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[Intervention Review]

Chinese medicinal herbs for measles

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ABSTRACT

Background

Measles is an infectious disease caused by the *Morbillivirus*. Chinese physicians believe that medicinal herbs are effective in alleviating symptoms and preventing complications. Chinese herbal medicines are dispensed according to the particular symptoms. This is the second update of a Cochrane Review first published in 2006.

Objectives

To assess the effectiveness and possible adverse effects of Chinese medicinal herbs for measles.

Search methods

We searched the Cochrane Central Register of Controlled Clinical Trials (CENTRAL Issue 1, 2011) which contains the Cochrane Acute Respiratory Infections Group's Specialised Register, MEDLINE (1966 to March week 5, 2011), EMBASE (1980 to April 2011), Web of Science (2005 to 30 April 2011), AMED (1985 to 30 April 2011), Chinese Biomedical Database (1976 to 30 June 2011), VIP Information (1989 to 30 June 2011), China National Knowledge Infrastructure (CNKI) (1976 to 30 June 2011), Chinese Journals full-article database (1994 to 30 June 2011) and the *metaRegister* of Controlled Trials for ongoing trials.

Selection criteria

Randomised controlled trials (RCTs) of Chinese medicinal herbs in patients with measles (without complications).

Data collection and analysis

Two review authors (SC, TW) independently assessed trial quality and extracted data. We telephone interviewed the trial authors for missing information regarding participant allocation. Some trials allocated participants according to the sequence they were admitted to the trials, that is to say, by using a pseudo-random allocation method. None of the trials concealed the allocation or used blinding methods.

Main results

We did not identify any suitable trials for inclusion. In this updated review we identified 80 trials which claimed to use random allocation. We contacted 32 trial authors by telephone and learned that the allocation methods used were not randomised. We excluded 34 studies because the participants experienced complications such as pneumonia. We excluded 10 trials because of non-random allocation and complications experienced by the participants. We were unable to contact the remaining four trials' authors, so they require further assessment and have been allocated to the 'Studies awaiting classification' section.

Chinese medicinal herbs for measles (Review)

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Authors' conclusions

There is no RCT evidence for or against Chinese medicinal herbs as a treatment for measles. We hope high-quality, robust RCTs in this field will be conducted in the future.

PLAIN LANGUAGE SUMMARY

Chinese medicinal herbs for measles

Measles (rubeola) is an infectious disease caused by multiplication of a single-strand ribonucleic acid (RNA) virus of the genus *Morbillivirus* in the upper respiratory tract and conjunctiva. It can lead to serious complications and death. Chinese herbal medicines are believed to be effective in alleviating symptoms and shortening the duration of measles, and are widely used as the main or adjunctive therapy to treat measles in China and other countries.

The review authors found a large number of clinical studies providing evidence of Chinese herbal medicines in the treatment of measles. Some of these reports claimed to be randomised controlled trials. However, after telephone interviewing 32 trial authors, we found that none of them used acceptable randomisation procedures to allocate participants and 34 studies included participants with measles complicated with other diseases, for example, pneumonia. Ten trials were non-randomised controlled studies and four trials require further classification. In this update, we were unable to include any randomised controlled trial for assessment. Although no trials were included, the authors reviewed the articles and found no reports of adverse events in the use of Chinese herbal medicines for treating measles. High-quality and large trials are needed.

BACKGROUND

Description of the condition

Measles (rubeola) is an infection caused by multiplication of a single-strand ribonucleic acid (RNA) virus of the genus *Morbillivirus* (Budd 2002) in the upper respiratory tract and conjunctiva. Measles was identified in ancient times and it continues to cause serious problems in many parts of the world. A dramatic decline in both morbidity and mortality has been achieved with the use of measles vaccines (Nemir 1990). In 2008 it was estimated that a total of 164,000 deaths were caused by measles globally (WHO 2011). The only source of infection is from acutely infectious patients.

The measles pathogen exists in secretions from the nasopharynx, mouth and conjunctiva of infected persons; and in sputum, urine and blood, especially in leukocytes. It is spread by droplets or on direct contact with nasal or throat secretions. Less commonly, it is spread by airborne means or by articles freshly soiled with secretions of the nose and throat (WHO 2004). The virus can be very dangerous. Ninety-five per cent of people who have not been vaccinated can be infected after contact with an infectious patient (Zhou 2003). Children between six months and five years of age are the most likely to be infected. Measles is one of the most readily transmitted communicable diseases and probably the best known of the serious childhood rash with fever illnesses (WHO 2004). Patients with immunological deficiencies, malnutrition and particularly vitamin A deficiency may have severe and often fatal forms of measles.

Measles has two clinical manifestations: typical and atypical. The former can be divided into three stages: a prodromal stage, an eruption stage and a subsidence stage. The latter clinical manifestation has several types: mild measles, severe measles, adult measles and heterotypic measles (WHO 2011). Following an incubation period of six to 18 days, the first clinical signs appear and include profuse mucoserous nasal discharge, sneezing, excessive formation of tears and development of photophobia, cough, Koplik spots and fever (Nemir 1990). Three to four days later, the rash develops and symptoms become more severe. The rash generally disappears three to five days later and the temperature decreases (WHO 2011). Complications occur in approximately 30% of cases (Hussey 2003). Pneumonia is the most common and most dangerous complication. In addition, laryngitis, carditis, otitis media and cephalitis may develop. Diagnosis of typical measles is often based on the clinical signs and symptoms. Detecting the specific antibody in the serum and *Morbillivirus* in samples may not be needed. Diagnosis of atypical measles is more difficult and may require sero-diagnosis.

