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Chinese herbal medicine Huangqi type formulations for nephrotic syndrome (Review)

Feng M, Yuan W, Zhang R, Fu P, Wu T

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[Intervention Review]

Chinese herbal medicine Huangqi type formulations for nephrotic syndrome

Mei Feng[1,2], Wei Yuan[3], Renzhong Zhang[1], Ping Fu[1], Taixiang Wu[4]

[1]Department of Nephrology, West China Hospital, Sichuan University, Chengdu, China. [2]Radiation Oncology, Sichuan Cancer Hospital, Chengdu, China. [3]Tianjin First Center Hospital, Tianjin, China. [4]Chinese Clinical Trial Registry, Chinese Ethics Committee of Registering Clinical Trials, West China Hospital, Sichuan University, Chengdu, China

Contact: Taixiang Wu, Chinese Clinical Trial Registry, Chinese Ethics Committee of Registering Clinical Trials, West China Hospital, Sichuan University, No. 37, Guo Xue Xiang, Chengdu, Sichuan, 610041, China. txwutx@hotmail.com.

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ABSTRACT

Background

Patients with primary nephrotic syndrome mostly need immunosuppression to achieve remission, but many of them either relapse after immunosuppression therapy or resistant to it. On the other hand, immunosuppression therapy could increase the adverse effect. Huangqi and Huangqi type formulations have been used to treat nephrotic syndrome for years in China, however the effects and safety of these formulations have not been systematically reviewed. This is an update of a review first published in 2008.

Objectives

To assess the benefits and harms of Huangqi and Huangqi type formulations in treating nephrotic syndrome in any age group, either as sole agents or in addition to other drug therapies.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, Chinese Biomedicine Database (CBM), CNKI, VIP and reference lists of articles. There was no language restriction.
Date of search: April 2011.

Selection criteria

All randomised controlled trials (RCTs) assessing the use of Huangqi or Huangqi type formulations in treating nephrotic syndrome in adults and children, either as sole agents or in addition to other drug therapies.

Data collection and analysis

Two authors independently assessed study quality and extracted data. For dichotomous outcomes results were expressed as relative risk (RR) and 95% confidence intervals (CI). Continuous outcomes were expressed as mean difference (MD) with 95% CI.

Main results

Nine studies were identified. One was judged to be at high risk of bias for random sequence, the rest were judged to be at low risk of bias. All studies had high risk of bias for allocation concealment and performance bias; unclear risk for detection bias and low risk for attrition bias. Two studies had unclear risk reporting bias and the rest had low risk. No other potential threats to validity were found. Compared to control interventions, Huangqi type formulations had a positive effect on plasma albumin (MD 6.41 g/dL, 95% CI 4.24 to 8.59), urine albumin excretion (-0.57 g/24 h, 95% CI -1.04 to -0.10), cholesterol (MD -1.70 mmol/L, 95% CI -2.60 to -1.13) and triglycerides (-0.33 mmol/

L, 95% CI -0.63 to -0.03); and more patients showed improvement at three months (RR 0.41, 95% CI 0.20 to 0.84). There was no significant difference between Huangqi type formulations and control interventions for complete (RR 1.59, 95% CI 0.29 to 8.65) or partial remission (RR 1.22, 95% CI 0.57 to 2.58). While some formulations showed improvement in the number of patients achieving complete or partial remission, the number of studies (usually one per formulation), and the number patients (ranging from 38 to 78) were small. Relapse was reported at varying time points, ranging from three months to three years, and therefore these results were not pooled. Complications of nephrotic syndrome and adverse events were only reported by two studies; Only one study reported complications of nephrotic syndrome (infection) and another reported adverse reactions to treatment (Cushing's syndrome, steroid withdrawal syndrome, respiratory tract infection, and upper gastrointestinal haemorrhage). Both studies reported those treated with Huangqi type formulations had significantly less complications or adverse reactions.

Authors' conclusions

Huangqi and Huangqi type formulations may have some positive effects in treating nephrotic syndrome by increasing plasma albumin and reducing urine albumin excretion, blood cholesterol and triglycerides, and decreasing the number who don't show improvement at three months. Some formulations showed an increase in the number of patients achieving complete or partial remission, however study and participant numbers were small.

PLAIN LANGUAGE SUMMARY

Chinese herbal medicine Huangqi type formulations for nephrotic syndrome

Heavy proteinuria (protein in the urine), hypoalbuminaemia (low blood albumin levels), oedema (a build-up of fluid, resulting in swelling) and hypercholesterolaemia (high blood cholesterol) are the major characteristics of nephrotic syndrome. At present, the primary drugs for nephrotic syndrome are corticosteroids, alkylating agents and cyclosporin. However there are many adverse effects associated with their use. This review identified nine studies (461 participants) comparing Huangqi type formulations with control drugs. The results of this review suggest that Huangqi type formulations may have a positive effect on nephrotic syndrome by increasing plasma albumin and reducing urine albumin excretion, blood cholesterol and triglycerides. Huangqi type formulation may reduce some adverse effects of other drugs used for treating nephrotic syndrome, however these were only reported in two studies. The methodological quality of the nine included studies was poor and was the major limitation of this review. The types of pathology, sex and age of the patients, as well as the duration and dosage of the Huangqi type formulations could not be analysed.

BACKGROUND

Nephrotic syndrome is a condition that is often caused by any disease that damages the kidneys. Heavy proteinuria (> 3.5 g/d), hypoalbuminaemia (serum albumin < 2.5 g/dL), oedema and hypercholesterolaemia are the main characteristics (Cohen 2011; UMMC 2009). It can be divided into two types - primary and secondary nephrotic syndrome. Primary nephrotic syndrome may occur in association with a diverse array of glomerular disorders including;

- minimal change disease (MCD) responsible for about 80% of nephrotic syndrome in children, and about 20% in adults,
- focal segmental glomerulosclerosis (FSGS) responsible for about 8% of nephrotic syndrome in children, and about 15% in adults,
- membranous glomerulonephritis (MGN) responsible for about 1% of nephrotic syndrome in children, and about 25% in adults,
- membranoproliferative glomerulonephritis (MPGN) responsible for about 5% of nephrotic syndrome in children, and about 12% in adults (UMMC 2009; Ye 2003).

Normally, proteins are restricted by a charge-selective barrier and a size-selective barrier (McCarthy 2012). But in nephrotic syndrome, the barriers are damaged, which let proteins leak into the urine (Cohen 2011). As a result, plasma protein and colloid osmotic pressure (COP) decrease, which result in the shift of fluid from the blood vessels into the body tissues causing oedema. Sodium retention causes a greater shift in fluid and thus an increase in oedema and occurs in some patients with nephrotic syndrome (Koomans 2003). Hypoalbuminaemia is caused not only by urinary loss of albumin but also results from increased catabolism, decreased synthesis, and increased gastrointestinal loss (Lane 2011). Hypercholesterolaemia (high levels of cholesterol, VLDL, IDL, LDL, lipoprotein (a) (Lp (a)) and triglyceride) is thought to be the consequence of both increased synthesis and decreased catabolism of lipoprotein. Abnormal function of enzymes or regulatory proteins such as lecithin-cholesterol acyltransferase, lipoprotein lipase, and cholesteryl ester transfer protein also contribute to the hypercholesterolaemia (Doucet 2000; Saland 2002).

Immunosuppression therapy is the most important treatment for the primary nephrotic syndrome. However, many patients may relapse or resistant after the therapy. For example, while up to 90% of adults with MCD will respond to initial therapy with prednisone, approximately one-third of these same patients will relapse within 6 months and require further immunosuppression(Palmer 2008; Waldman 2007).With diseases such as idiopathic membranous nephropathy (IMN) and FSGS, for which first-line therapies produce substantially lower response rates than for MCD, physicians are often compelled to use second-, third-, and even fourth-line therapies to achieve remission(Cattran 1999; Cattran 2007; Segarra 2009).There is no standard therapy for patients with frequent relapsing, steroid-dependent or resistant nephrotic syndrome. Prolonged or repeated steroid therapy can lead to a variety of serious side effects. Achieving remission is an important goal that predicts an excellent long-term prognosis (Das 2009). Antibiotics may be needed to control infections. Angiotensin converting enzyme inhibitors, diuretic medications and a low-protein diet are also used to treat nephrotic syndrome. Treatment depends on the underlying disorder which has caused nephrotic syndrome. Though many of these drugs are effective on the treatment of primary nephrotic syndrome, they also cause many adverse effects including infection, osteoporosis, suppression of bone marrow and liver damage. All in all, the lack of efficacy and safety of existing treatment protocols make the treatment of nephrotic syndrome difficult (Meyrier 2004; Orth 1998; Ye 2003).

