT Simple randomisation No blinding	
Participants	Treatment group (males): 30 (18) Control group: 30 (not available) Age Treatment group: 6-43 years; Control group: not available Inclusion: Epilepsy Exclusion: space occupying lesions on CT scan Seizure type: not available Duration of epilepsy Treatment group: 3 months to 10 years; Control group: not available Baseline seizure frequency: not available Number of AEDs taken: not available	
Interventions	Treatment group: acupuncture at 7 acupoints every 3-5 days for 20-30 times Control group: phenytoin 100 mg tds +/- oryzanol Duration of treatment: 60-150 days	
Outcomes	75% or greater reduction in seizure frequency: Treatment group: 22; Control group: 14 50% or greater reduction in seizure frequency: Treatment group: 29; Control group: 28	
Notes	Jadad score: 2 Comparability of groups at baseline was uncertain since there was no data age and gender distribution and duration of epilepsy of the control group, etiology of epilepsy, current AED treatments, and frequency of seizures No dropouts Duration of follow up: 6 months	
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Zhang 2006

Methods	RCT Simple randomisation No blinding	
Participants	Treatment group 1 (catgut implantation at acupoints) (males): 30 (14) Treatment group 2 (needle acupuncture + valproate): 30 (12) Control group: 30 (12) Age Treatment group 1: mean 33.56 (SD 12.75) years; Treatment group 2: mean 35.02 (SD 12.05) years; Control group: mean 31.79 (SD 11.77) years Inclusion: generalised tonic-clonic epilepsy Exclusion: nil Seizure type: generalised tonic-clonic epilepsy Duration of epilepsy Treatment group 1: mean 7.3 (SD 7.03) years; Treatment group 2: mean 7.96 (SD 7.28) years; Control group: mean 7.68 (SD 6.94) years. Baseline seizure frequency: not available Number of AEDs taken: not available	
Interventions	Treatment group 1: catgut implantation in 17 acupoints (17 points divided into 4 groups: group 1 to group 3 each contains 4 points, group 4 contains 5 points, acupoints in the 1st 3 groups used in alternate cycles, each cycle also used 1 of 5 points from group 4. So each cycle used 5 acupoints in total); Implantation once every 15 days. Treatment group 2: needle acupuncture at same acupoints alternate days + valproate 200 mg tds Control group: Valproate 200 mg tds Duration of treatment: 3 months	
Outcomes	92% or greater reduction in seizure frequency: Treatment group 1: 3; Treatment group 2: 2; Control group: 2 75% or greater reduction in seizure frequency: Treatment group 1: 15; Treatment group 2: 8; Control group: 4 50% or greater reduction in seizure frequency: Treatment group 1: 25; Treatment group 2: 19; Control group: 10 25% or greater reduction in seizure frequency: Treatment group 1: 28; Treatment group 2: 26; Control group: 23 Seizure score after treatment: Treatment group 1: mean 7.86 (SD 4.3); Treatment group 2: mean 8.22 (SD 4.06); Control group: mean 8.09 (SD 5.21)	
Notes	Jadad score: 2 Comparability of groups at baseline was uncertain since there was no data on etiology of epilepsy, current AED treatments, and frequency of seizures No dropouts Duration of follow up: 3 months	
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Zhou 2000

Methods	RCT Simple randomisation No blinding	
Participants	Treatment group (males): 60 (32) Control group: 30 (17) Age Treatment group: 0.5 to 65 years; Control group: 1 to 59 years. Inclusion: epilepsy Exclusion: nil Seizure type: Treatment group: generalised epilepsy (46), partial epilepsy (14); Control group: generalised epilepsy (20), partial epilepsy (10) Duration of epilepsy: not available Baseline seizure frequency: not available Number of AEDs taken: not available	
Interventions	Treatment group: acupuncture at 12 standard acupoints + 1-2 additional acupoints according to different diagnosis in Traditional Chinese Medicine, daily for 30 days then weekly for 5 months Control: phenytoin Duration of treatment: 6 months	
Outcomes	75% or greater reduction in seizure frequency: Treatment group: 46; Control group: 8 50% or greater reduction in seizure frequency: Treatment group: 56; Control group: 14 25% or greater reduction in seizure frequency: Treatment group: 58; Control group: 18 Seizure frequency after treatment: Treatment group: 2.3 (SD 4.2) times/year; Control group: 27.4 (SD 30.2) times/year	
Notes	Jadad score: 2 The treatment group had lower baseline seizure frequency. No dropouts Duration of follow up: 6 months	
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Zhuang 2006

Methods	RCT Simple randomisation No blinding	
Participants	Treatment group (males): 50 (22) Control group: 50 (27) Age Treatment group: mean 30.05 (SD 12.03) years; Control group: mean 33.2 (SD 11.65) years. Inclusion: generalised epilepsy Exclusion: nil Seizure type: generalised epilepsy	

Zhuang 2006 (Continued)

	Duration of epilepsy: not available Baseline seizure frequency: not available Number of AEDs taken: not available	
Interventions	Treatment group: catgut implantation in 17 acupoints (17 points divided into 4 groups: group 1 to group 3 each contains 4 points, group 4 contains 5 points, acupoints in the 1st 3 groups used in alternate cycles, each cycle also used 1 of 5 points from group 4. So each cycle used 5 acupoints in total); Implantation once every 15 days. Control group: Valproate 200 mg tds Duration of treatment: 3 months	
Outcomes	92% or greater reduction in seizure frequency: Treatment group: 11; Control group: 5 75% or greater reduction in seizure frequency: Treatment group: 33; Control group: 10 50% or greater reduction in seizure frequency: Treatment group: 42; Control group: 22 25% or greater reduction in seizure frequency: Treatment group: 47; Control group: 41 Seizure score after treatment: Treatment group 1: mean 8.35 (SD 4.76); Control group: mean 7.84 (SD 5.14)	
Notes	Jadad score: 2 Comparability of groups at baseline was uncertain since there was no data on etiology of epilepsy, current AED treatments, and frequency of seizures No dropouts Duration of follow up: 3 months	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Characteristics of excluded studies [ordered by study ID]

Deng 2001b	Acupuncture combined with Chinese herbs compared with antiepileptic drugs. No placebo or sham or no-treatment control.
Kuang 1996	Acupuncture combined with Chinese herbs compared with acupuncture only. No placebo or sham or no-treatment control.
Xu 2004	Acupuncture combined with Chinese herbs compared with sodium valproate. No placebo or sham or no-treatment control.

DATA AND ANALYSES

Comparison 1. Needle acupuncture plus Chinese herbs versus Chinese herbs alone

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 50% or greater reduction in seizure frequency	2	120	Risk Ratio (M-H, Fixed, 95% CI)	1.13 [0.97, 1.31]
2 75% or greater reduction in seizure frequency	2	120	Risk Ratio (M-H, Fixed, 95% CI)	1.52 [1.12, 2.05]
3 25% or greater reduction in seizure frequency	2	120	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.91, 1.10]
4 50% or greater reduction in seizure duration	2	120	Risk Ratio (M-H, Fixed, 95% CI)	1.29 [1.03, 1.62]
5 75% or greater reduction in seizure duration	2	120	Risk Ratio (M-H, Fixed, 95% CI)	1.9 [0.97, 3.74]
6 4 points or greater improvement in EEG	1	52	Risk Ratio (M-H, Fixed, 95% CI)	1.67 [0.89, 3.11]
7 2 points or greater improvement in EEG	1	52	Risk Ratio (M-H, Fixed, 95% CI)	1.04 [0.87, 1.25]
8 Abnormal EEG after treatment	1	60	Risk Ratio (M-H, Fixed, 95% CI)	0.76 [0.51, 1.15]

Comparison 2. Needle acupuncture plus valproate versus valproate alone

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 50% or greater reduction in seizure frequency	1	60	Risk Ratio (M-H, Fixed, 95% CI)	1.9 [1.07, 3.38]
2 92% or greater reduction in seizure frequency	1	60	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.15, 6.64]
3 75% or greater reduction in seizure frequency	1	60	Risk Ratio (M-H, Fixed, 95% CI)	2.0 [0.67, 5.94]
4 25% or greater reduction in seizure frequency	1	60	Risk Ratio (M-H, Fixed, 95% CI)	1.13 [0.89, 1.44]
5 Seizure score after treatment	1	60	Mean Difference (IV, Fixed, 95% CI)	0.13 [-2.23, 2.49]

Comparison 3. Needle acupuncture versus sham acupuncture

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Percentage reduction in seizure frequency			Other data	No numeric data
2 Reduction in seizure frequency	1	34	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.40, 2.83]
3 No increase in seizure frequency	1	34	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.58, 1.66]
4 Percentage increase in seizure-free weeks			Other data	No numeric data
5 Quality of life raw score (QOLIE-89 score)	1	28	Mean Difference (IV, Fixed, 95% CI)	-0.80 [-12.05, 10.45]
6 Quality of life T-score (QOLIE-89 score)	1	28	Mean Difference (IV, Fixed, 95% CI)	-0.5 [-7.68, 6.68]
7 Mean improvement in quality of life raw score (QOLIE-89 score)			Other data	No numeric data

Comparison 4. Needle acupuncture versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Reduction in seizure frequency	4	214	Risk Ratio (M-H, Fixed, 95% CI)	1.05 [0.94, 1.17]

Comparison 5. Needle acupuncture versus phenytoin

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 50% or greater reduction in seizure frequency	2	150	Risk Ratio (M-H, Random, 95% CI)	1.43 [0.46, 4.44]
2 75% or greater reduction in seizure frequency	2	150	Risk Ratio (M-H, Fixed, 95% CI)	2.14 [1.47, 3.10]
3 25% or greater reduction in seizure frequency	1	90	Risk Ratio (M-H, Fixed, 95% CI)	1.61 [1.20, 2.17]
4 Seizure frequency after treatment	1	90	Mean Difference (IV, Fixed, 95% CI)	-25.10 [-35.96, -14.24]