Description of the intervention

There is no specific treatment for measles. Therapy should be aimed at alleviating symptoms and preventing complications. For uncomplicated measles, rest and supportive treatment aids recovery for most people. Therapies for reducing fever and pain, for example, antipyretics and extra fluids during the febrile period and cough suppressants are necessary (Perry 2002). Aspirin should be used with caution because a correlation has been found between children taking aspirin and the development of Reye's syndrome (Starko 1980). Vitamin A is used in low-income countries to treat measles. There is no significant reduction in overall mortality, but it can reduce mortality in children under two years age (Yang 2011).

Many Chinese physicians believe that herbal medicines are effective in alleviating symptoms and shortening the duration of the disease. Herbal medicines are not only routinely used for most respiratory diseases in hospitals but are also commonly used by many Chinese people at home. Chinese medical theory is based on the belief that measles is caused by an invasion of an 'exterior unhealthy influence'. Accordingly, appropriate drugs (treating the unhealthy influence) are used in the early stage of the disease. These drugs are thought to promote sweating to reduce fever and clear 'toxic material'. Drugs thought to improve immunity are used in later stages to speed recovery from measles.

How the intervention might work

Herbs are dispensed depending on the symptoms. Pharmacological experiments suggest that Ge Gen (*Radix puerariae*) (Dou 2004), Sheng ma (*Rhizoma cimicifugae*) (Zhao 2004b), Jing Jie (*Herba schizonepetae*) (Zhao 2004a) and Lian qiao (*Fructus forsythiae*) (Deng 2004) may abate fever. In addition, Sheng ma (*Rhizoma cimicifugae*) (Zhao 2004b) and Jing Jie (*Herba schizonepetae*) (Zhao 2004a) might act as analgesics and sedatives. Bo he (*Herba menthae*) is used to induce perspiration and loosen sputum (Wang 2004a). Jing Jie (*Herba schizonepetae*) (Zhao 2004a) and Jie geng (*Radix platycodi*) (Xuan 2004) may have an antitussive effect and loosen sputum. Sang ye (*Folium mori*) (Wang 2004b) and Zi Cao (*Radix arnebiae*) (Hou 2004) may have an anti-inflammatory effect. Mai dong (*Radix ophiopogonis*) might improve immunity (Tao 2004). Ideally, it is thought that Chinese medicinal herbs should be used according to the practice of traditional Chinese medicine.

Why it is important to do this review

A large number of studies of treatment of measles with traditional Chinese herbs have been published. These have shown significant benefits in the clinical setting. However, the benefits and adverse reactions of these treatments have not yet been systematically reviewed.

OBJECTIVES

To assess the effectiveness and possible adverse effects of Chinese medicinal herbs in treating measles.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs).

Types of participants

We included adults and children diagnosed with measles. Diagnosis is generally based on positive signs and symptoms. Sero-diagnosis can be used when necessary. To be consistent with changes in classification and diagnostic criteria of the disease, the diagnosis should have been established using standard criteria that were valid at the beginning of the trial. Changes in diagnostic criteria may produce significant variability in the clinical characteristics of the patients included, as well as in the results obtained. These differences were to be considered, documented and explored in a sensitivity analysis. We excluded measles with complications. We excluded patients concurrently infected with other infections.

Types of interventions

We compared Chinese medicinal herbs or injections extracted from herbs with placebo or with another intervention regimen.

Types of outcome measures

Primary outcomes

1. Death from any cause resulting from secondary complications during treatment.
2. Improvement in overall symptoms.

The measures of 'recovery' and 'no improvement' are as follows. We defined recovery as: fever had abated to normal limits within three days after starting treatment; the symptoms had vanished completely. We used the following outcomes to measure recovery:

1. fast improvement - the fever had abated within 48 hours following treatment; and
2. marked improvement - meaning the fever had abated within three to five days after treatment.

We defined no improvement as: there were no significant changes in the symptoms at the end of day seven after administering Chinese medical herbs. We also considered the following outcomes: participants with a high fever treated with interventions such as ice applications to the forehead, applying alcohol over the body or antibiotics for clearance of fever during treatment.

Secondary outcomes

1. Marked improvement: fever abatement time occurred within three to five days of Chinese medical herbs being administered and most of the symptoms had cleared up.
2. Improvement: temperature returned to normal after Chinese medical herbs had been administered and the rash disappeared within six to seven days.
3. Fever clearance time.

Adverse events

We defined serious adverse events according to the International Conference on Harmonisation (ICH) Guidelines (ICHEWG 1997) to include any event that leads to death, was life-threatening, required inpatient hospitalisation or prolongation of existing hospitalisation, resulted in persistent or significant disability or any important medical event which may have jeopardised the participant or required an intervention to prevent such an event. All other adverse events were considered as non-serious.