In China, traditional Chinese herbal medicines are commonly used in the treatment of nephrotic syndrome (Wang 2001a). Most of the physicians consider them could increase the remission rate and reduce the adverse effect. Huangqi and Huangqi type formulations have been used to treat nephrotic syndrome for years in China, such as Huangqi intravenous injection, Huangqi oral solution, Yiqibushen soup, Shenkanglin doction and Huangqi-Danggui mixture. Huangqi with Danggui mixture could increase the synthesis of liver protein on the mRNA level, and decrease the blood lipid level (Tong 2003). Huangqi, Taizishen and Shanyao have an effect on strengthening spleen, supplementing qi, inducing diuresis for removing oedema (Lan 2005). Huangqi could improve anaemia, and also the status of water-sodium retention (Liu 2001a). Huangqi is a one of the traditional Chinese herbal medicines. It is the dried root of Huangqi membranaceus (Fisch.) Bge. Var. mongholicus (Bge.) Hsiao or Huangqi membranaceus (Fisch.) Bge. Or Hedysarum polybotrys Hand.-Mazz (fam. Leguminosae) (Deng 1998). Huangqi contains many active components, including calycosin 7-O-beta-D-glucoside, formononetin 7-O-beta-D-glucoside, (6 alpha R, 11 alpha R) 3-hydroxy-9,10-dimethoxypterocarpan-3-O-beta-D-glucoside, 7,2'-dihydroxy-3',4'-dimethoxyisoflavan-7-O-beta-D-glucoside, calycosin and formononetin (Wu 2005). Studies in patients and experimental animals suggest that Huangqi reduces proteinuria, hypoalbuminaemia, hyperlipidaemia and acts as a diuretic (Peng 2005). Huangqi may reduce proteinuria by:

- protecting both the charge-selective and size-selective barrier (Bao 2003),
- correct hypoalbuminaemia through promoting the transcription of albumin gene, enhancing the synthesis of albumin in the liver (Wang 2004b),
- alleviate nephrotic hyperlipidaemia by up-regulating the expression of hepatic LDL-R gene and increasing the activities of serum LPL and LCAT (Li 2000).

As a result, degradation of VLDL and reverse transportation of cholesterol are accelerated, which is beneficial to the decrease of serum VLDL. These effects are favourable for preventing further kidney injury caused by hyperlipidaemia (Li 2000). The diuretic effect of Huangqi relieves the oedema resulting from water and sodium retention (Su 2000b; Wang 2002).

Although Huangqi and its formulations have been widely used for nephrotic syndrome in China, the effectiveness and adverse effect have not been reviewed systematically.

OBJECTIVES

To assess the benefits and harms of Huangqi and Huangqi type formulations in treating nephrotic syndrome in adults and children, either as sole agents or in addition to other drug therapies.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials (RCTs) assessing the use of Huangqi and Huangqi type formulations in treating nephrotic syndrome in adults and children, either as sole agents or in addition to other drug therapies. The first period of randomised crossover studies were also included.

Types of participants

Adults and children with primary nephrotic syndrome. In the absence of an explicit definition of nephrotic syndrome, the diagnosis of nephrotic syndrome in adults was based on the excretion of large amount of protein in the urine/d (> 3.5 g/24 h urine) and low serum protein (< 30 g/L), and in children with proteinuria > 3+ on dipstick, urinary protein-creatinine ratio > 0.2 g/mmol, > 40 mg/m^2/h or > 50 mg/kg/d.

Patients with secondary nephrotic syndrome were excluded as it is in the majority of cases a renal manifestation of a systemic general illness. The common causes of secondary nephrotic syndrome are diabetes mellitus, lupus erythematosus, viral infection, amyloidosis and paraproteinemias, and malignant tumours.

Types of interventions

- Huangqi or Huangqi type formulations versus other drugs, formulations or placebo.
- Huangqi or Huangqi type formulations in addition to other drugs versus other drugs.

Types of outcome measures

Primary outcomes

- Mortality
- Complete remission at three months: urine protein (nil), proteinuria ≤ 0.2 g/24 h, plasma albumin ≥ 35 g/L, normal kidney function, disappearance of all the nephrotic syndrome symptoms (e.g. oedema, hypertension)
- Partial remission at three months: urine protein decreased, proteinuria < 3.0 g/24 h, improved plasma albumin, improved kidney function
- Urinary protein excretion (g/24 h)
- Plasma albumin

Secondary outcomes

- Triglycerides
- Total cholesterol
- Oedema remission (days to remission)
- No improvement in nephrotic syndrome at three months: urine protein unimproved, plasma albumin unimproved, nephrotic syndrome symptoms do not disappear, kidney function unchanged. Complete remission and partial remission constitute improvement.
- The number and proportion of patients developing hypertension, chronic kidney disease (CKD) or end-stage kidney disease (ESKD)
- The number and proportion of patients who relapse. Relapse was defined as urine protein changing from negative to positive longer than two weeks within three months after complete remission
- The duration of remission
- Complications of nephrotic syndrome: infection, thrombosis, acute kidney injury
- Adverse effects
- Traditional Chinese Medicine (TCM) outcomes: the tongue picture, pulse picture and symptoms
- Cost

Search methods for identification of studies

Electronic searches

We used the following data-bases to search all relevant studies (Appendix 1 -*Electronic search strategies*).

- The Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library*, Issue 2, 2011).
- MEDLINE (June 2006 to May 2011)
- EMBASE (June 2006 to May 2011)
- The Chinese Biomedicine Database (CBM) (June 2006 to May 2011).
- CNKI (June 2006 to May 2011)
- VIP (June 2006 to May 2011)

The MEDLINE search strategy was modified as required to search other databases.

We also searched for ongoing studies in the National Research Register, Meta-Register of Controlled Trials, Medical Research Council Clinical Trials Directory and the Cochrane Complimentary Medicine Field's trials register.

Searching other resources

We checked the references of published studies to identify additional studies. We contacted study authors to identify any unpublished papers, but were not able to contact pharmaceutical companies who produced relevant products. There was no language restriction.

Data collection and analysis

Selection of studies

The search strategy was used to obtain citations that may be relevant to the review. The titles and abstracts of all retrieved citations were screened independently by two authors who discarded citations that were not applicable. All citations for studies and reviews that might report relevant data or information on available studies were retained initially. The same two authors independently assessed retrieved abstracts and, if necessary, the full text of these studies, to determine which studies satisfied the inclusion criteria. Two authors telephoned the original authors of Chinese articles to identify the randomisation procedure and other methodological issues to insure the included studies were RCTs. If the required information was not available, the articles were added to Studies awaiting classification. Reasons for exclusion from the review were recorded to Characteristics of excluded

studies. Disagreements during the study selection were resolved in consultation with a third author.

Data extraction and management

The quality of the studies included was assessed independently by two authors by means of using a piloted data extraction form. There were no disagreements. We extracted the formulation contents of the included studies (Table 1 - *Preparation and composition of the herbal medicines in the included studies*). Where more than one publication of one study exists, reports were grouped together and the publication with the most complete data was used in the analyses.

Assessment of risk of bias in included studies

For this update the following items were independently assessed by five authors using the risk of bias assessment checklist (Higgins 2011) (*see* Appendix 2). Disagreements during the assessment of risk of bias in included studies were resolved by discussion between all authors.

- Was there adequate sequence generation (selection bias)?
- Was allocation adequately concealed (selection bias)?
- Was knowledge of the allocated interventions adequately prevented during the study (detection bias)?
  - Participants and personnel
  - Outcome assessors
- Were incomplete outcome data adequately addressed (attrition bias)?
- Are reports of the study free of suggestion of selective outcome reporting (reporting bias)?
- Was the study apparently free of other problems that could put it at a risk of bias?

Measures of treatment effect

For dichotomous outcomes (mortality, relapse, complications, adverse effects, no improvement at three months, the duration of remission, the number and proportion of patients developing hypertension, CKD or ESKD), results were expressed as risk ratios (RR) and 95% confidence intervals (CI). RR and 95% CI within individual studies were calculated from the number of events and numbers of participants at risk extracted from each included study. For continuous outcomes (urine albumin excretion, triglycerides, cholesterol, plasma albumin, oedema remission), results were expressed as mean difference (MD) with 95% CI.