Comparison 6. Needle acupuncture versus valproate

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Seizure freedom	1	80	Risk Ratio (M-H, Fixed, 95% CI)	1.81 [0.78, 4.24]
2 50% or greater reduction in seizure frequency	1	80	Risk Ratio (M-H, Fixed, 95% CI)	1.44 [1.05, 1.98]

Comparison 7. Catgut implantation at acupoints plus valproate or carbamazepine versus valproate or carbamazepine alone

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 50% or greater reduction in seizure frequency	1	129	Risk Ratio (M-H, Fixed, 95% CI)	1.09 [0.97, 1.22]
2 92% or greater reduction in seizure frequency	1	129	Risk Ratio (M-H, Fixed, 95% CI)	1.66 [0.85, 3.23]
3 75% or greater reduction in seizure frequency	1	129	Risk Ratio (M-H, Fixed, 95% CI)	1.42 [1.07, 1.88]
4 25% or greater reduction in seizure frequency	1	129	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.96, 1.07]
5 Abnormal EEG after treatment	1	387	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.67, 1.24]
5.1 Severe abnormality	1	129	Risk Ratio (M-H, Fixed, 95% CI)	0.44 [0.12, 1.61]
5.2 Moderate abnormality	1	129	Risk Ratio (M-H, Fixed, 95% CI)	0.62 [0.38, 1.01]
5.3 Mild abnormality	1	129	Risk Ratio (M-H, Fixed, 95% CI)	1.43 [0.94, 2.19]

Comparison 8. Catgut implantation at acupoints versus valproate alone

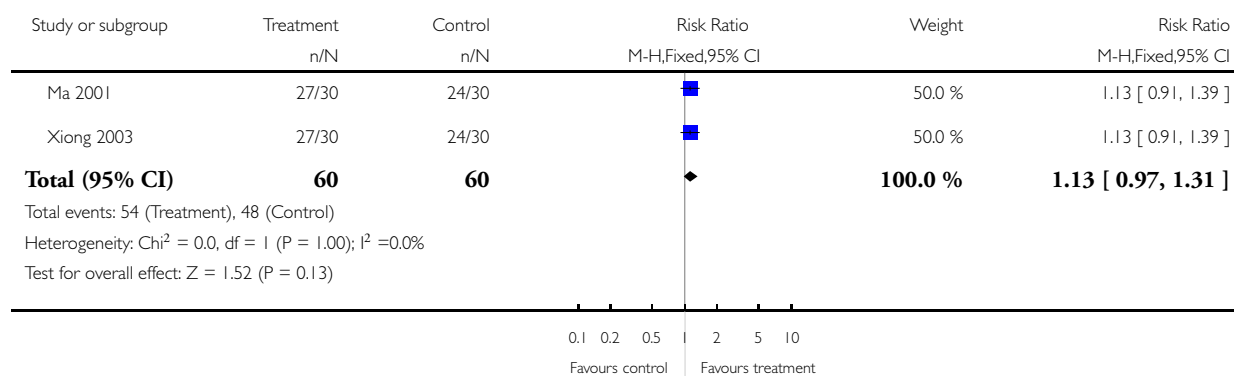
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Seizure freedom	2	181	Risk Ratio (M-H, Random, 95% CI)	3.43 [0.20, 57.97]
2 50% or greater reduction in seizure frequency	4	341	Risk Ratio (M-H, Random, 95% CI)	1.42 [0.93, 2.16]
3 92% or greater reduction in seizure frequency	2	160	Risk Ratio (M-H, Fixed, 95% CI)	2.0 [0.86, 4.68]
4 75% or greater reduction in seizure frequency	3	223	Risk Ratio (M-H, Random, 95% CI)	2.33 [1.01, 5.36]
5 25% or greater reduction in seizure frequency	2	160	Risk Ratio (M-H, Fixed, 95% CI)	1.17 [1.04, 1.33]
6 Seizure score after treatment	2	160	Mean Difference (IV, Fixed, 95% CI)	0.22 [-1.29, 1.73]

Analysis 1.1. Comparison 1 Needle acupuncture plus Chinese herbs versus Chinese herbs alone, Outcome 1 50% or greater reduction in seizure frequency.

Review: Acupuncture for epilepsy

Comparison: 1 Needle acupuncture plus Chinese herbs versus Chinese herbs alone

Outcome: 1 50% or greater reduction in seizure frequency

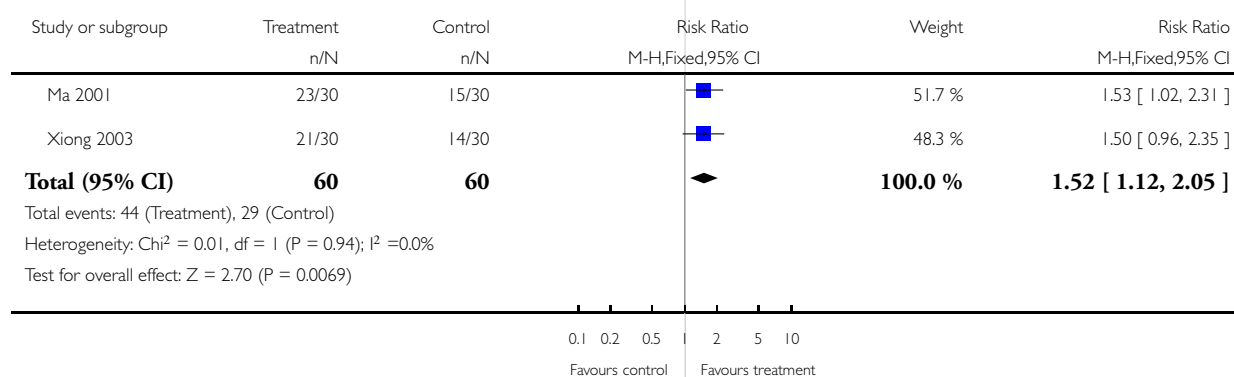


Analysis 1.2. Comparison 1 Needle acupuncture plus Chinese herbs versus Chinese herbs alone, Outcome 2 75% or greater reduction in seizure frequency.

Review: Acupuncture for epilepsy

Comparison: 1 Needle acupuncture plus Chinese herbs versus Chinese herbs alone

Outcome: 2 75% or greater reduction in seizure frequency

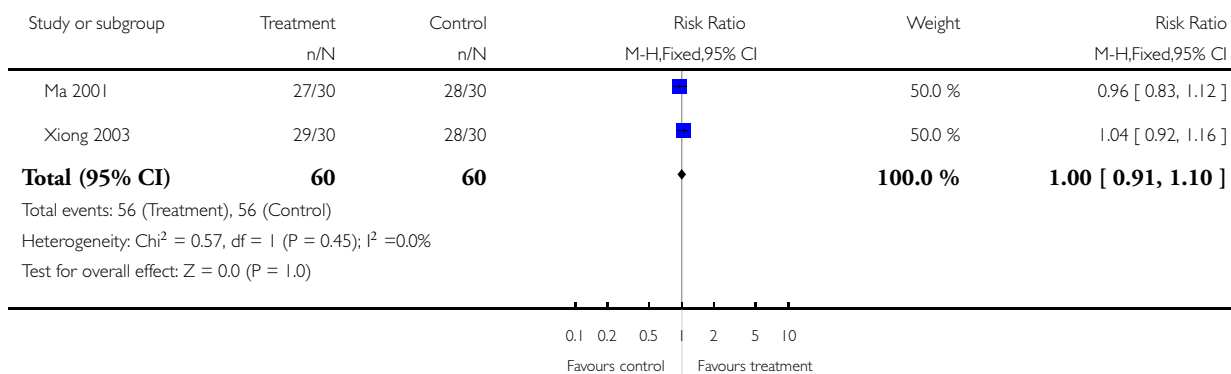


Analysis 1.3. Comparison 1 Needle acupuncture plus Chinese herbs versus Chinese herbs alone, Outcome 3 25% or greater reduction in seizure frequency.

Review: Acupuncture for epilepsy

Comparison: 1 Needle acupuncture plus Chinese herbs versus Chinese herbs alone

Outcome: 3 25% or greater reduction in seizure frequency

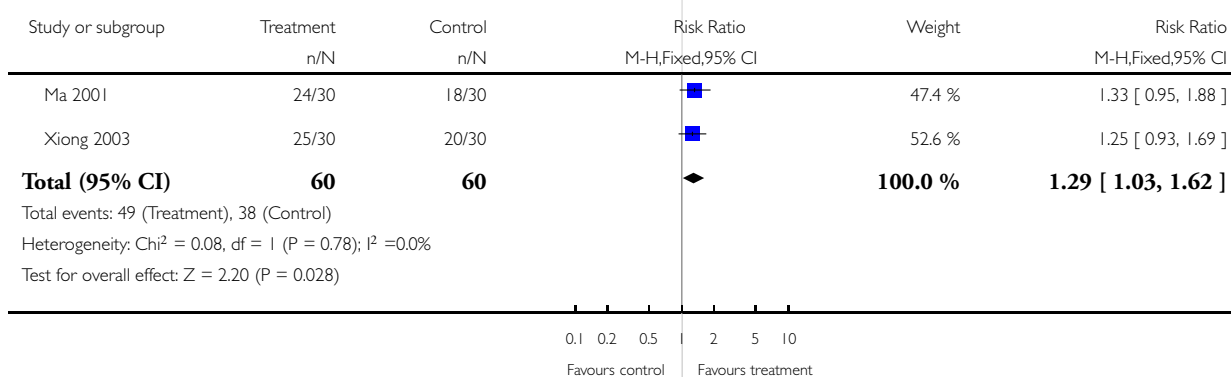


Analysis 1.4. Comparison 1 Needle acupuncture plus Chinese herbs versus Chinese herbs alone, Outcome 4 50% or greater reduction in seizure duration.