Search methods for identification of studies

Electronic searches

For this 2011 update we searched the Cochrane Central Register of Controlled Trials (CENTRAL) 2011, Issue 1, part of *The Cochrane Library*, www.thecochranelibrary.com (accessed 11 April 2011), which contains the Cochrane Acute Respiratory Infections Group's Specialised Register, MEDLINE (March 2009 to March week 5, 2011), EMBASE (March 2009 to 30 April 2011), Web of Science (2009 to 30 April 2011), AMED (2009 to 30 April 2011), Chinese Biomedical Database (2009 to 30 June 2011), VIP Information (2009 to 30 June 2011), China National Knowledge Infrastructure (CNKI) (2009 to 30 June 2011), Chinese Journals full-article database (2009 to 30 June

2011) and the WHO ICTRP Search Portal for ongoing trials. See [Appendix 1](#) for details of previous searches.

We used the following search strategy to search MEDLINE and CENTRAL. We did not use a filter to identify randomised trials in MEDLINE as there were too few results.

MEDLINE (Ovid)

```
1 exp Measles/
2 exp Measles virus/
3 measles.tw.
4 Morbillivirus/ (223)
5 (morbilli virus* or morbillivirus*).tw.
6 rubeola.tw.
7 or/1-6
8 Medicine, Chinese Traditional/
9 Medicine, East Asian Traditional/
10 Drugs, Chinese Herbal/
11 Plants, Medicinal/
12 (chinese adj3 (medicin* or herb*)).tw.
13 (medicin* adj3 herb*).tw.
14 or/8-13
15 7 and 14
```

We modified the search strategy to search Web of Science, EMBASE, AMED, VIP, Chinese Biomedical Database, CNKI and Chinese Journals full-article database. We did not impose any language or publication restrictions (see [Appendix 2](#); [Appendix 3](#); [Appendix 4](#); [Appendix 5](#); [Appendix 6](#); [Appendix 7](#); [Appendix 8](#) for the search strategies applied to the individual databases).

Searching other resources

We attempted to identify additional studies by searching the reference lists of relevant trials, reviews, conference proceedings and journals. In particular, with respect to journals, we searched those not indexed in the electronic databases.

We contacted organisations (including the WHO (www.who.int), the Chinese Trial Registry (www.chictr.org), individual researchers working in the field and medicinal herbal manufacturers) in order to obtain additional references, unpublished trials, ongoing trials, confidential reports and raw data of published trials.

Data collection and analysis

We followed the instructions given in the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](#)) and the Cochrane Acute Respiratory Infections Group's [Module](#).

Selection of studies

Three review authors (SC, XYK, YH) independently clarified the authenticity of each supposed RCT by telephone interviewing the original trial authors. We excluded trials that failed to meet our inclusion criteria and the reasons are listed in the [Characteristics of excluded studies](#) table. There were no disagreements about the selection of studies.

Data extraction and management

One review author (SC) extracted relevant population and intervention characteristics using a standard data extraction template. Another author (TW) resolved any disagreements by discussion. We pilot tested the data extraction form prior to using it.

We sought all relevant missing information about the trials from the original authors of the articles. We resolved disagreements through discussion.

Assessment of risk of bias in included studies

We planned to assess risk of bias of randomised controlled trials by the following quality criteria specified in *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011):

1. Sequence generation (checking for possible selection bias)

The methods used to generate the allocation sequence are categorised as:

- adequate (any truly random process, e.g. random number table; computer random number generator);
- inadequate (any non-random process, e.g. odd or even date of birth; hospital or clinic record number); or
- unclear.

2. Allocation concealment (checking for possible selection bias)

The method used to conceal the allocation sequence in sufficient detail and determine whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment. Methods are categorised as:

- adequate (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes);
- inadequate (open random allocation; unsealed or non-opaque envelopes, alternation; date of birth); or
- unclear.

3. Blinding (checking for possible performance bias)

We judged studies at low risk of bias if they were blinded, or if we judged that the lack of blinding could not have affected the results. We assessed blinding separately for different outcomes or classes of outcomes. Methods are categorised as:

- low risk: the outcome assessors were blinded;
- high risk: no blinding was used; or
- unclear.

4. Incomplete outcome data (checking for possible attrition bias through withdrawals, drop-outs, protocol deviations)

We planned to assess whether attrition and exclusions were reported; the numbers included in the analysis at each stage (compared with the total randomised participants); reasons for attrition or exclusion where reported; and whether missing data were balanced across groups or were related to outcomes. The data are categorised as:

- low risk of incomplete outcome data bias: trials where few drop-out/losses to follow-up are noted and an intention-to-treat analysis is possible;
- high risk of incomplete outcome data bias: the rate of exclusion was at least 20%, or wide differences in exclusions between groups whatever the intention-to-treat was used; or
- unclear.

5. Selective reporting bias

We planned to investigate the possibility of selective outcome reporting bias and what we found. The data are categorised as:

- low risk of reporting bias (where it is clear that all of the study's prespecified outcomes and all expected outcomes of interest to the review have been reported);
- high risk of reporting bias (where not all the study's prespecified outcomes have been reported; one or more reported primary outcomes were not prespecified; outcomes of interest are reported incompletely and so cannot be used; study fails to include results of a key outcome that would have been expected to have been reported); or
- unclear.