Data synthesis

Heterogeneity was analysed, where applicable, using a chi-squared test on N-1 degrees of freedom, with an alpha of 0.05 used for statistical significance and with the I^2 test (Higgins 2003). I^2 values of 25%, 50% and 75% corresponded to low, medium and high levels of heterogeneity. The sensitivity analysis was done, and there was no statistical significance between the fixed-effects and random-effects model in the data synthesis. So the random-effect model in the studies was used in the study. Data for each study were analysed and expressed as RRs and mean difference. Subgroup analysis was planned to explore the heterogeneity in different interventions. We used a meta-analysis to calculate the pooled effect size of these studies.

RESULTS

Description of studies

Results of the search

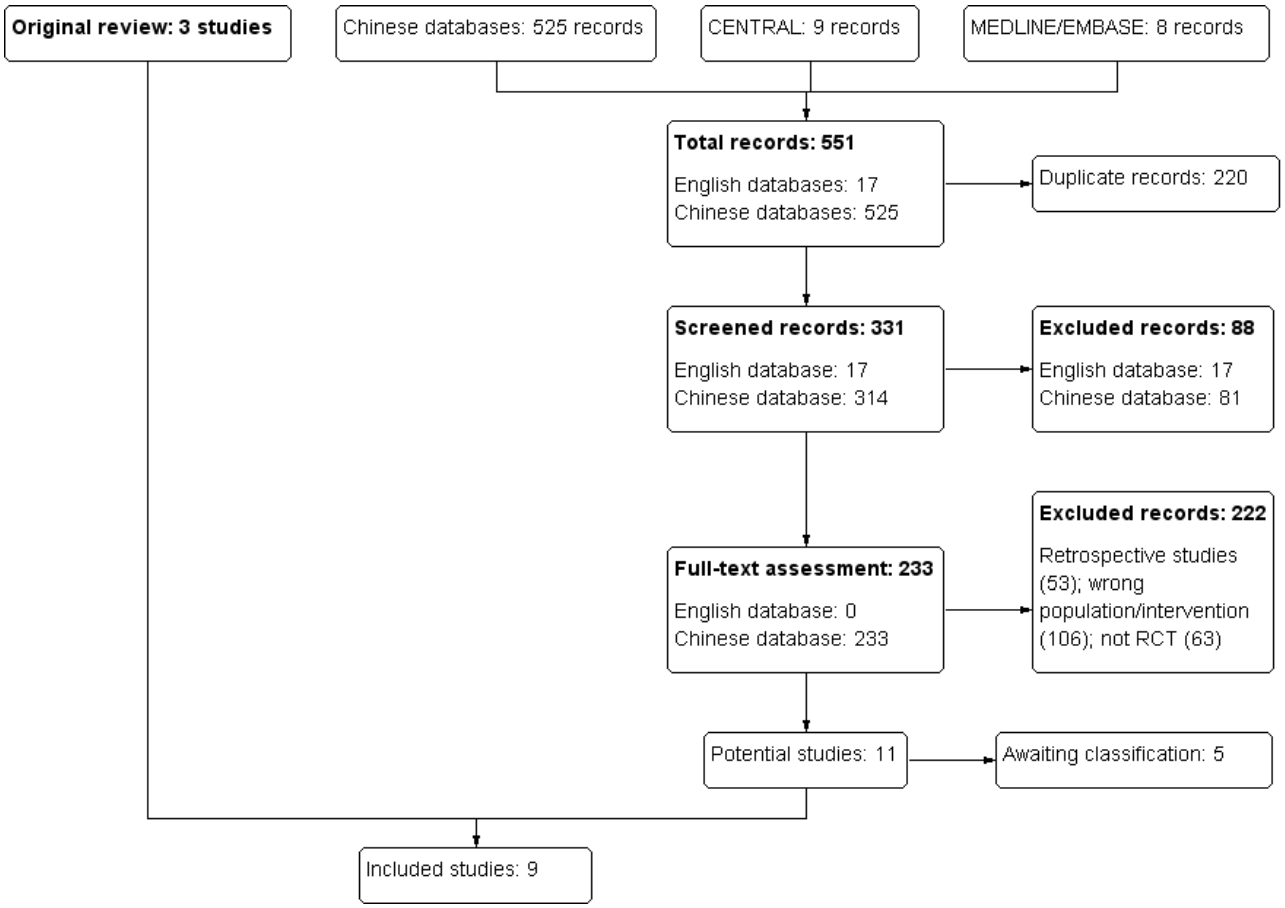
Initial review

A total of 188 studies were retrieved that claimed to be randomised. We successfully contacted 93 study authors by telephone. Of these studies, 87 were excluded, because the study authors misunderstood true random allocation. Ninety five studies were listed in Studies awaiting classification as we could not locate the original study authors to identify the randomisation method. Six reports were identified as true RCTs. Of these, three were excluded. The data for Chang 2002b (two reports) was not in accordance with the study description, and the outcomes reported in Lin 2006 (L-10) were not relevant to this review. Three studies were included (Chang 2002a; Hu 2002; Yuan 2004). The total number of patients randomised was 128. All the studies were conducted in China.

Review update

In this updated review, a total of 551 studies were retrieved that claimed to be randomised (Figure 1). After title and abstract screening, 320 were excluded and 233 potentially eligible studies were retrieved for further assessment. Through the full text screening, 222 studies were excluded because: the study authors misunderstood true random allocation; the articles were retrospective studies; the interventions did meet our inclusion criteria; secondary nephrotic patients were not excluded; or they were not clinical trials. Five studies are awaiting assessment (Studies awaiting classification) as we could not locate the original study authors to identify the randomisation method. Six studies were identified as true RCTs in and have been included in this update (Ai 2008; Lin 2008; Luo 2008; Wang 2006a; Zhou 2010; Zou 1997). In the original review, 95 studies were listed in Studies awaiting classification. During this update, we successfully contacted 86 study authors by telephone. Of these 86 studies, 85 studies were excluded because the study authors misunderstood true random allocation; the articles were retrospective studies; the inclusion criteria were not in accordance with our protocol; and one study was identified as a true RCT (Wang 2006a) which had already been included in this new update. A total of 14 studies are listed in Studies awaiting classification in this update. This update has identified an additional six studies (333 participants) (Ai 2008; Lin 2008; Luo 2008; Wang 2006a; Zhou 2010; Zou 1997). This brings the total number of studies included in this review to nine (461 participants). All the studies were conducted in China.

Figure 1. Study flow diagram.



Included studies

Study characteristics are shown in the table Characteristics of included studies.

- Chang 2002a compared Huangqi-Danggui mixture with control drugs (N = 30). The article did not describe pathology, baseline kidney function of the patients and course of disease. The control group received prednisone, dipyridamole and heparin. The experimental group received Huangqi with Danggui mixture in addition to the drugs the control group received.
- Hu 2002 compared Huangqi intravenous injection with control drugs (N = 38). The article did not describe pathology, baseline kidney function of the patients and course of disease. The control group received corticosteroid, anticoagulants and diuretics. The experimental group received Huangqi intravenous injection in addition to the drugs the control group received.
- Yuan 2004 compared Huangqi and Hongzao with control drugs (N = 60). The study only included patients with refractory nephrotic syndrome (mesangial proliferative glomerulonephritis). The article did not describe baseline kidney function of the patients and course of disease. The control group received prednisone and best support care. The experimental group received Huangqi with Hongzao mixture in addition to the drugs the control group received.
- Ai 2008 compared Shenkanglin decoction with control drugs (N = 68). The study only included frequent relapse nephropathy of children. The average course of disease in the experiment group was 1.42 ± 0.67 years, and that in the control group was 1.32 ± 0.44 years. The article did not describe pathology and baseline kidney function of the patients. The control group received prednisone, when prednisone was inefficacy or partial efficacy, MMF or CsA was used. The experimental group received Shenkanglin decoction in addition to the drugs the control group received.
- Lin 2008 compared Huangqi intravenous injection with control drugs (N = 81). The article did not describe pathology, baseline kidney function of the patients and course of disease. The control group received prednisone and anti-inflammation therapy. The experimental group received Huangqi intravenous injection in addition to the drugs the control group received.
- Luo 2008 compared Shenzongerjia soup with control drugs (N = 78). The study only included patients with refractory nephrotic syndrome. The average course of disease in the experiment group was 3.1 years, and that in the control group was 2.9 years. The article did not describe pathology and baseline kidney function of the patients. The control group received prednisone, anticoagulation therapy, low salt diet, decrease blood lipid, control blood pressure, diuretics and calcium supplement. The experimental group received Shenzongerjia soup in addition to the drugs the control group received.
- Wang 2006a compared Huangqi oral solution with control drugs (N = 30). The article did not describe pathology, baseline kidney function of the patients and course of disease. The control group received prednisone and symptomatic treatment. The

experimental group received Huangqi oral solution in addition to the drugs the control group received.