Review: Acupuncture for epilepsy

Comparison: 1 Needle acupuncture plus Chinese herbs versus Chinese herbs alone

Outcome: 4 50% or greater reduction in seizure duration

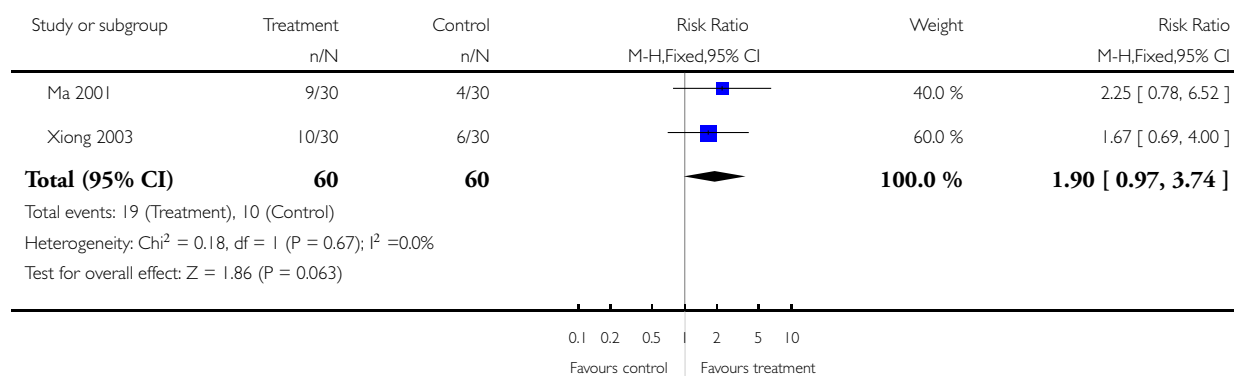


Analysis 1.5. Comparison 1 Needle acupuncture plus Chinese herbs versus Chinese herbs alone, Outcome 5 75% or greater reduction in seizure duration.

Review: Acupuncture for epilepsy

Comparison: 1 Needle acupuncture plus Chinese herbs versus Chinese herbs alone

Outcome: 5 75% or greater reduction in seizure duration

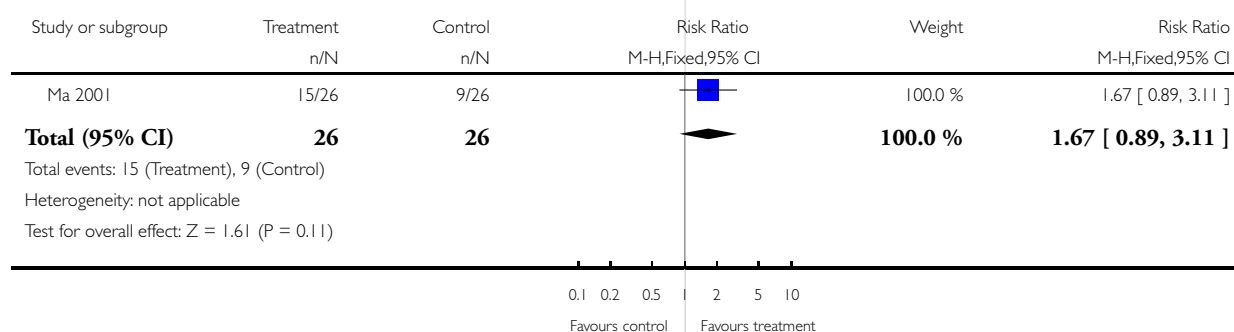


Analysis 1.6. Comparison 1 Needle acupuncture plus Chinese herbs versus Chinese herbs alone, Outcome 6 4 points or greater improvement in EEG.

Review: Acupuncture for epilepsy

Comparison: 1 Needle acupuncture plus Chinese herbs versus Chinese herbs alone

Outcome: 6 4 points or greater improvement in EEG

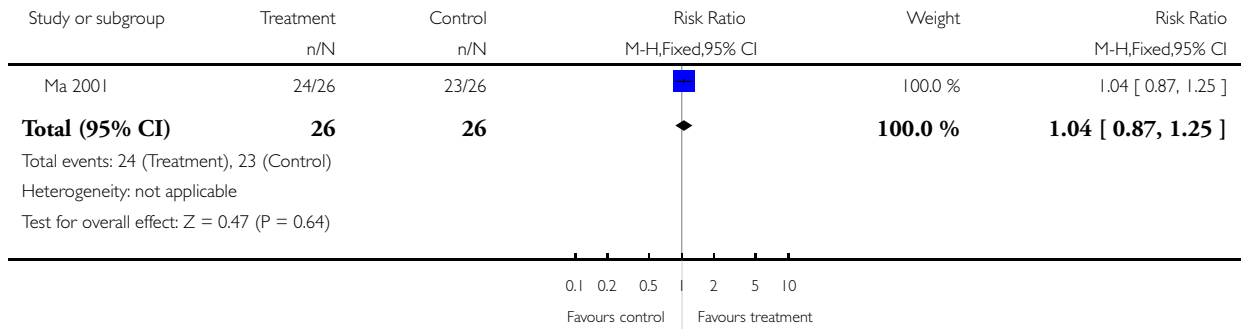


Analysis 1.7. Comparison 1 Needle acupuncture plus Chinese herbs versus Chinese herbs alone, Outcome 7 2 points or greater improvement in EEG.

Review: Acupuncture for epilepsy

Comparison: 1 Needle acupuncture plus Chinese herbs versus Chinese herbs alone

Outcome: 7 2 points or greater improvement in EEG

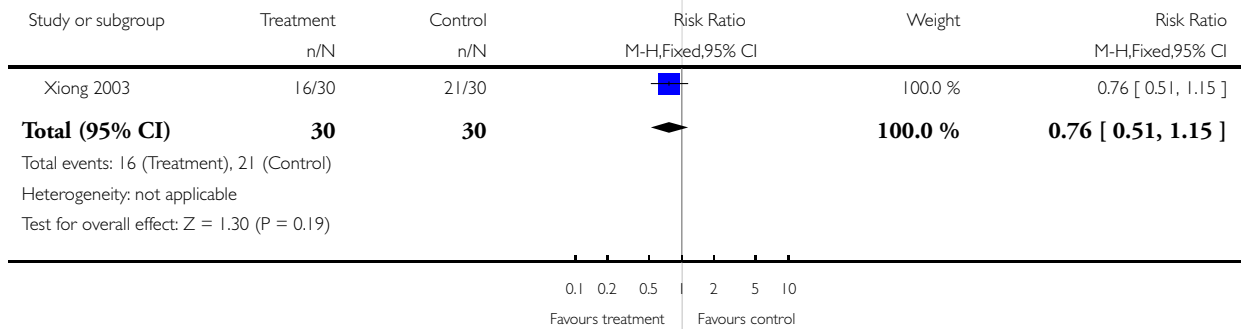


Analysis 1.8. Comparison 1 Needle acupuncture plus Chinese herbs versus Chinese herbs alone, Outcome 8 Abnormal EEG after treatment.

Review: Acupuncture for epilepsy

Comparison: 1 Needle acupuncture plus Chinese herbs versus Chinese herbs alone

Outcome: 8 Abnormal EEG after treatment

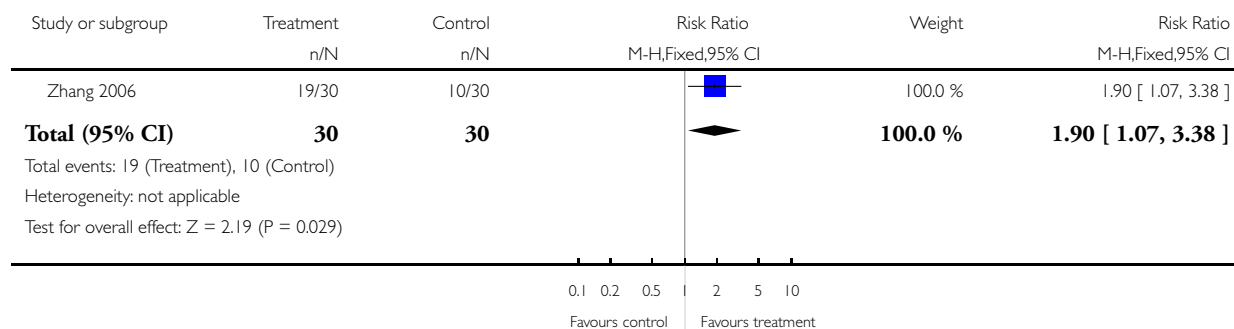


Analysis 2.1. Comparison 2 Needle acupuncture plus valproate versus valproate alone, Outcome 1 50% or greater reduction in seizure frequency.

Review: Acupuncture for epilepsy

Comparison: 2 Needle acupuncture plus valproate versus valproate alone

Outcome: 1 50% or greater reduction in seizure frequency

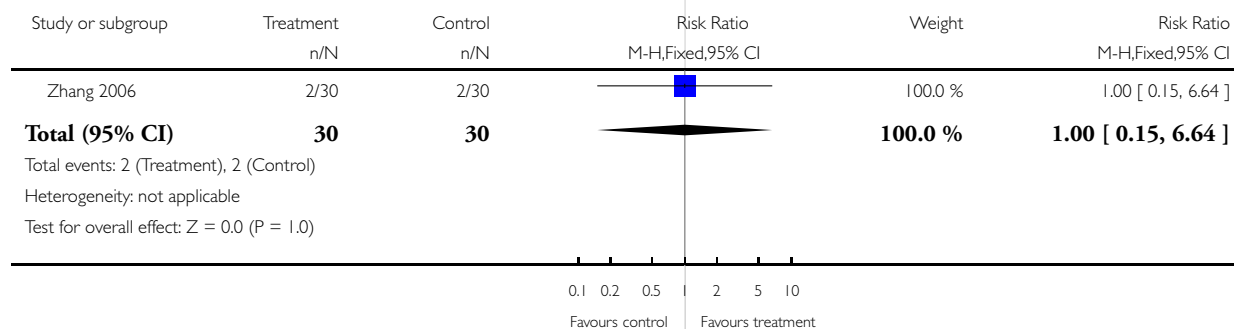


Analysis 2.2. Comparison 2 Needle acupuncture plus valproate versus valproate alone, Outcome 2 92% or greater reduction in seizure frequency.