(6) Other sources of bias

We assessed whether each study was free of other problems that could put it at risk of bias:

- yes;
- no; or
- unclear

Measures of treatment effect

In future we will express dichotomous data as risk ratios (RR) with 95% confidence intervals (CI). If the events probability is small, we will use the Peto odds ratio (OR). Continuous variables are expressed as mean differences (MD) with 95% CI.

Unit of analysis issues

The unit of analysis will be the individual.

Dealing with missing data

We will obtain relevant missing data from trial authors if feasible and carefully perform an evaluation of important numerical data such as screened, randomised patients as well as intention-to-treat (ITT), as-treated and per-protocol (PP) population. We will investigate attrition rates, for example, drop-outs, losses to follow-up and withdrawals, and critically appraise issues of missing data and imputation methods, for example, last observation carried forward (LOCF).

Assessment of heterogeneity

Study results are not reported as meta-analytically pooled effect estimates in the event of substantial clinical or methodological or statistical heterogeneity. We will identify heterogeneity by visual inspection of the forest plots, by using a standard Chi² test and a significance level of $\alpha = 0.1$, in view of the low power of this test. We will specifically examine heterogeneity with the I² statistic, quantifying inconsistency across studies to assess the impact of heterogeneity on the meta-analysis, where an I² statistic of 75% and more indicates a considerable level of inconsistency (Higgins 2011). When heterogeneity is found, we will attempt to determine the potential causes by examining individual studies and subgroup characteristics.

Assessment of reporting biases

We will test for publication bias by using the funnel plot in future updates if there are sufficient trials to include in our review.

Data synthesis

We will statistically summarise data if they are available, sufficiently similar and of sufficient quality. We plan to perform statistical analyses according to the statistical guidelines referenced in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

We will summarise data in a narrative format and analyse different comparisons separately when data are reported in various forms that could not be easily converted into a standard measure.

For meta-analyses, we will process data as follows: data are included in a meta-analysis if they are of sufficient quality and sufficiently similar. We expect both event (dichotomous) data and continuous data. We will express dichotomous data as RR. We may use the Peto OR as an alternative to the RR if the rate of events is low, for example, the rate of goitre and mortality. We will express continuous data as MD. If RR or MD are used, we will calculate overall results based on the random-effects model.

Subgroup analysis and investigation of heterogeneity

We planned to conduct an overall analysis and subgroup analyses in order to explore effect size differences between groups as follows:

1. by different controls to compare the relative effects;

2. by different age group: child (six months to 14 years) versus adult (15 years or older); or
3. by different preparations or different forms of traditional Chinese medicine (TCM), for example, injection versus decoction.

Sensitivity analysis

We plan to carry out a sensitivity analysis to examine the effects of removing studies at high risk of bias (studies with poor or unclear allocation concealment) from the analysis. We considered a study to be of high quality if it was graded as adequate in both the randomisation and allocation concealment and in either blinding or loss to follow-up.

RESULTS

Description of studies

Results of the search

In this update, we identified 24 studies comparing Chinese medicinal herbs with placebo or with another intervention, which mentioned random allocation. We interviewed the original trial authors to ascertain whether the method of allocation was truly randomised or not. We successfully contacted 25 trial authors (Figure 1).

Figure 1. Study flow diagram.

Included studies

We did not identify any trials eligible for inclusion.

Excluded studies

In total, we excluded 80 studies. From the potential 29 studies identified in this update review we were able to excluded 24

studies. The allocation methods were inadequately randomised in nine excluded studies (Fang 2010; Ji 2008; Liao 2011; Luo 2009; Nu 2010; Sun 2009; Zheng 2003; Zhou 2010; Zhou 2009). Ten studies were excluded because the participants had measles complicated by pneumonia (Bo 2010; Guan 2009; Guo 2010; Li 2009; Liu 2009; Liu 2010; Ma 2009; Ma 2009a; Yan 2009; Zhang 2010). One study was excluded because the participant developed

encephalitis (Chen 2010). Five studies were excluded because the participants had measles with multiple complications such as laryngitis, bronchitis, respiratory failure, heart failure, diarrhoea, pneumothorax, pneumonia, hepatitis, enteritis, renal damage or heart damage (Cheng 2002; Chu 2011; Dong 2011; Xia 2011; Zhang 2009). We were still unable to contact the authors of the remaining four studies (Cui 1994; Feng 1994; Jiao 2001; Liu 1996). These require further assessment and have been allocated to the [Studies awaiting classification](#) section.

Risk of bias in included studies

Allocation

Eighty studies claimed to have "randomly allocated patients". After telephone interviewing the trial authors, we identified 43 studies as non-RCTs in which the participants were allocated by the trial authors and randomisation was misunderstood.

Blinding

None of the studies used blinding.

Incomplete outcome data

We did not identify any suitable trials for inclusion.

Selective reporting

We did not identify any suitable trials for inclusion.

Other potential sources of bias

Almost all the Chinese medicines were prepared by the trial authors, so there was a high risk of conflict of interest.

Effects of interventions

In the absence of any suitable RCTs, we were unable to perform any analyses.