- Zhou 2010 compared Huangqi granules with control drugs (N = 46). The article did not describe pathology or baseline declining kidney function of the patients. The control group received prednisone, symptomatic and supportive therapy. The experimental group received Huangqi granules in addition to the drugs the control group received.
- Zou 1997 compared Ciwujia with Huangqi mixture with control drugs (N = 30). The article did not describe pathology or baseline declining kidney function of the patients. The control group received steroid and best support care. The experimental group received Ciwujia with Huangqi mixture in addition to the drugs the control group received.

Risk of bias in included studies

See Figure 2 and Figure 3 for summary of risk of bias assessment

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

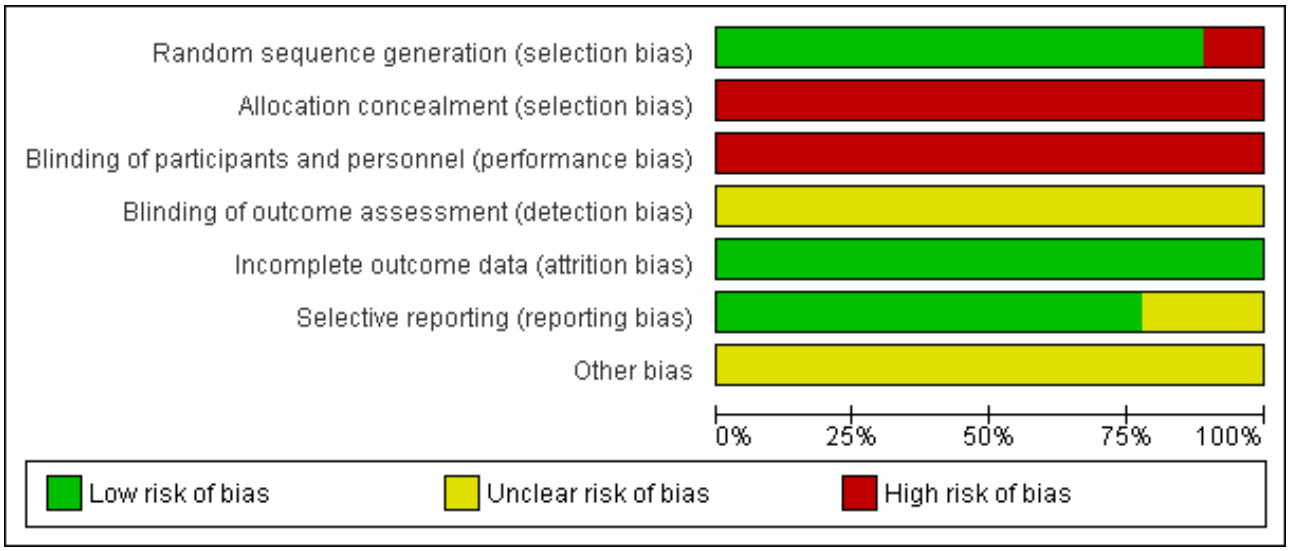
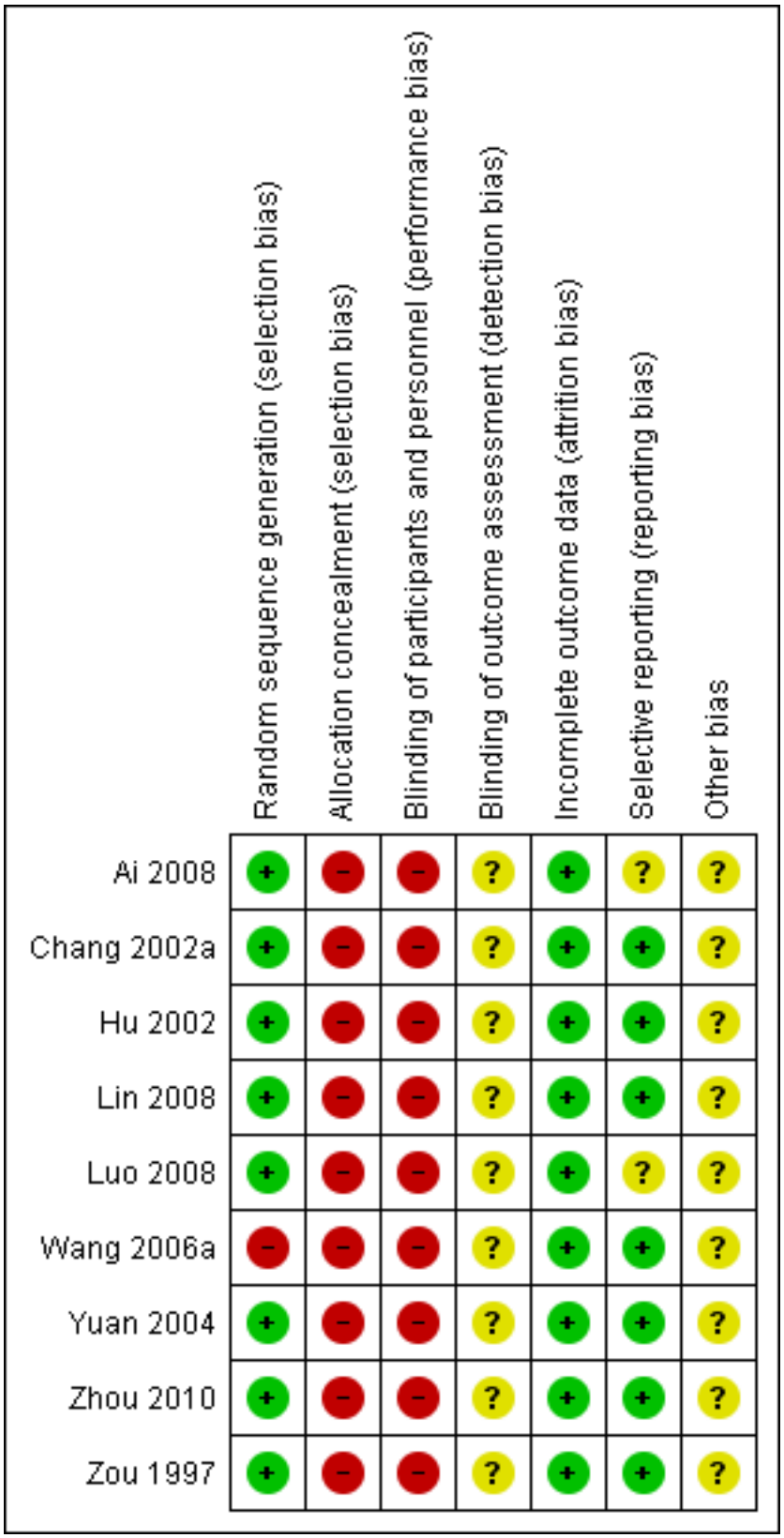


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

All nine studies mentioned "randomly allocating the participants", and one study described the use of a random number table (Zhou 2010). After telephoning the other eight study authors, we determined that five used random number tables (Chang 2002a; Ai 2008; Luo 2008; Lin 2008; Zou 1997), one used computer software (Yuan 2004), one used minimised imbalance index distribution (Hu 2002), and one drew lots (Wang 2006a).

All nine studies did not provide any information about allocation concealment. After telephoning the study authors, we established all the studies had a high risk of allocation concealment (investigator knew the intervention group before eligible participants entered in the study).

Blinding

In terms of performance bias, single blinding (patients were blinded) was used in two studies (Chang 2002a; Yuan 2004). The remaining seven studies did not use blinding (Hu 2002; Ai 2008; Luo 2008; Lin 2008; Wang 2006a; Zhou 2010; Zou 1997). All studies were determined to be at high risk of bias because it was highly likely that the patients knew if they were taking Chinese herbal medicine.

Blinding of outcome assessors was not reported in any of the included studies.

Incomplete outcome data

There were no withdrawals or dropouts from any of the included studies. All data were reported.