Review: Acupuncture for epilepsy

Comparison: 2 Needle acupuncture plus valproate versus valproate alone

Outcome: 2 92% or greater reduction in seizure frequency

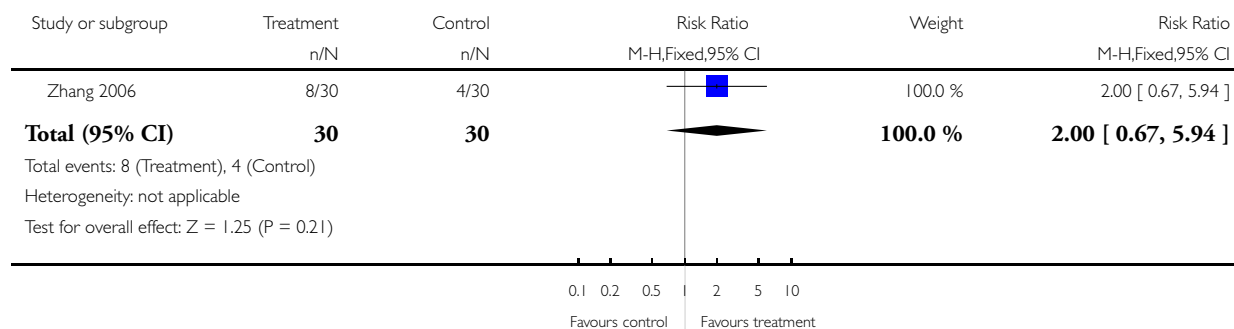


Analysis 2.3. Comparison 2 Needle acupuncture plus valproate versus valproate alone, Outcome 3 75% or greater reduction in seizure frequency.

Review: Acupuncture for epilepsy

Comparison: 2 Needle acupuncture plus valproate versus valproate alone

Outcome: 3 75% or greater reduction in seizure frequency

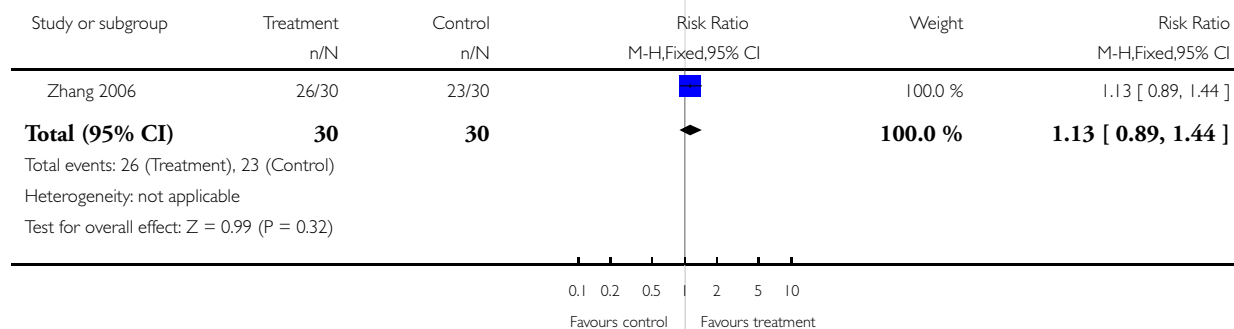


Analysis 2.4. Comparison 2 Needle acupuncture plus valproate versus valproate alone, Outcome 4 25% or greater reduction in seizure frequency.

Review: Acupuncture for epilepsy

Comparison: 2 Needle acupuncture plus valproate versus valproate alone

Outcome: 4 25% or greater reduction in seizure frequency

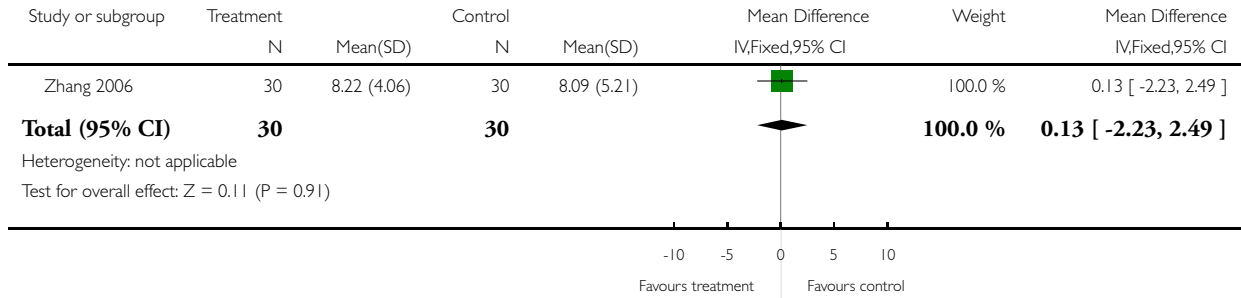


Analysis 2.5. Comparison 2 Needle acupuncture plus valproate versus valproate alone, Outcome 5 Seizure score after treatment.

Review: Acupuncture for epilepsy

Comparison: 2 Needle acupuncture plus valproate versus valproate alone

Outcome: 5 Seizure score after treatment



Analysis 3.1. Comparison 3 Needle acupuncture versus sham acupuncture, Outcome 1 Percentage reduction in seizure frequency.

Percentage reduction in seizure frequency

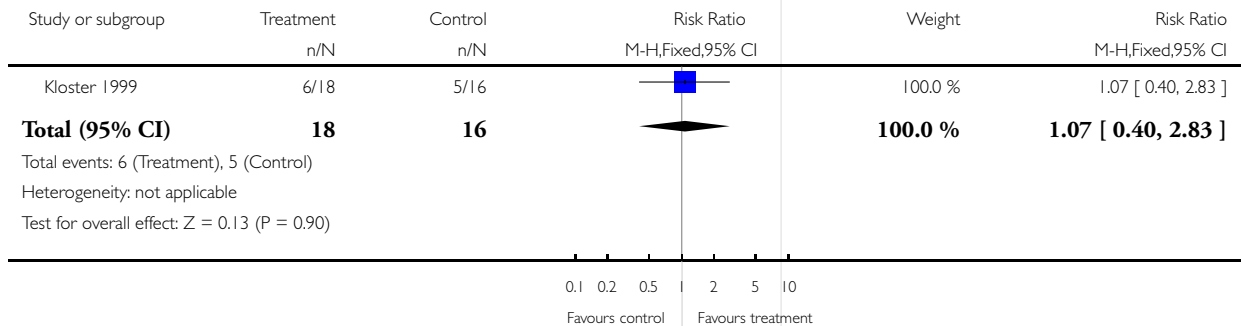
Kloster 1999	45% (n=18)	20% (n=16)
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Analysis 3.2. Comparison 3 Needle acupuncture versus sham acupuncture, Outcome 2 Reduction in seizure frequency.

Review: Acupuncture for epilepsy

Comparison: 3 Needle acupuncture versus sham acupuncture

Outcome: 2 Reduction in seizure frequency

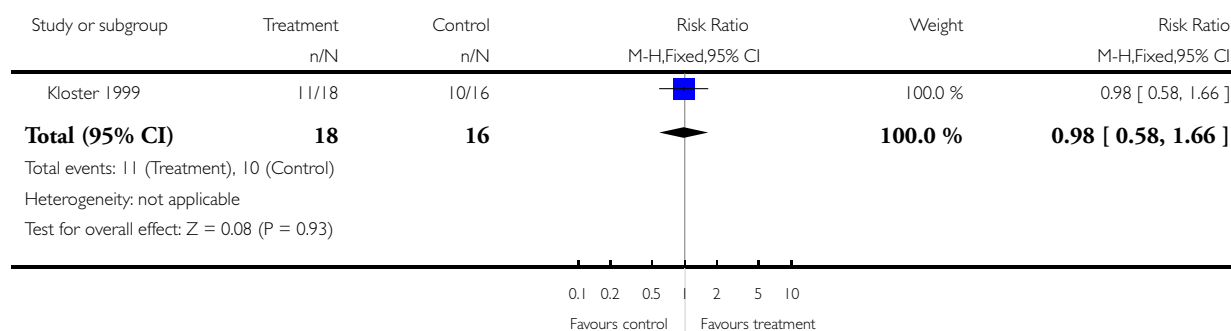


Analysis 3.3. Comparison 3 Needle acupuncture versus sham acupuncture, Outcome 3 No increase in seizure frequency.

Review: Acupuncture for epilepsy

Comparison: 3 Needle acupuncture versus sham acupuncture

Outcome: 3 No increase in seizure frequency



Analysis 3.4. Comparison 3 Needle acupuncture versus sham acupuncture, Outcome 4 Percentage increase in seizure-free weeks.

Percentage increase in seizure-free weeks

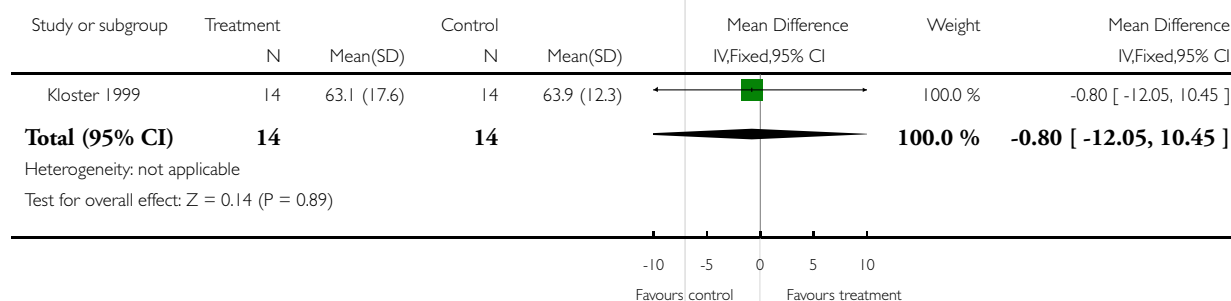
Kloster 1999	50% (n=18)	100% (n=16)
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Analysis 3.5. Comparison 3 Needle acupuncture versus sham acupuncture, Outcome 5 Quality of life raw score (QOLIE-89 score).