DISCUSSION

Summary of main results

We have no data to report.

Overall completeness and applicability of evidence

Although Chinese medicinal herbs are widely used to treat measles in China and many relevant clinical studies have been completed and published, we were unable to identify any randomised controlled trials (RCTs). We hope high-quality RCTs in this field will be conducted in the future.

Quality of the evidence

The results of the telephone interviews demonstrated that the designs of the clinical studies we identified were not randomised, even though all of the identified studies mentioned randomisation. Some studies allocated patients voluntarily. Some studies allocated patients according to the patients' admitting sequence, making it a pseudo-random allocation. None of the trials concealed patient allocation or used a blinding method.

Potential biases in the review process

Allocation concealment is important in preventing selection bias. None of the studies related to our question concealed the allocation process, which could lead to a high risk of selection bias.

Blinding was not used, which could lead to a high risk of performance and detection bias. Chinese medicinal herbs usually differ from Western medicines in terms of appearance, taste and smell. Therefore, blinding was difficult. However, a double-dummy technique could be used and the outcome assessors could be blinded. Publication bias may exist as all of the studies were published in Chinese and no primary articles reported negative results.

An additional problem was that most Chinese medicinal herbal preparations were tested in one study only and most of the trials were conducted in country hospitals or smaller clinics. This means that most of the trials did not receive ethical approval and therefore may not be true trials but analysis reports from case notes.

Agreements and disagreements with other studies or reviews

We did not identify any suitable trials for inclusion.

AUTHORS' CONCLUSIONS

Implications for practice

There were no randomised controlled trials (RCTs) for or against Chinese medicinal herbs as a treatment for measles.

Implications for research

Further research in Chinese medicinal herbs seems justified by both the claims of the doctors and the popularity of alternative therapies in general. RCTs are urgently needed in order to define the efficacy and acceptability of these interventions for measles.

Well-designed, multi-centre RCTs are required to evaluate Chinese medicinal herbs for measles. Outcome measures should include overall symptom and fever clearance times. Adverse events should be critically assessed by standardised monitoring or an effective self reporting system. Attention should be paid to long-term adverse effects of Chinese medicinal herbs.

Although Chinese herbal medicine as a treatment for measles and its method of manufacture are widely accepted in China, most of the constituents of the pharmacological preparations used in trials cannot be clearly specified. This is in marked contrast to pharmacological agents used in Western medicine, in which the chemical constituents, the quantities and the percentage of any impurities or contaminants are precisely known, and the variation between different production batches is kept within specified limits. Variation between formulations and batches of treatments are an inevitable consequence of traditional Chinese medicines, though the Chinese Government also specifies the limits of variation that are acceptable. This variation is a factor that may contribute to any heterogeneity between different study results.

Furthermore, one must accept that the overall treatment concept for traditional Chinese medicine is different to that used in Western medicine. When a study uses a self prepared herbal formulation,

the quality of herbs and methods of preparation should be stated in detail, in order to achieve consistent effects.

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CHARACTERISTICS OF STUDIES

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Ai 2004	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the method of allocation, which had been described as "according to the administration sequence", was not an adequate randomisation approach. Participants suffered from measles with pneumonia
Bo 2010	Participants were described as having "measles with pneumonia". Pneumonia is a complication of measles
Cai 2004	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the method of allocation, which had been described as "according to the administration sequence", was not an adequate randomisation approach. There was no random number table or other adequate randomisation approach
Chen 2010	The condition (measles) was described as "atypical measles". The trial author has not yet confirmed the diagnosis of measles
Cheng 2002	Participants were described as having "measles with heart failure". Heart failure is a complication of measles
Chu 2011	Most participants had complications of measles, such as laryngitis, bronchitis, pneumonia, liver damage or diarrhoea
Cui 1999	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "according to administration sequence", was not an adequate randomisation approach. There was no random number table or other adequate randomisation
Cui 2006	Participants had "childhood measles with pneumonia". Pneumonia is one of the complications of measles
Ding 2008	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "arbitrary", was not an adequate randomisation approach. There was no random number table or other adequate randomisation and no protocol before clinical trial
Dong 2005	Participants had "childhood measles with pneumonia". Pneumonia is one of the complications of measles
Dong 2011	Participants were described as having "measles with heart failure". Heart failure is a complication of measles
Du 2008	Most participants had complications of measles, such as laryngitis, bronchitis, respiratory failure, heart failure, diarrhoea or pneumothorax
Fan 2006	The condition (measles) was described as "atypical measles". The trial author has not yet confirmed the diagnosis of measles
Fan 2006b	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "arbitrary and not strict", was not an adequate randomisation approach. There was no random number table or other adequate randomisation and no protocol before clinical trial
Fang 2010	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "according to the sequence of administration", was not an adequate randomisation approach