Selective reporting

In two studies (Ai 2008; Luo 2008) not all pre-defined outcomes were reported (complete blood count, urinary routine examination). All the clinically relevant and reasonably expected outcomes were reported in the other seven studies.

Other potential sources of bias

No other potential threats to validity were found in the nine studies.

Effects of interventions

All studies compared Huangqi type compounds versus control drugs.

Mortality

No study reported mortality.

Complete remission

There was no significant difference in the number of patients achieving complete remission between Huangqi type compounds and the control drugs (Analysis 1.1 (3 studies, 176 participants): RR 1.59, 95% CI 0.29 to 8.65; I^2 = 97%) (Luo 2008; Hu 2002; Yuan 2004).

Huangqi with Hongzao versus control drugs

One study reported all patients achieved complete remission in both the Huangqi with Hongzao treatment group and the control drugs group (Analysis 1.1.1 (1 study, 60 participants): RR 1.00, 95% CI 0.94 to 1.07) (Yuan 2004).

Shenzongerjia soup versus control drugs

One study reported no significant difference in complete remission between Shenzongerjia soup and the control drugs (Analysis 1.1.2 (1 study, 78 participants): RR 1.52, 95% CI 0.79 to 2.92) (Luo 2008).

Huangqi intravenous injection versus control drugs

One study reported Huangqi intravenous injection significantly increased the number of patients achieving complete remission compared to the control drugs (Analysis 1.1.3 (1 study, 38 participants): RR 2.78, 95% CI 1.05 to 7.32) (Hu 2002).

Partial remission

There was no significant difference in the number of patients achieving partial remission between the Huangqi type compounds and the control drugs (Analysis 1.2 (2 studies, 116 participants): RR 1.22, 95% CI 0.57 to 2.58; I^2 = 0%) (Hu 2002; Luo 2008).

Huangqi intravenous injection versus control drugs

One study reported no significant difference in the number of patients achieving partial remission between Huangqi intravenous injection and the control drugs (Analysis 1.2.1 (1 study, 38 participants): RR 1.11, 95% CI 0.38 to 3.22) (Hu 2002).

Shenzongerjia soup versus control drugs

One study reported no significant difference in partial remission between Shenzongerjia soup and the control drugs (Analysis 1.2.2 (1 study, 78 participants): RR 1.33, 95% CI 0.46 to 3.83) (Luo 2008).

Urinary protein excretion

Huangqi type formulations significantly decreased urinary protein excretion when compared to the control drugs (Analysis 1.3 (3 studies, 176 participants): MD -0.57 g/24 h, 95% CI -1.04 to -0.10; I^2 = 85%) (Ai 2008; Luo 2008; Wang 2006a).

Shenzongerjia soup versus control drugs

One study reported Shenzongerjia soup significantly decreased urinary protein excretion when compared to the control drugs (Analysis 1.3.1 (1 study, 78 participants): MD -0.98 g/24 h, 95% CI -1.37 to -0.59) (Luo 2008).

Huangqi oral solution versus control drugs

One study reported Huangqi oral solution significantly decreased urinary protein excretion when compared to the control drugs (Analysis 1.3.2 (1 study, 30 participants): MD -0.59 g/24 h, 95% CI -0.98 to -0.20) (Wang 2006a).

Shenkanglin decoction versus control drugs

One study reported Shenkanglin decoction significantly decreased urinary protein excretion when compared to the control drugs (Analysis 1.3.3 (1 study, 68 participants): MD -0.21 g/24 h, 95% CI -0.40 to -0.02) (Ai 2008).

Plasma albumin

Huangqi type formulations significantly increased plasma albumin compared to the control drugs (Analysis 1.4 (5 studies, 295 participants): MD 6.41 g/dL, 95%CI 4.24 to 8.59; I^2 = 68%) (Ai 2008; Hu 2002; Lin 2008; Luo 2008; Wang 2006a).

Huangqi intravenous injection versus control drugs

Huangqi intravenous injection significantly increased plasma albumin compared to the control drugs (Analysis 1.4.1 (2 studies, 199 participants): MD 8.28 g/dL, 95% CI 6.17 to 10.39; I^2 = 9%) (Hu 2002; Lin 2008).

Huangqi oral solution versus control drugs

One study reported Huangqi oral solution significantly increased plasma albumin compared to the control drugs (Analysis 1.4.2 (1 study, 30 participants): MD 3.26 g/dL, 95% CI 1.02 to 5.50) (Wang 2006a).

Shenzongerjia soup versus control drugs

One study reported Shenzongerjia soup significantly increased plasma albumin compared to the control drugs (Analysis 1.4.3 (1 study, 78 participants): MD 5.86 g/dL, 95% CI 3.04 to 8.68) (Luo 2008).

Shenkanglin decoction versus control drugs

One study reported Shenkanglin decoction significantly increased plasma albumin compared to the control drugs (Analysis 1.4.4 (1 study, 68 participants): MD 7.27, 95% CI 4.21 to 10.33) (Ai 2008).

Triglycerides

Huangqi type formulations significantly decreased triglycerides compared to the control drugs (Analysis 1.5 (4 studies, 217 participants): MD -0.33 mmol/L, 95%CI -0.63 to -0.02; I^2 = 41%) (Ai 2008; Chang 2002a; Hu 2002; Lin 2008).

Huangqi intravenous injection versus control drugs

There was no significant difference in triglycerides between Huangqi intravenous injection and the control drugs (Analysis 1.5.1 (2 studies, 119 participants): MD -0.43 mmol/L, 95% CI -1.20 to 0.34; I^2 = 64%) (Hu 2002; Lin 2008).

Huangqi with Danggui mixture versus control drugs

One study reported no significant difference in triglycerides between Huangqi with Danggui mixture and the control drugs (. Analysis 1.5.2 (1 study, 30 participants): MD -0.11 mmol/L, 95% CI -0.49 to 0.27) (Chang 2002a).

Shenkanglin decoction versus control drugs

One study reported Shenkanglin decoction significantly decreased triglycerides when compared to control drugs (Analysis 1.5.3 (1 study, 68 participants): MD -0.52 mmol/L, 95% CI -0.89 to -0.15) (Ai 2008).

Cholesterol

Huangqi type formulation significantly decreased cholesterol when compared to control drugs (Analysis 1.6 (4 studies, 217 participants): MD -1.70 mmol/L, 95%CI -2.26 to -1.13; I^2 = 43%) (Ai 2008; Chang 2002a; Hu 2002; Lin 2008).

Huangqi intravenous injection versus control drugs

Huangqi intravenous injection significantly decreased cholesterol when compared to control drugs (Analysis 1.6.1 (2 studies, 119 participants): MD -2.01 mmol/L, 95% CI -2.60 to -1.43; I^2 = 0%) (Hu 2002; Lin 2008).

Huangqi with Danggui mixture versus control drugs

One study reported a decrease in cholesterol when Huangqi with Danggui was compared to control drugs (Analysis 1.6.2 (1 study, 30 participants): MD -0.85 mmol/L, 95% CI -1.70 to 0.00) (Chang 2002a).

Shenkanglin decoction versus control drugs

One study reported a significant decrease cholesterol when Shenkanglin decoction was compared to control drugs (Analysis 1.6.3 (1 study, 68 participants): MD -1.91 mmol/L, 95% CI -2.82 to -1.00) (Ai 2008).

Oedema remission

One study reported Huangqi oral solution significantly reduced the number of days to oedema remission (Analysis 1.7.1 (1 study, 30 participants): MD -5.00 days, 95% CI -6.62 to -3.38) (Wang 2006a).

No improvement at three months

Huangqi type formulation significantly improved clinical and physical symptoms at three months (without complete or partial remission) when compared to control drugs (Analysis 1.8 (3 studies, 176 participants): MD -0.41, 95%CI -0.20 to -0.84; I^2 = 0%) (Hu 2002; Luo 2008; Yuan 2004).

Huangqi intravenous injection versus control drugs

One study reported no significant improvement in clinical and physical symptoms at three months (without complete or partial remission) when Huangqi oral solution was compared to control drugs (Analysis 1.8.1 (1 study 38 participants): RR 0.22 95% CI 0.03 to 1.73) (Hu 2002).

Huangqi with Hongzao mixture versus control drugs

One study reported all patients achieved complete remission in both the Huangqi with Hongzao mixture group and the control drugs group (Yuan 2004).

Shenzongerjia soup versus control drugs

One study reported a significant improvement in clinical and physical symptoms at three months (without complete or partial remission) when Shenzongerjia soup was compared to control drugs (Analysis 1.8.3 (1 study, 78 participants): RR 0.44, 95% CI 0.20 to 0.97) (Luo 2008).