Review: Acupuncture for epilepsy

Comparison: 3 Needle acupuncture versus sham acupuncture

Outcome: 5 Quality of life raw score (QOLIE-89 score)

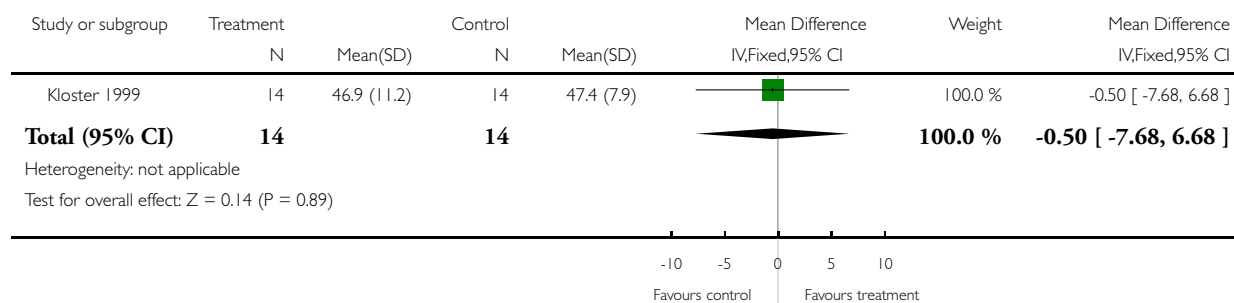


Analysis 3.6. Comparison 3 Needle acupuncture versus sham acupuncture, Outcome 6 Quality of life T-score (QOLIE-89 score).

Review: Acupuncture for epilepsy

Comparison: 3 Needle acupuncture versus sham acupuncture

Outcome: 6 Quality of life T-score (QOLIE-89 score)



Analysis 3.7. Comparison 3 Needle acupuncture versus sham acupuncture, Outcome 7 Mean improvement in quality of life raw score (QOLIE-89 score).

Mean improvement in quality of life raw score (QOLIE-89 score)

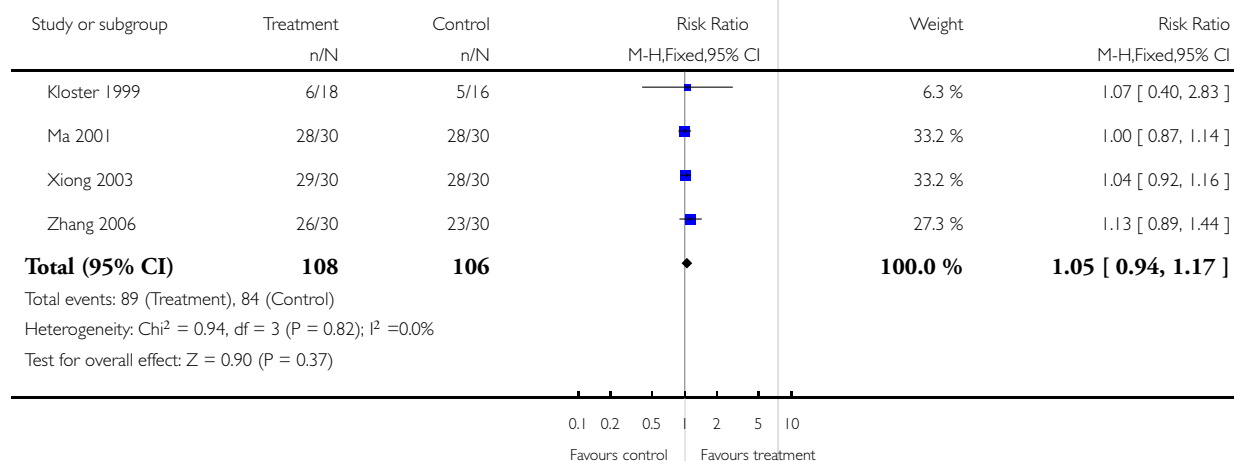
Kloster 1999	-1.7 (n=12)	1.7 (n=10)
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Analysis 4.1. Comparison 4 Needle acupuncture versus control, Outcome 1 Reduction in seizure frequency.

Review: Acupuncture for epilepsy

Comparison: 4 Needle acupuncture versus control

Outcome: 1 Reduction in seizure frequency

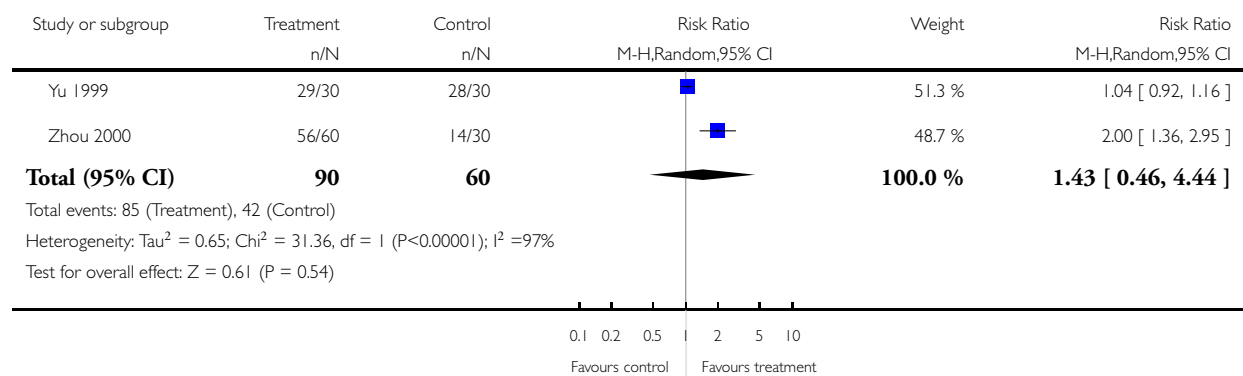


Analysis 5.1. Comparison 5 Needle acupuncture versus phenytoin, Outcome 1 50% or greater reduction in seizure frequency.

Review: Acupuncture for epilepsy

Comparison: 5 Needle acupuncture versus phenytoin

Outcome: 1 50% or greater reduction in seizure frequency

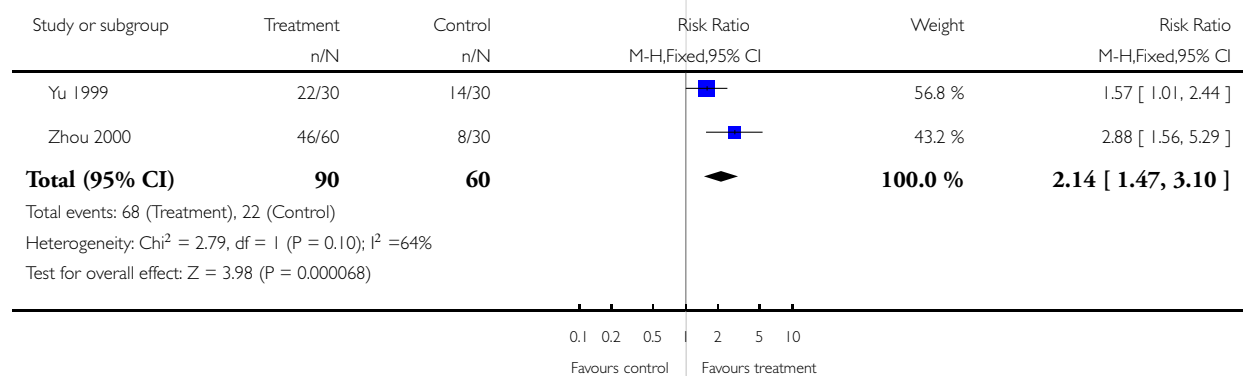


Analysis 5.2. Comparison 5 Needle acupuncture versus phenytoin, Outcome 2 75% or greater reduction in seizure frequency.

Review: Acupuncture for epilepsy

Comparison: 5 Needle acupuncture versus phenytoin

Outcome: 2 75% or greater reduction in seizure frequency

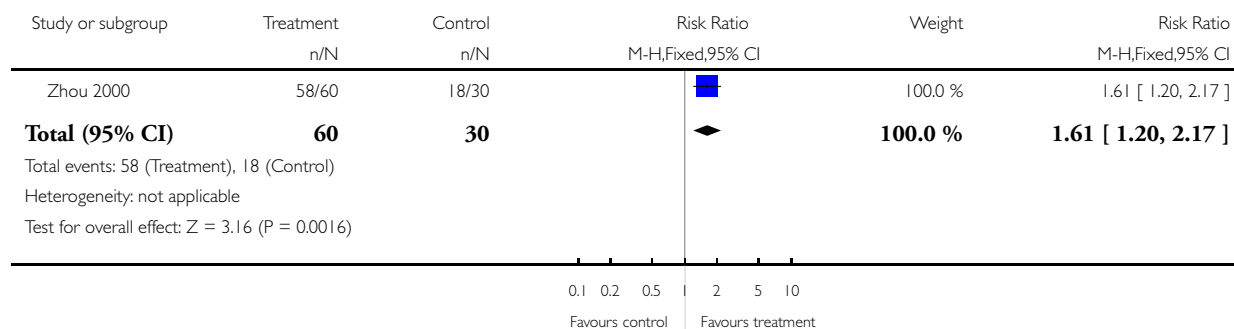


Analysis 5.3. Comparison 5 Needle acupuncture versus phenytoin, Outcome 3 25% or greater reduction in seizure frequency.