Study	Reason for exclusion
Gu 2005	Participants were described as having "measles with myocardial damage". Myocardial damage is a complication of measles
Guan 2009	Participants were described as having "measles with pneumonia". Pneumonia is a complication of measles
Gui 2008	Participants were described as having "measles with acute tracheal bronchitis". Acute tracheal bronchitis is an infection caused by other pathogens
Guo 2008	Participants were described as having "measles with pneumonia". Pneumonia is a complication of measles
Guo 2010	Participants were described as having "childhood measles with pneumonia". Pneumonia is a complication of measles
Han 2006a	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "arbitrary", was not an adequate randomisation approach. There was no random number table or other adequate randomisation and no protocol before clinical trial
Han 2006b	Participants were described as having "childhood measles with pneumonia". Pneumonia is a complication of measles
Hu 2006	Participants were described as having "measles with pneumonia". Pneumonia is a complication of measles
Ji 2008	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "according to the sequence of administration", was not an adequate randomisation approach. The trial author knows the randomisation was incorrect
Li 1999	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "voluntary", was not an adequate randomisation approach. Participants had measles with pneumonia
Li 2000	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "according to the sequence of administration", was not an adequate randomisation approach. The trial author knows the randomisation was incorrect
Li 2002	Participants had measles and pneumonia
Li 2003	Participants had measles and encephalitis
Li 2005	Participants were described as having "measles combined with bronchial pneumonia". Bronchial pneumonia is a complication of measles
Li 2008	Participants were described as having "measles complicated by bronchial pneumonia". Bronchial pneumonia is a complication of measles
Li 2009	Participants were described as having "childhood measles with pneumonia". Pneumonia is a complication of measles
Liang 2007	Participants were described as "measles complicated by bronchial pneumonia". Bronchial pneumonia is a complication of measles

Study	Reason for exclusion
Liao 2011	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "voluntary", was not an adequate randomisation approach
Liu 2000b	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "voluntary", was not an adequate randomisation approach. Patients suffered from measles complicated with pneumonia
Liu 2005	Participants were described as having "measles complicated by pneumonia". Pneumonia is a complication of measles
Liu 2007	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "arbitrary and not strict", was not an adequate randomisation approach. There was no random number table or other adequate randomisation and no protocol before clinical trial
Liu 2009	Participants were described as "measles complicated by pneumonia". Pneumonia is a complication of measles
Liu 2010	Participants were described as having "childhood measles with pneumonia". Pneumonia is a complication of measles
Lou 2010	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "voluntary", was not an adequate randomisation approach
Lu 2008	"Randomised" was mentioned, but in the context we discovered that the method of allocation, which had been described as "according to the administration sequence and according to the odd-even number", was not an adequate randomisation approach. By telephone interviewing the trial author we know that the method was incorrect
Luo 2009	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "voluntary", was not an adequate randomisation approach
Ma 2009	Participants were described as having "childhood measles with pneumonia". Pneumonia is a complication of measles
Ma 2009a	Participants were described as having "childhood measles with pneumonia". Pneumonia is a complication of measles
Mei 2002	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "voluntary", was not an adequate randomisation approach
Niu 2005	Participants were described as having "measles complicated by bronchial pneumonia". Bronchial pneumonia is a complication of measles
Niu 2006	Participants were described as "patients with severe measles". Severe measles is defined as measles with at least one of the following complications: 1. Pneumonia, moderate dyspnoea (Grade 2, needs to walk more slowly than others of the same age or has to stop for breath when walking at own pace on level ground. It gives a severity scale for dyspnoea developed by the American Thoracic Society). 2. Heart failure 3. Toxic encephalitis

Study	Reason for exclusion
Nu 2010	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "according to the sequence of administration", was not an adequate randomisation approach
Pan 2005	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "voluntary", was not an adequate randomisation approach. Participants had measles complicated with pneumonia
Pei 2004	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "voluntary", was not an adequate randomisation approach. Participants had measles complicated with pneumonia
Qian 2003	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "according to the sequence of administration", was not an adequate randomisation approach. Participants had measles complicated by pneumonia.
Sun 2009	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "voluntary", was not an adequate randomisation approach
Tan 2001	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "according to the sequence of administration", was not an adequate randomisation approach. Participants had measles complicated by pneumonia.
Wang 1994	Participants had measles complicated by pneumonia.
Wang 1995a	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "according to the sequence of administration", was not an adequate randomisation approach. The trial author knows the randomisation was incorrect. Participants had measles complicated by pneumonia.
Wang 1995b	"Randomised" was mentioned, but by interviewing the trial author by telephone we understood that the method of allocation was described as "arbitrary and subjective", but without any adequate random approach
Wang 1996	"Randomised" was mentioned, but by interviewing the trial author by phone we understood that the method of allocation was described as "according to the administration sequence" without any adequate random approach. Participants had measles complicated by pneumonia.
Wang 1997	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "voluntary", was not an adequate randomisation approach
Wang 2008a	Participants were described as having "childhood measles with pneumonia". Pneumonia is a complication of measles
Wang 2008b	Most participants had "pneumonia, hepatitis, enteritis, renal damage or heart damage". These are complications of measles
Wu 2004	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "voluntary", was not an adequate randomisation approach
Xia 2011	Most participants had complications of measles, such as laryngitis, bronchitis, respiratory failure, heart failure, diarrhoea or pneumothorax