Hypertension, CKD or ESKD

The number developing hypertension, CKD or ESKD were not reported.

Relapse

The studies reporting relapse were not pooled as each measured relapse at different time points.

Huangqi with Hongzao versus control drugs (12 and 24 months)

One study reported no significant difference in the number who relapsed between Huangqi with Hongzao and the control drugs at 12 months (Analysis 1.9.1 (1 study 60 participants): RR 0.75, 95% 0.18 to 3.07) and 24 months (Analysis 1.9.2 (1 study, 60 participants): RR 0.08, 95% 0.00 to 1.31) (Yuan 2004).

Huangqi granules versus control drugs (3 months)

One study reported a significant decrease in the number who relapsed when Huangqi granules were compared to control drugs at three months (Analysis 1.9.3 (1 study, 46 participants): RR 0.2, 95% CI 0.07 to 0.59) (Zhou 2010).

Shenzongerjia soup versus control drugs (12 months)

One study reported no significant difference in relapse between Shenzongerjia soup and the control drugs at 12 months (Analysis 1.9.4 (1 study, 78 participants): RR 0.43, 95% 0.17 to 1.13) (Luo 2008).

Ciwujia with Huangqi mixture versus control drugs (36 months)

One study reported a significant decrease in the number who relapsed when Ci Wu Jia with Huangqi mixture were compared to control drugs at 36 months (Analysis 1.9.5 (1 study, 30 participants): RR 0.36, 95% CI 0.15 to 0.89) (Zou 1997).

Complications

One study reported a significant decrease in infection when Huangqi granules was compared to control drugs (Analysis 1.10 (1 study, 46 participants): RR 0.61, 95% CI 0.39 to 0.95) (Zhou 2010).

Adverse reactions

Only one study reported adverse reactions(Yuan 2004). Huangqi with Hongzao mixture significantly reduced the occurrence of Cushing's syndrome (Analysis 1.11.1 (1 study, 60 participants): RR 0.55, 95% CI 0.32 to 0.94), steroid withdrawal syndrome (Analysis 1.11.2 (1 study, 60 participants): RR 0.58 95% CI 0.39 to 0.85) and respiratory tract infection (Analysis 1.11.3 (1 study, 60 participants): RR 0.27, 95% CI 0.08 to 0.88) when compared to control drugs. This study also reported that the use of Huangqi with Hongzao mixture did not increase upper gastrointestinal haemorrhage.

TCM outcomes

TCM outcomes (the tongue picture, pulse picture, symptoms) were not reported.

Cost

Cost was not reported.

DISCUSSION

Summary of main results

Based on nine studies enrolling 461 participants conducted in China, Huangqi type formulations may have a beneficial effect on increasing plasma albumin, and reducing urine albumin excretion, triglycerides and cholesterol, and increasing the number reporting improvement in clinical and physical symptoms at three months. Huangqi type formulations may also reduce the number to days to oedema remission, number of infections and the adverse reactions of other drugs. There was insufficient evidence to demonstrate if Huangqi type formulations improve complete or partial remission, or reduce or delay the number of patients who relapse. No adverse events of Huangqi type formulation were reported. However, studies of Huangqi type formulations for nephrotic syndrome lacked sufficient power to provide reliable estimates of their effectiveness and adverse effects, due to poor study design and methodological quality.

Overall completeness and applicability of evidence

We were unable to determine the benefits and harms of Huangqi and Huangqi type formulations in treating nephrotic syndrome in any age group, either as sole agents or in addition to other drug therapies. All nine studies were conducted in China. Eight studies involved patients with all types of nephrotic syndrome (Chang 2002a; Hu 2002; Zhou 2010; Ai 2008; Lin 2008; Luo 2008; Wang 2006a; Zou 1997) and did not mention the histological subtype of nephrotic syndrome; Yuan 2004 only involved patients with mesangial proliferative glomerulonephritis type nephrotic syndrome. Different histological subtype of primary nephrotic syndrome may lead to different responds to the same therapy. We could not perform any subgroup analyses to investigate this based on the limited data.

Three studies included both adults and children but none reported the number of adults or children (Chang 2002a; Hu 2002; Yuan 2004). Five studies only included children (Ai 2008; Lin 2008; Wang 2006a; Zhou 2010; Zou 1997), and Luo 2008 included only adults. Children are more likely to respond to therapy than adults, even when adults have minimal change disease, and this may have had an influence on the results. Again, we could not do subgroup analysis because of limited data.

Patient diagnoses also varied. Five studies included nephrotic syndrome patients who had not been previously treated (Chang 2002a; Hu 2002; Lin 2008; Wang 2006a; Zou 1997), and two studies (Ai 2008; Yuan 2004) only included relapsing nephrotic syndrome patients. Two studies (Luo 2008; Zhou 2010) enrolled both patients presenting for the first time with nephrotic syndrome and those with relapsing nephrotic syndrome, however data were not presented separately. The therapeutic effect may be totally different between these two groups although they received the same therapy, so this may influence the results.

Four studies (Chang 2002a; Hu 2002; Lin 2008; Zhou 2010) used Huangqi as the intervention, and five studies used Huangqi type formulation (Ai 2008; Luo 2008; Wang 2006a; Yuan 2004; Zou 1997). Complete remission (three studies), partial remission (two studies), urine albumin excretion (three studies), plasma albumin (five studies), triglycerides (four studies), cholesterol (four studies), time to oedema remission (one study), no improvement at three months (three studies), relapse (four studies), complications (one study) and adverse reactions (1 study) were reported. Mortality, number and proportion of patients developing hypertension, CKD or ESKD, the duration of remission, TCM outcome and cost were not reported. The timing of outcome measurements were not clearly reported in six studies (Chang 2002a; Hu 2002; Yuan 2004; Luo 2008; Lin 2008; Wang 2006a). Three studies reported when the outcomes were assessed, however each study measured these at different time points. Zhou 2010 evaluated the effects of therapy after one month treatment; Zou 1997 measured the immune index after six weeks treatment and evaluated relapse after three years; and Ai 2008 assessed the outcomes after three months of treatment. None of the studies reported who measured these outcomes.

The standard first line medication for nephrotic syndrome is prednisolone or prednisone. However, many patients may relapse or are resistant to therapy. While Chinese herbal medicine is not widely used in treating nephrotic syndrome patients outside China, many hospitals in China use immunosuppression combined with Chinese herbal medicine, such as Huangqi to treat nephrotic

syndrome with the aim of increasing the efficacy and safety of the immunosuppression therapy. In our review, Huangqi type formulations may have some positive effects in treating nephrotic syndrome by increasing plasma albumin and reducing urine albumin excretion, blood cholesterol and triglycerides. It may also decrease the number of days to oedema remission, the number of patients who relapse, the number of patients with no improvement at three months, infection and adverse events. There were no significant differences between Huangqi type formulations and control drugs on complete or partial remission.

Quality of the evidence

The methodological quality of the included studies was poorly reported. One study described the use of a random number table to create the random sequence (Zhou 2010); one stated they used simple randomisation (Ai 2008); and seven studies did not describe random sequence generation. We telephoned the authors of these seven studies and established that they were all RCTs. Overall, six studies used a random number table (Chang 2002a; Lin 2008; Luo 2008; Zou 1997; Zhou 2010; Ai 2008), one used computer software (Yuan 2004), one used minimised imbalance index distribution (Hu 2002) and one used simple randomisation (drawing lots) (Wang 2006a). Allocation concealment and blinding were also not mentioned in any of the included studies. By telephoning the authors, we were able to confirm that no study used allocation concealment; single blinding was used in two studies (Chang 2002a; Yuan 2004) and no blinding was used in the other seven studies (Ai 2008; Hu 2002 Lin 2008; Luo 2008; Wang 2006a; Zhou 2010; Zou 1997). These three characteristics may lead to selection, performance and detection bias and may result in false positive findings. All nine studies reported the outcome data of the included participants, and the risk of attrition bias was assessed to be low. Luo 2008 and Ai 2008 did not report all the pre-defined outcomes, such as complete blood count, routine urine examination and kidney function. This may lead to both selection and reporting bias.