Review: Acupuncture for epilepsy

Comparison: 5 Needle acupuncture versus phenytoin

Outcome: 3 25% or greater reduction in seizure frequency

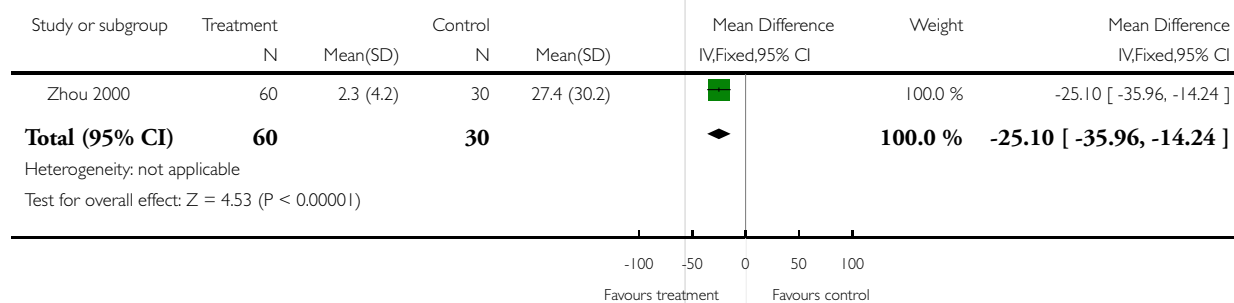


Analysis 5.4. Comparison 5 Needle acupuncture versus phenytoin, Outcome 4 Seizure frequency after treatment.

Review: Acupuncture for epilepsy

Comparison: 5 Needle acupuncture versus phenytoin

Outcome: 4 Seizure frequency after treatment

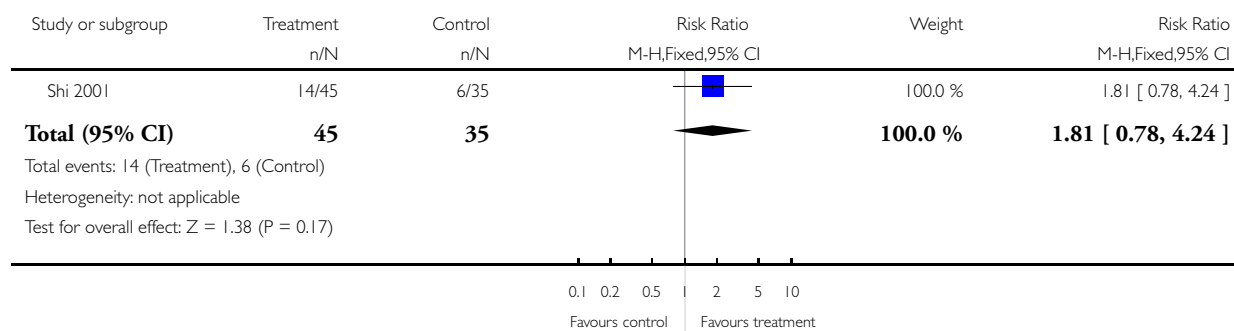


Analysis 6.1. Comparison 6 Needle acupuncture versus valproate, Outcome 1 Seizure freedom.

Review: Acupuncture for epilepsy

Comparison: 6 Needle acupuncture versus valproate

Outcome: 1 Seizure freedom

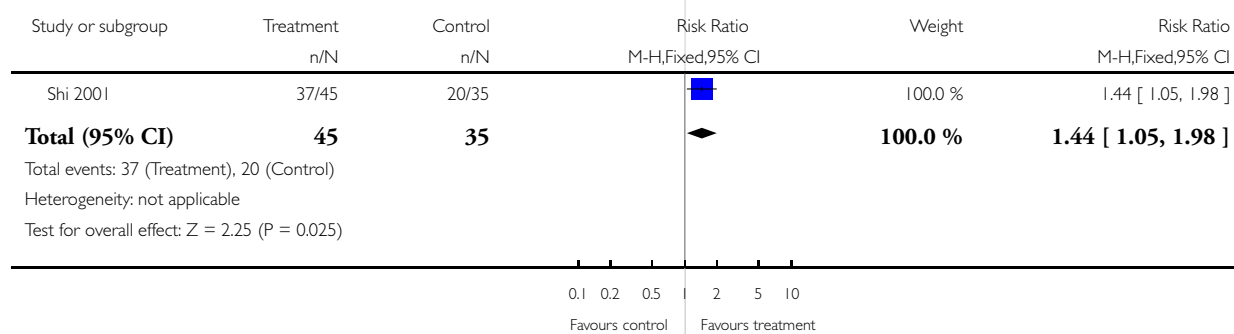


Analysis 6.2. Comparison 6 Needle acupuncture versus valproate, Outcome 2 50% or greater reduction in seizure frequency.

Review: Acupuncture for epilepsy

Comparison: 6 Needle acupuncture versus valproate

Outcome: 2 50% or greater reduction in seizure frequency

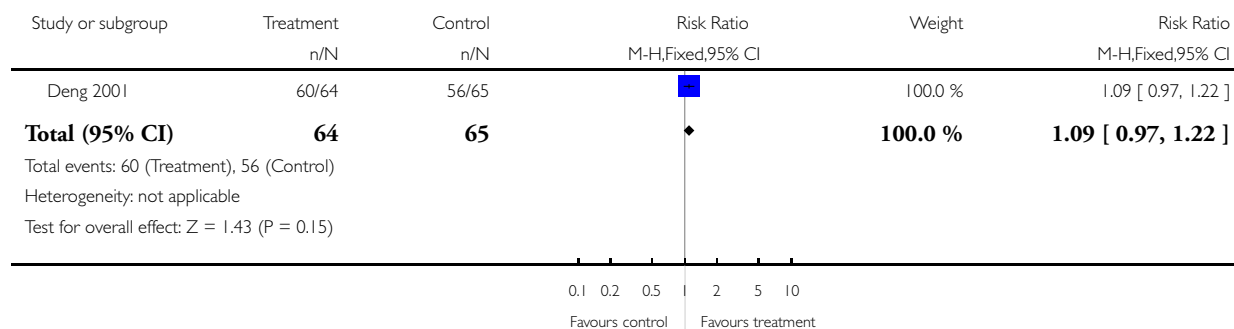


Analysis 7.1. Comparison 7 Catgut implantation at acupoints plus valproate or carbamazepine versus valproate or carbamazepine alone, Outcome 1 50% or greater reduction in seizure frequency.

Review: Acupuncture for epilepsy

Comparison: 7 Catgut implantation at acupoints plus valproate or carbamazepine versus valproate or carbamazepine alone

Outcome: 1 50% or greater reduction in seizure frequency

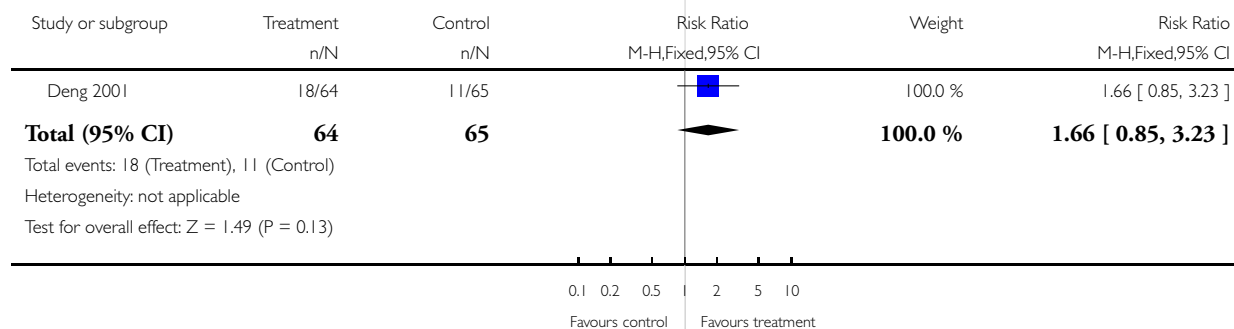


Analysis 7.2. Comparison 7 Catgut implantation at acupoints plus valproate or carbamazepine versus valproate or carbamazepine alone, Outcome 2 92% or greater reduction in seizure frequency.

Review: Acupuncture for epilepsy

Comparison: 7 Catgut implantation at acupoints plus valproate or carbamazepine versus valproate or carbamazepine alone

Outcome: 2 92% or greater reduction in seizure frequency

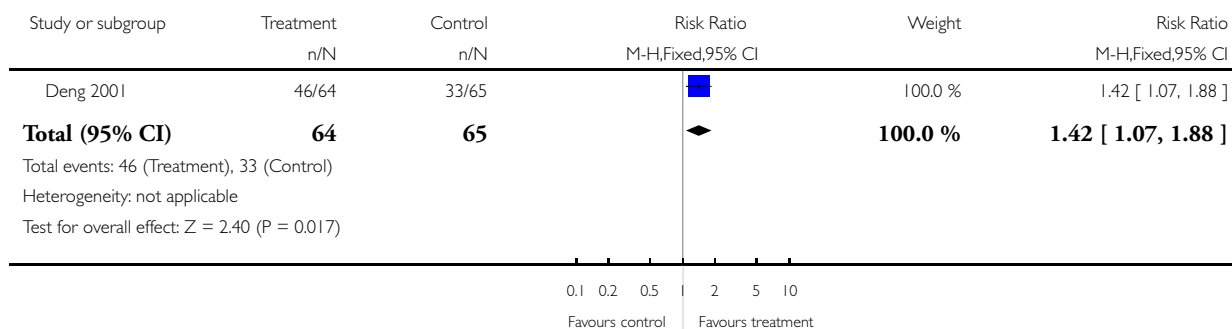


Analysis 7.3. Comparison 7 Catgut implantation at acupoints plus valproate or carbamazepine versus valproate or carbamazepine alone, Outcome 3 75% or greater reduction in seizure frequency.