Study	Reason for exclusion
Xu 2005	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "according to administration sequence", was not an adequate randomisation approach. There was no random number table or other adequate randomisation and no protocol before clinical trial
Xue 2006	"Randomised" was mentioned, but in the context we discovered that the method of allocation, which had been described as "according to the administration sequence", was not an adequate randomisation approach. By telephone interviewing the trial author we know that the method was incorrect
Yan 2009	Participants were described as having "childhood measles with pneumonia". Pneumonia is a complication of measles
Yang 2006a	Participants were described as having "childhood measles with pneumonia". Pneumonia is a complication of measles
Yang 2006b	Participants were described as having "childhood measles with pneumonia". Pneumonia is a complication of measles
Yang 2008	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "voluntary", was not an adequate randomisation approach. Participants had measles complicated with pneumonia
Zhang 2004	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method to decide who would receive Qingre Jiedutang, or who would not, was described as "voluntary"; this is not considered to be a true RCT
Zhang 2006a	Participants were described as having "childhood measles with pneumonia". Pneumonia is a complication of measles
Zhang 2006b	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the method of allocation, which had been described as "arbitrary and non-formal", was not an adequate randomisation approach. The author knows that the method was incorrect. There was no protocol before the clinical trial
Zhang 2008	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "arbitrary", was not an adequate randomisation approach. There was no random number table or other adequate randomisation and no protocol before clinical trial
Zhang 2009	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "arbitrary", was not an adequate randomisation approach. There was no random number table or other adequate randomisation and no protocol before clinical trial
Zhang 2010	Participants were described as having "childhood measles with pneumonia". Pneumonia is a complication of measles
Zhao 2002	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the allocation method, which was described as "voluntary", was not an adequate randomisation approach. Participants had measles complicated with pneumonia
Zhao 2005	Participants were described as having "childhood measles with bronchial pneumonia". Bronchial pneumonia is a complication of measles

Study	Reason for exclusion
Zheng 2003	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the method of allocation, which had been described as "according to the administration sequence", was not an adequate randomisation approach.
Zhou 2006	Participants were described as having "childhood measles with pneumonia". Pneumonia is a complication of measles
Zhou 2009	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the method of allocation, which had been described as "according to the administration sequence", was not an adequate randomisation approach
Zhou 2010	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the method of allocation, which had been described as "according to the administration sequence", was not an adequate randomisation approach
Zhu 1994	"Randomised" was mentioned, but by telephone interviewing the trial author we discovered that the method of allocation, which had been described as "according to the administration sequence", was not an adequate randomisation approach. The review author knows that the method was incorrect

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

[Cui 1994](#)

Methods	"The patients were randomly allocated" mentioned, but lack of detailed information about the method of randomisation
Participants	
Interventions	
Outcomes	
Notes	

[Feng 1994](#)

Methods	"The patients were randomly allocated" mentioned, but lack of detailed information about the method of randomisation
Participants	
Interventions	
Outcomes	
Notes	

Jiao 2001

Methods	"The patients were randomly allocated" mentioned, but lack of detailed information about the method of randomisation
Participants	
Interventions	
Outcomes	
Notes	

Liu 1996

Methods	"The patients were randomly allocated" mentioned, but lack of detailed information about the method of randomisation
Participants	
Interventions	
Outcomes	
Notes	

APPENDICES

Appendix 1. Previous search

We searched the Cochrane Central Register of Controlled Clinical Trials (CENTRAL) (*The Cochrane Library* 2009, Issue 1) which contains the Cochrane Acute Respiratory Infections Group's Specialised Register; MEDLINE (1966 to March 2009); EMBASE (1980 to March 2009); the Chinese Biomedical Database (1976 to March 2009); VIP Information (1989 to March 2009); and China National Knowledge Infrastructure (CNKI) (1994 to March 2009). We searched the *metaRegister* of Controlled Trials for ongoing trials at www.controlled-trials.com.

We searched for trials in MEDLINE by combining the following search terms with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity-maximising version (2008 revision) (Lefebvre 2008).

MEDLINE (Ovid)

```
#1 exp Measles/
#2 exp Measles virus/
#3 measles
#4 rubeola
#5 or/1-4
#6 exp Medicine, Chinese Traditional/
#7 exp Medicine, Oriental Traditional/
#8 exp Drugs, Chinese Herbal/
#9 exp Plants, Medicinal/
#10 herb*
#11 or/6-10
#12 5 AND 11
```

We modified the search strategy to search EMBASE, VIP and CNKI. We did not impose any language or publication restrictions (see Appendix 1, Appendix 2; Appendix 3; Appendix 4; Appendix 5; Appendix 6; Appendix 7 for the search strategies applied to the individual databases).