Potential biases in the review process

This systematic review involved a comprehensive search strategy and only included RCTs. We searched English and Chinese language databases to identify all possible RCTs. We acknowledge that there may be studies of Huangqi type formulation published in other languages, however by searching CENTRAL (which contains over 500,000 reports of studies from indexed, non-indexed and handsearched journals and conference proceedings in many languages) we do not believe we have missed any major study. Data extraction, analysis and methodological quality assessments were performed by two or more authors. We found a large number of clinical trials investigating Huangqi type formulation for the treatment of nephrotic syndrome. We contacted authors to clarify how the study was conducted; this resulted in the exclusion of 363 reports. Most investigators misunderstood true random allocation resulting in poor methodological quality and ineligible study design.

Agreements and disagreements with other studies or reviews

Two systematic reviews investigating Huangqi or Huangqi type formulation for the treatment of nephrotic syndrome have been previously published (Li 2006f; Zhou 2009d). Li 2006f included four studies (Chen 2001a; Wu 1998b; Zhao 1999c; Zhang 1998) and concluded Buyanghuanwu soup (Huangqi, Guiwei, Chishao, Dilong, Chuanqiong, Taoren, Honghua) improved the effective rate and safety of primary nephrotic syndrome. In our review we excluded these four studies. On phoning the authors we determined that these four studies were not randomised. Zhou 2009d included 20 studies (Chen 2008b; Dai 2006; Deng 2003; Dong 2001; Kang 2005; Li 1999a; Li 2003b; Li 2007g; Lin 2007; Ning 2002; Shi 2004; Wang 1997; Wang 2001c; Wang 2002f; Wang 2006a; Wu 2005a; Xu 2000a; Yu 2001; Yu 2003; Zhang 2001c). This review concluded that *Radix astragali* could increase the therapeutic effect of prednisone and immunosuppression for primary nephrotic syndrome and reduce its recurrence. *Radix Astragali* also increased plasma albumin and decreased 24 hour proteinuria and plasma cholesterol. Again on phoning the authors of these 20 studies we excluded 19 for the same reasons as for Li 2006f - the studies were not randomised. The reason for this obvious difference in study selection might be that these two review authors did not telephone the study authors to confirm study design, and in particular random sequence generation. Five studies in our review enrolled children (Ai 2008; Lin 2008; Wang 2006a; Zou 1997; Zhou 2010), however only one of the four studies published before the completion of Zhou 2009d was included (Wang 2006a). We performed a comprehensive search using a well-defined search strategy and contacted all authors of potentially eligible studies.

AUTHORS' CONCLUSIONS

Implications for practice

Huangqi and Huangqi type formulations may have a positive effect on nephrotic syndrome. However, limited by the small number of poorly-designed RCTs enrolling small number of participants, there is currently insufficient evidence to support the use of Huangqi type formulations for the treatment of nephrotic syndrome.

Implications for research

Large, properly randomised, controlled and double blind studies are needed to evaluate the effect of Huangqi type formulations. The following factors should be considered for future studies.

- sample size should be calculated before commencement of the study
- randomisation and allocation concealment procedures should be reported
- studies should be blinded and this should be described in detail
- baseline characteristics of the participants should be described in detail
- the histological subtype of participants should be described in detail
- the name and dose of all the drugs used in the control groups should be described in detail
- outcomes should be clearly defined
- the composition, dosage and course of the drugs (intervention and control) should be clearly described
- describe the outcomes (methods and units of measure) and the time to measure in detail
- long-term follow-up is needed to evaluate the benefits and harms of Huangqi type formulations.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Ai 2008

Methods	• Study design: parallel RCT
Participants	• Country: China • Primary nephrotic syndrome patients (proteinuria: > 3+ on dipstick; urinary protein-creatinine ratio: > 0.2 g/mmol, > 40 mg/m^2/h or > 50 mg/kg/d). All the patients achieved remission after standard hormone therapy, but they relapsed more than 2 times in 6 months or 3 times in one year (relapse: urine protein goes from negative to positive lasting longer than 2 weeks) • Number: treatment group (35); control group (33) • Mean age ± SD years: treatment group (5.87 ± 3.09); control group (7.57 ± 1.20) • Sex (M/F): treatment group (21/14); control group (19/14)
Interventions	Treatment group

Ai 2008 *(Continued)*

	• Shenkanglin decoction
	  ○ Huangqi 20 g; Shendi 15 g; Shanyu 9 g; Huaishan 9 g; Zexie 9 g; Fulin 9 g; Taizishen 20 g; Zhimu 6 g; Danshen 15 g; Shanlizhi 15 g; Xiuhuazhen 15 g
	  ○ Shenkangling decoction taken once a day, until 2 months after prednisone was withdrawn
	• Drugs the control group received
	
	Control group
	
	• Prednisone
	  ○ Initial dose 1.5-2.0 mg/kg/d
	  ○ 2 weeks after urine protein became negative, 2 mg/kg was used every other day for 4 weeks. Dose was then reduced gradually 2.0-2.5mg every 2-4 weeks. The total therapy time was longer than 1 year.
	• Anticoagulation and best support care

Outcomes	• Plasma NF-KB • Plasma TXB2 • Plasma 6-keto-PGF1a • Plasma albumin • Plasma protein • 24 hours urine protein • Blood cholesterol • Blood triglyceride
Notes	• Baseline declining kidney function: NS • Remission: NS • Pathology: NS • Relapse: NS • Time to relapse: NS • Mean follow-up: NS • Dosage: described in detail • Prepare method: NS • Source of funding: none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	We interviewed the author by telephone, a random number table was used for generating the allocation sequence
Allocation concealment (selection bias)	High risk	The random number table was produced by themselves. Investigator knew the intervention group before eligible participants entered in the study.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Blinding was not used in the study.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NS
Incomplete outcome data (attrition bias) All outcomes	Low risk	The data for all 68 patients were reported.

Ai 2008 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Not all pre-defined outcomes were reported, such as complete blood count, routine urine exam and kidney function.
Other bias	Unclear risk	The study did not show any interest.

Chang 2002a

Methods	• Study design: parallel RCT
Participants	• Country: China • Primary nephrotic syndrome patients (proteinuria > 3.5 g; plasma albumin < 30 g/L) • Number: treatment group (15); control group (15) • Age range: 15 to 42 years • Sex (M/F): 18/12

Interventions	Treatment group
	• Huangqi-Danggui mixture
	  ◦ 1 mL/kg/d (0.5 g Huangqi and 0.5 g Danggui)
	• Drugs the control group received
	Control group
	• Prednisone
	  ◦ Initial dose 1.5 to 2.0 mg/kg/d
	• Dipyridamole
	• Heparin

Outcomes	• Triglyceride • Cholesterol
Notes	• Baseline declining kidney function: NS • Pathology: NS • Relapse: NS • Time to relapse: NS • Mean follow-up: NS • The author prepared the Huangqi with Danggui mixture • Source of funding: none • TCM sign: NS • Time to measure outcomes: NS

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	We interviewed the author by telephone, a random number table was used for generating the allocation sequence
Allocation concealment (selection bias)	High risk	The random number table was produced by themselves. Investigator knew the intervention group before eligible participants entered in the study.
Blinding of participants and personnel (performance bias)	High risk	Simple blinding was used, but the doctors and data analysts knew who took the Huangqi-Danggui mixture.

Chang 2002a *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NS
Incomplete outcome data (attrition bias) All outcomes	Low risk	The data for all 30 patients were reported.
Selective reporting (reporting bias)	Low risk	All clinically relevant and reasonably expected outcomes were reported.
Other bias	Unclear risk	The study did not show any interest.

Hu 2002

Methods	• Study design: parallel RCT
Participants	• Country: China • Primary nephrotic syndrome patients (proteinuria > 3.5 g/d; plasma albumin < 30/dL; high oedema; hyperlipidaemia) • Number: treatment group (18); control group (20) • Age range: 14 to 50 years • Sex (M/F): 17/21

Interventions	Treatment group
	• Huangqi intravenous injection
	  ◦ 40 mL Huangqi + 250 mL 5% glucose/d
	• Drugs control group received
	Control group
	• Prednisone
	  ◦ Initial dose 1.5 to 2.0 mg/kg/d
	• Anticoagulant
	• Diuretics

Outcomes	• Plasma albumin • Blood cholesterol • Blood triglyceride • No improvement: urine protein unchanged, symptoms not disappeared, kidney function unchanged, plasma albumin unchanged
Notes	• Baseline declining kidney function: NS • Pathology: NS • Remission: described in detail • Relapse: NS • Time to relapse: NS • Mean follow-up: 20 days • Dosage: described in detail • Prepare method: NS • Source of funding: none

Hu 2002 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	We interviewed the author by telephone, they used simple randomisation.
Allocation concealment (selection bias)	High risk	The random number table was produced by themselves. Investigator knew the intervention group before eligible participants entered in the study.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Blinding was not used in the study.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NS
Incomplete outcome data (attrition bias) All outcomes	Low risk	The data for all 38 patients were reported.
Selective reporting (reporting bias)	Low risk	All clinically relevant and reasonably expected outcomes were reported.
Other bias	Unclear risk	The study did not show any interest.