Review: Acupuncture for epilepsy

Comparison: 7 Catgut implantation at acupoints plus valproate or carbamazepine versus valproate or carbamazepine alone

Outcome: 3 75% or greater reduction in seizure frequency

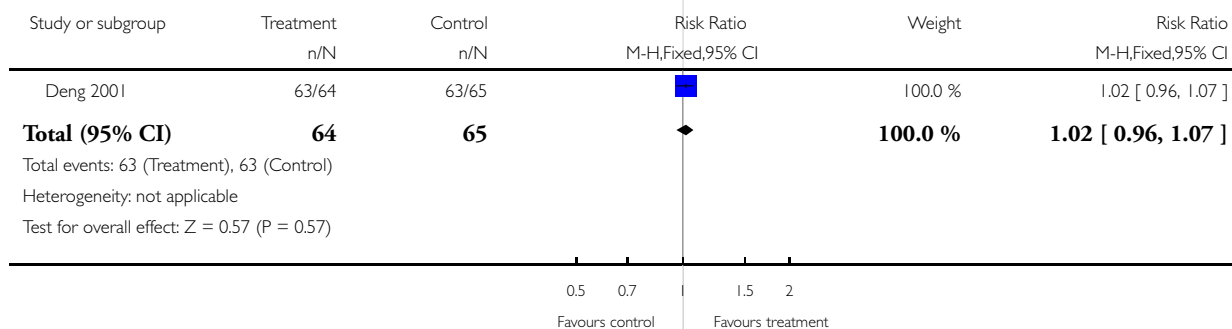


Analysis 7.4. Comparison 7 Catgut implantation at acupoints plus valproate or carbamazepine versus valproate or carbamazepine alone, Outcome 4 25% or greater reduction in seizure frequency.

Review: Acupuncture for epilepsy

Comparison: 7 Catgut implantation at acupoints plus valproate or carbamazepine versus valproate or carbamazepine alone

Outcome: 4 25% or greater reduction in seizure frequency

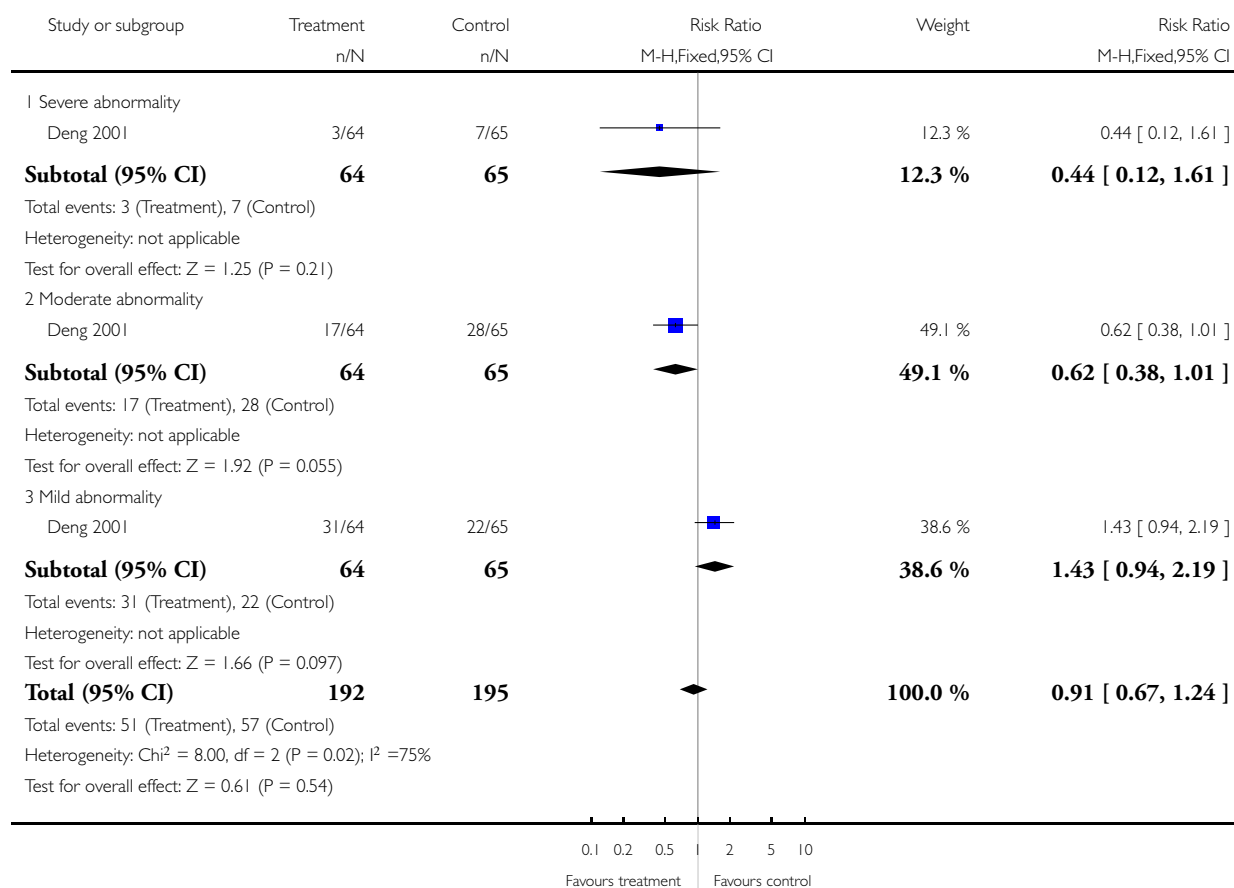


Analysis 7.5. Comparison 7 Catgut implantation at acupoints plus valproate or carbamazepine versus valproate or carbamazepine alone, Outcome 5 Abnormal EEG after treatment.

Review: Acupuncture for epilepsy

Comparison: 7 Catgut implantation at acupoints plus valproate or carbamazepine versus valproate or carbamazepine alone

Outcome: 5 Abnormal EEG after treatment

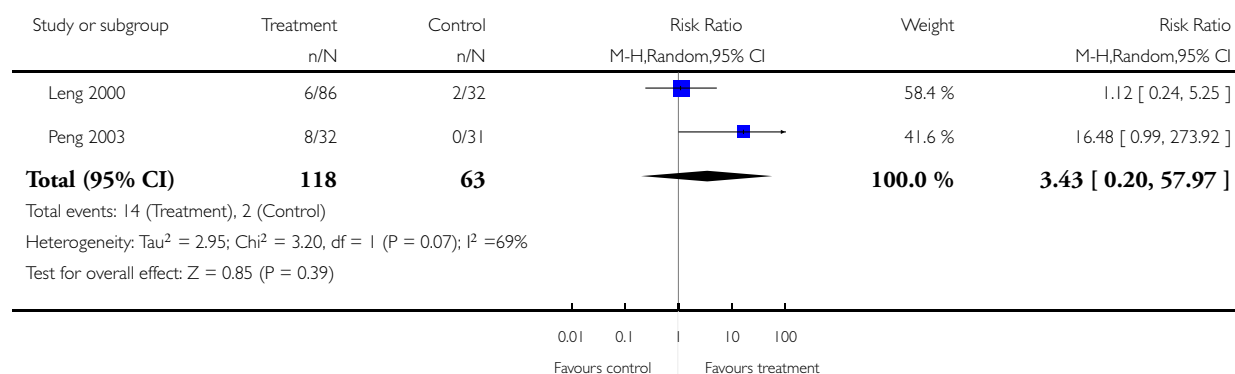


Analysis 8.1. Comparison 8 Catgut implantation at acupoints versus valproate alone, Outcome 1 Seizure freedom.

Review: Acupuncture for epilepsy

Comparison: 8 Catgut implantation at acupoints versus valproate alone

Outcome: 1 Seizure freedom

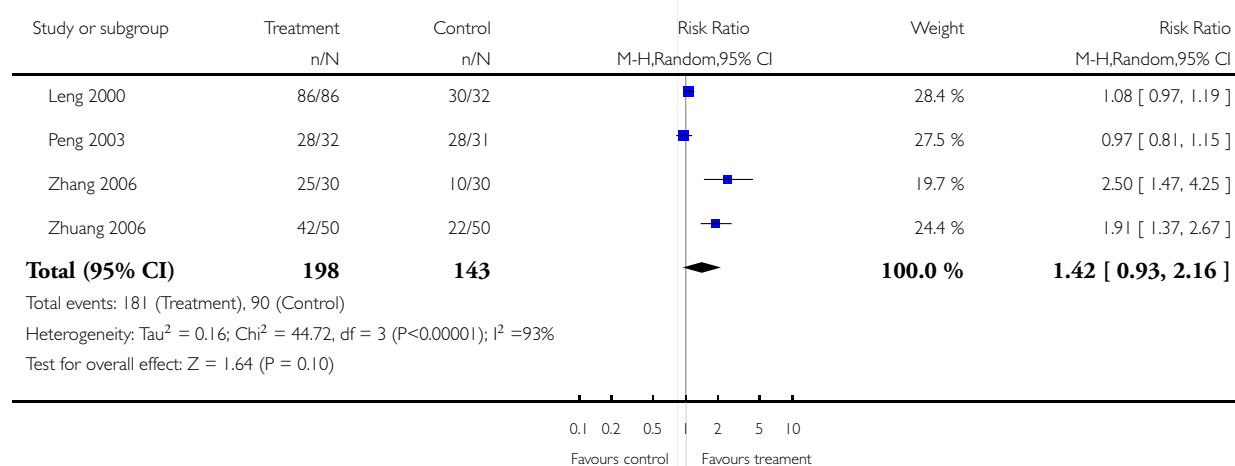


Analysis 8.2. Comparison 8 Catgut implantation at acupoints versus valproate alone, Outcome 2 50% or greater reduction in seizure frequency.