Appendix 2. Strategy for Web of Science Search

Topic=(measles or "measles virus" or rubeola or morbilli) AND Topic=("chinese medicine" or "chinese traditional medicine" or "chinese herb*" or "oriental medicine" or "oriental traditional medicine" or "medicinal plant*" or herb*)

Appendix 3. Embase.com search strategy

#13. #7 AND #12 17 10 Apr 2011
#12. #8 OR #9 OR #10 OR #11 23,130 10 Apr 2011
#11. (herb* NEAR/3 medicin*):ab,ti AND [embase]/lim 8,057 10 Apr 2011
#10. (chinese NEAR/3 (medicin* OR herb*)):ab,ti AND [embase]/lim 13,049 10 Apr 2011
#9. 'oriental medicine'/de AND [embase]/lim 173 10 Apr 2011
#8. 'chinese medicine'/de AND [embase]/lim 11,372 10 Apr 2011
#7. #1 OR #2 OR #3 OR #4 OR #5 OR #6 15,375 10 Apr 2011
#6. rubeola:ab,ti AND [embase]/lim 230 10 Apr 2011
#5. morbillivirus*:ab,ti OR 'morbilli virus':ab,ti AND [embase]/lim 366 10 Apr 2011
#4. 'morbillivirus infection'/de AND [embase]/lim 7 10 Apr 2011
#3. 'measles virus'/de AND [embase]/lim 5,349 10 Apr 2011
#2. measles:ab,ti AND [embase]/lim 11,590 10 Apr 2011
#1. 'measles'/de AND [embase]/lim 8,449 10 Apr 2011

Appendix 4. Strategy for AMED search

Database: AMED (Allied and Complementary Medicine)

1 measles/
2 measles.tw.
3 morbilli.tw.
4 rubeola.tw.
5 or/1-4
6 exp traditional medicine chinese/
7 exp drugs chinese herbal/
8 exp plants medicinal/
9 exp herbal drugs/
10 herb*.tw.
11 (chinese adj5 medicine).tw.
12 or/6-11
13 12 and 5
14 from 13 keep 1-9

Appendix 5. Strategy for VIP Chinese Science and Technique Journals Database search

Topic/Keyword=(measles or "measles virus" or rubeola or morbilli) AND Topic/Keyword=("chinese medicine" or "chinese traditional medicine" or "chinese herb*" or "oriental medicine" or "oriental traditional medicine" or "medicinal plant*" or herb*)

Timespan=1989 to June 2011

Appendix 6. Strategy for The Chinese Biomedical Database search

Database: The Chinese Biomedical Database <1994 to June 2011>

1 measles/
2 measles.tw.
3 morbilli.tw.
4 rubeola.tw.
5 4 or 1 or 3 or 2
6 exp traditional medicine chinese/
7 exp drugs chinese herbal/
8 exp plants medicinal/
9 exp herbal drugs/
10 herb*.tw.
11 (chinese adj5 medicine).tw.
12 8 or 6 or 11 or 7 or 10 or 9
13 12 and 5
14 from 13 keep 1-9

Appendix 7. Strategy for China National Infrastructure (CNKI) search

Title/Topic/Keyword=(measles or "measles virus" or rubeola or morbilli) AND Title/Topic/Keyword=("chinese medicine" or "chinese traditional medicine" or "chinese herb*" or "oriental medicine" or "oriental traditional medicine" or "medicinal plant*" or herb*)

Timespan=1994 to June 2011

Appendix 8. Strategy for Chinese Journals Full-article Database search

Topic=(measles or "measles virus" or rubeola or morbilli) AND Topic=("Chinese medicine" or "Chinese traditional medicine" or "Chinese herb*" or "oriental medicine" or "oriental traditional medicine" or "medicinal plant*" or herb*)

Timespan=Latest 5 years

WHAT'S NEW

Date	Event	Description
30 June 2011	New search has been performed	Searches conducted. Twenty-four new trials were excluded (Bo 2010 ; Chen 2010 ; Cheng 2002 ; Chu 2011 ; Dong 2011 ; Fang 2010 ; Guan 2009 ; Guo 2010 ; Li 2009 ; Liao 2011 ; Liu 2009 ; Liu 2010 ; Luo 2009 ; Ma 2009 ; Ma 2009a ; Nu 2010 ; Sun 2009 ; Xia 2011 ; Yan 2009 ; Zhang 2009 ; Zhang 2010 ; Zheng 2003 ; Zhou 2009 ; Zhou 2010). The conclusions remain unchanged.
11 April 2011	New citation required but conclusions have not changed	Three new authors, Drs' Shuo Chen, Xiangyu Kong and Hao Yuan joined the team to update this review.

HISTORY

Protocol first published: Issue 4, 2005

Review first published: Issue 2, 2006

Date	Event	Description
20 March 2009	New search has been performed	Searches conducted.
2 August 2008	Amended	Converted to new review format.
31 May 2005	New search has been performed	Searches conducted.

CONTRIBUTIONS OF AUTHORS

Chen S and Wu T are responsible for the second update of this review.

Chen S, Kong XY and Hao Y are responsible for telephoning the original authors to identify the studies.

Zheng Y Gu R and Wu T are responsible for the first update of this review.

Shi YY was responsible for telephone interviewing the trial authors of claimed RCTs in the original version of this review.

Zhang M was responsible for searching for trials and data extraction for the original version of this review.

Liu G was responsible for data analysis for the original version of this review.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- Chinese Cochrane Centre, West China Hospital of Sichuan University, Chinese Medical Board of New York (CMB), China.

External sources

- Cochrane Acute Respiratory Infections (ARI) Group, Australia.

INDEX TERMS

Medical Subject Headings (MeSH)

Antiviral Agents [adverse effects] [*therapeutic use]; Drugs, Chinese Herbal [adverse effects] [*therapeutic use]; Measles [*drug therapy]

MeSH check words

Adult; Child; Humans