Review: Acupuncture for epilepsy

Comparison: 8 Catgut implantation at acupoints versus valproate alone

Outcome: 2 50% or greater reduction in seizure frequency

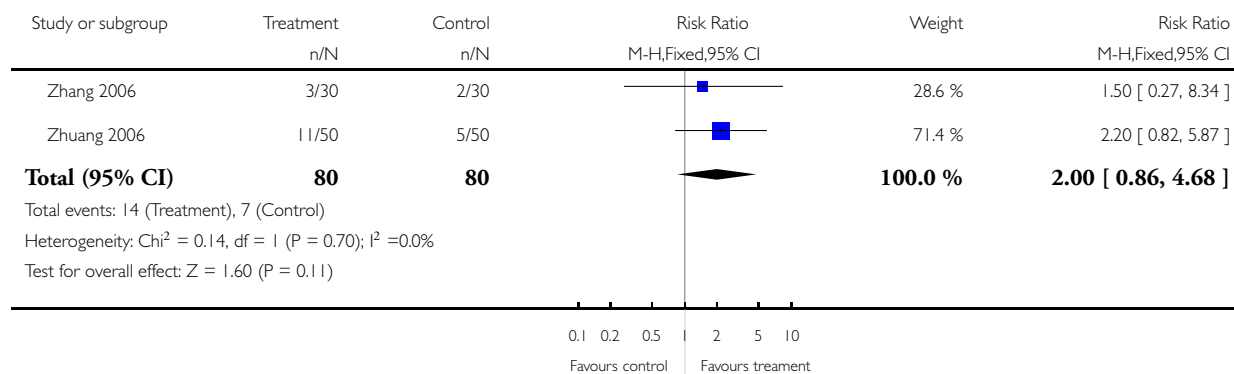


Analysis 8.3. Comparison 8 Catgut implantation at acupoints versus valproate alone, Outcome 3 92% or greater reduction in seizure frequency.

Review: Acupuncture for epilepsy

Comparison: 8 Catgut implantation at acupoints versus valproate alone

Outcome: 3 92% or greater reduction in seizure frequency

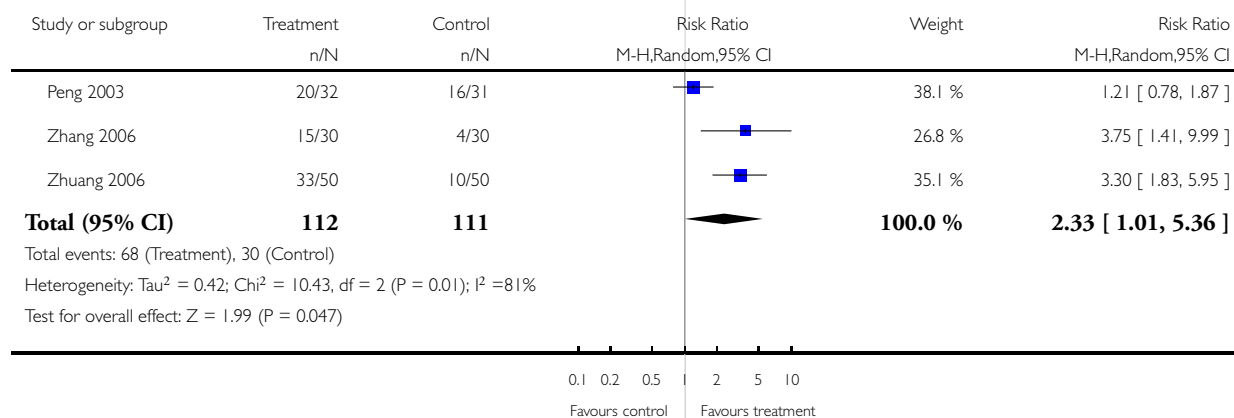


Analysis 8.4. Comparison 8 Catgut implantation at acupoints versus valproate alone, Outcome 4 75% or greater reduction in seizure frequency.

Review: Acupuncture for epilepsy

Comparison: 8 Catgut implantation at acupoints versus valproate alone

Outcome: 4 75% or greater reduction in seizure frequency

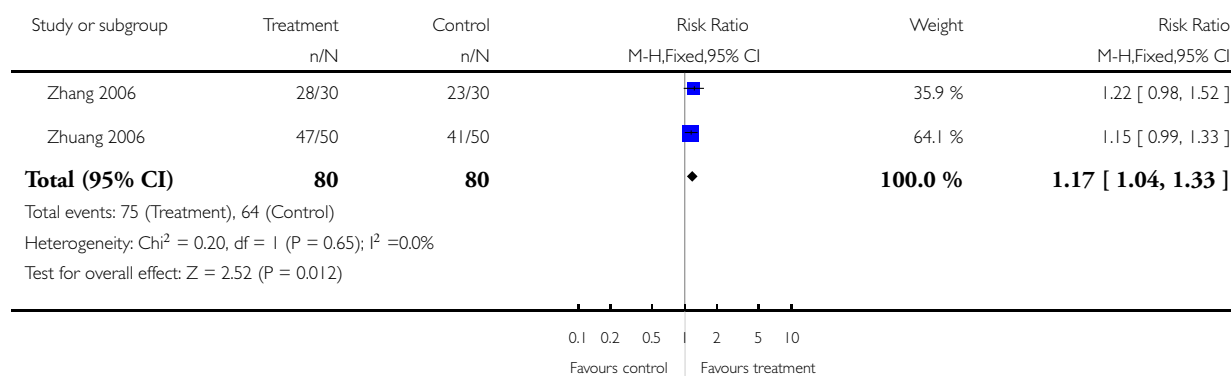


Analysis 8.5. Comparison 8 Catgut implantation at acupoints versus valproate alone, Outcome 5 25% or greater reduction in seizure frequency.

Review: Acupuncture for epilepsy

Comparison: 8 Catgut implantation at acupoints versus valproate alone

Outcome: 5 25% or greater reduction in seizure frequency

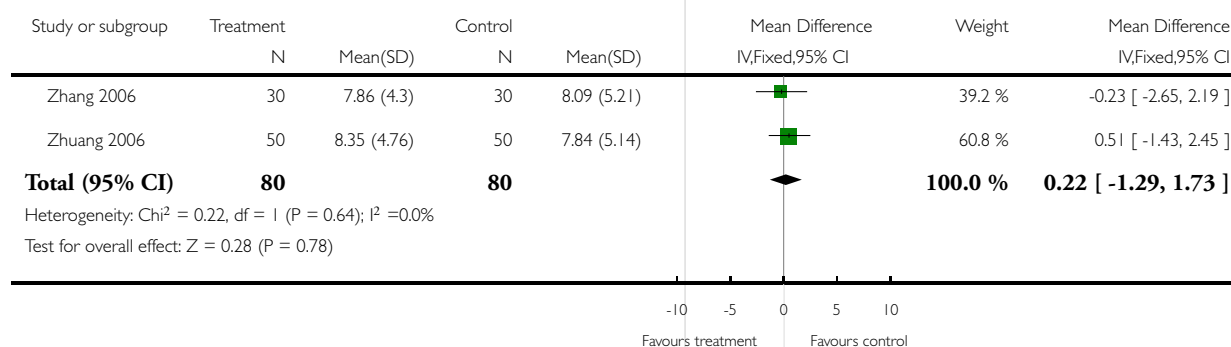


Analysis 8.6. Comparison 8 Catgut implantation at acupoints versus valproate alone, Outcome 6 Seizure score after treatment.

Review: Acupuncture for epilepsy

Comparison: 8 Catgut implantation at acupoints versus valproate alone

Outcome: 6 Seizure score after treatment



APPENDICES

Appendix I. MEDLINE search strategy

We used the following search strategy, that used a combination of controlled vocabulary and text word terms for MEDLINE, and was modified to suit other databases.

1. exp acupuncture/
2. acupuncture.tw
3. acupressure.tw
4. electroacupuncture.tw
5. meridians.tw
6. acupoint.tw
7. or/1-6
8. exp epilepsy/
9. epilep\$.tw
10. exp seizures/
11. seizu\$.tw
12. convuls\$.tw
13. or/8-12
14. 7 and 13

FEEDBACK

Query regarding excluded studies

Summary

The following query was made on 27 June 2006.

Why were trials which compared acupuncture alone with other treatments (pragmatic studies) excluded from the review? How many such trials were there? I think these are a valid form of evaluation and would like to know what data, if any, these studies yielded.

Reply

The objective of this review is to evaluate whether acupuncture is effective for treatment of epilepsy. Therefore only studies that yielded the net treatment effect of acupuncture were included. Net treatment effect of acupuncture can be determined by comparing acupuncture with placebo or sham or no treatment, or comparing acupuncture plus other treatments with the same other treatments. Studies comparing acupuncture with another treatment alone cannot help us to determine whether acupuncture itself is effective or not, because even though these studies show that acupuncture is more effective than another treatment e.g. antiepileptic drug or herbs, it does not necessarily mean that acupuncture per se is effective, as the drug may have negative impact on the outcomes, such that even no treatment or an ineffective treatment is better than the comparator drug. Therefore these studies comparing acupuncture with another treatment alone were excluded.

Studies comparing acupuncture with another treatment alone that we identified through a systematic search of the literature are included in the table of "Characteristics of excluded studies". The detailed findings of these studies are not shown but interested readers may refer to the references listed.

NB: 17 July 2008. Please note that this review has now been updated (issue 4/2008) to include the excluded studies i.e. studies comparing acupuncture with antiepileptic drugs.

Contributors

Comment made by Dr Catherine Zollman. Daniel Cheuk replied to the comment on behalf of the review authors for the review.

WHAT'S NEW

Last assessed as up-to-date: 15 July 2008.

11 August 2009	Amended	Contact details updated.
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HISTORY

Protocol first published: Issue 1, 2005

Review first published: Issue 2, 2006

24 October 2008	Amended	Search strategy amended to comply with RevMan 5.
17 July 2008	Amended	Converted to new review format.
17 July 2008	New citation required but conclusions have not changed	The review now includes eight new studies which previously appeared in the 'excluded studies' section. There are now a total of 914 participants.
1 March 2008	New search has been performed	The searches have been updated (1st March 2008).
17 August 2006	Feedback has been incorporated	Feedback incorporated along with contact author's response.

CONTRIBUTIONS OF AUTHORS

Both review authors contributed to the design, development and editing of the protocol and undertook all parts of the review.

DECLARATIONS OF INTEREST

None known.

INDEX TERMS

Medical Subject Headings (MeSH)

Acupuncture Therapy [*methods]; Drugs, Chinese Herbal [therapeutic use]; Epilepsy [*therapy]; Randomized Controlled Trials as Topic; Treatment Outcome

MeSH check words

Child; Humans