Lin 2008

Methods	• Study design: parallel RCT
Participants	• Country: China • Idiopathic nephrotic syndrome patients (urinary protein: > 50 mg/kg/d; plasma albumin: < 30 g/dL; hypoposia; hypercholesterolaemia) • Number: treatment group (41); control group (40) • Age range: treatment group (1.4 to 13 years); control group (1.5 to 12 years) • Sex (M/F): treatment group (27/14); control group (28/12) • Exclusions: secondary nephrotic syndrome

Interventions	Treatment group
	• Huangqi intravenous injection
	  ◦ 0.5 to 1 mL/kg/d or 1 to 2 g/kg/d + 5% glucose solution (100 to 250 mL) for 2 weeks
	• Drugs the control group received
	Control group
	• Prednisone
	  ◦ 1.5 to 2.0 mg/kg for 2 weeks
	• Anti-inflammation therapy for 2 weeks
	• Anticoagulation therapy for 2 weeks

Outcomes	• Blood lactic dehydrogenase • Blood creatinine kinase-MB isoenzyme

Lin 2008 *(Continued)*

	• Blood total cholesterol • Blood albumin • Blood high density lipoprotein • Blood total protein • Blood IgG • Blood IgA • Blood IgM • Blood IgE
Notes	• Baseline declining kidney function: NS • Pathology: NS • Remission: NS • Relapse: NS • Mean follow-up: NS • Time to relapse: NS • Prepare method: NS • Dosage: described in detail • Source of funding: none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	We interviewed the author by telephone, a random number table was used for generating the allocation sequence
Allocation concealment (selection bias)	High risk	The random number table was produced by themselves. Investigator knew the intervention group before eligible participants entered in the study.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Blinding was not used in the study. The patients in control group and doctors knew they did not receive the Huangqi injection.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NS
Incomplete outcome data (attrition bias) All outcomes	Low risk	The data for all 81 patients were reported.
Selective reporting (reporting bias)	Low risk	All clinically relevant and reasonably expected outcomes were reported.
Other bias	Unclear risk	The study did not show any interest.

Luo 2008

Methods	• Study design: parallel RCT
Participants	• Country: China • Idiopathic nephrotic syndrome patients (urinary protein > 50 mg/kg/d; plasma albumin < 30 g/dL; hypoposia; hypercholesterolaemia)

Luo 2008 *(Continued)*

- Number: treatment group (40); control group (38)
- Mean age: treatment group (26.7 years); control group (27.1 years)
- Sex (M/F): treatment group (22/18); control group (21/17)
- Exclusions: secondary nephrotic syndrome

Interventions	Treatment group
	• Shenzongerjia soup
	  ◦ Huangqi 15 g; Taizishen 15 g; Fulin 15 g; fried Baishu 15 g; Shudi 15 g; Guiban 15 g; Biejia 15 g; Danshen 15 g; Chuanqiong 10 g; Fangfeng 10 g; Chantui 10 g; Jiangchan 10 g; Dilong 12 g; Yimucao 30 g; Bai maogeng 30 g
	• Same drugs as the control group
	Control group
	• Prednisone
	  ◦ initial dose 1.0 mg/kg/d for 8 weeks; decreased by 5 mg/wk until 0.4 mg/kg/d, then 0.4 mg/kg every other day for 4 to 6 months. Dose was then reduced gradually by 2.5 mg every 2 weeks. Finally, decreased gradually until withdrawal.
	• Anticoagulation therapy, low salt diet, decrease blood lipid, control blood pressure, diuretics, calcium supplement

Outcomes	• Blood albumin • Blood creatinine • Blood urea nitrogen • 24 hour urinary protein • Complete remission: 24 h urine protein ≤ 0.2 g; plasma albumin ≥ 35 g/L; kidney function normal; symptoms disappeared • Partial remission: 24 h urine protein < 3.0 g, plasma albumin improved, kidney function improved • No improvement: urine proteinuria unchanged, plasma albumin unchanged, kidney function unchanged, symptoms unchanged • Frequent relapse: Relapse 3 times/year or 2 times/6 months during therapy, relapse was defined as proteinuria changing from negative to positive longer than 2 weeks within 3 months after complete remission
Notes	• Baseline declining kidney function: described in detail • Pathology: NS • Remission: described in detail • Relapse: described in detail • Mean follow-up: NS • Time to relapse: NS • Prepare method: NS • Dosage: described in detail • Source of funding: none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	We interviewed the author by telephone, a random number table was used for generating the allocation sequence.
Allocation concealment (selection bias)	High risk	The random number table was produced by themselves. Investigator knew the intervention group before eligible participants entered in the study.

Luo 2008 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Blinding was not used in the study. The patients in control group and doctors knew they did not receive the traditional Chinese medicine.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NS
Incomplete outcome data (attrition bias) All outcomes	Low risk	The data for all 78 patients were reported.
Selective reporting (reporting bias)	Unclear risk	Not all pre-defined outcomes were reported, such as complete blood count and routine urine exam.
Other bias	Unclear risk	The study did not show any interest.

Wang 2006a

Methods	• Study design: parallel RCT
Participants	• Country: China • Idiopathic nephrotic syndrome children (proteinuria: > 3+ on dipstick; urinary protein-creatinine ratio: > 0.2 g/mmol; > 40 mg/m^2/h or > 50 mg/kg/d) • Number: treatment group (15); control group (15) • Age range: treatment group (3 to 15 years); control group (3 to 15 years) • Sex (M/F): treatment group (7/8); control group (8/7) • Exclusions: secondary nephrotic syndrome

Interventions	Treatment group
	• Huangqi oral solution
	  ◦ 10 mL 3 times/d for 1 month
	• Same drugs as the control group
	Control group
	• Prednisone
	  ◦ 1.5 to 2.0 mg/kg/d for 1 month
	• Anticoagulation therapy
	• Symptomatic treatment

Outcomes	• Plasma albumin • 24 hour urine protein • Plasma β2-microglobulin • Urine β2-microglobulin • Time of oedema recession
Notes	• Baseline declining kidney function: NS • Pathology: NS • Remission: NS • Relapse: NS • Mean follow-up: NS

Wang 2006a *(Continued)*

- Time to relapse: NS
- Prepare method: NS
- Dosage: described in detail
- Source of funding: none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	We interviewed the author by telephone, drawing lots was used for generating the allocation sequence.
Allocation concealment (selection bias)	High risk	The random number table was produced by themselves. Investigator knew the intervention group before eligible participants entered in the study.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Blinding was not used in the study. The patients in control group and doctors knew they did not receive the traditional Chinese medicine.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NS
Incomplete outcome data (attrition bias) All outcomes	Low risk	The data all 30 patients were reported.
Selective reporting (reporting bias)	Low risk	All clinically relevant and reasonably expected outcomes were reported.
Other bias	Unclear risk	The study did not show any other bias.

Yuan 2004

Methods	• Study design: parallel RCT
Participants	• Country: China • Frequently relapsing nephrotic syndrome patients of mesangial proliferative glomerulonephritis type (proteinuria > 3.5 g/d; plasma albumin < 30 g/dL; hypoposia and hypercholesterolaemia; can have complete remission but relapse 3 times in 1 year or 2 times in 6 months. • Number: treatment group (30); control group (30) • Age range: treatment group (10 to 60 years); control group (8 to 60 years) • Sex (M/F): treatment group (18/12); control group (17/13) • Exclusions: secondary nephrotic syndrome
Interventions	Treatment group • Same drugs as the control group • Huangqi (25 g) and Hongzao (15 g) after prednisone had been used for 8-12 weeks Control group • Prednisone ○ Initial dose 1 mg/kg/d for 8-12 weeks. When urine protein (-), decreased 5 mg/wk until reduced to 0.5 mg/kg/d, then 1 mg/kg every other day for 6 months. Dose was then reduced gradually to 0.4

Yuan 2004 *(Continued)*

	mg/kg/d over 6 months and maintained at this dose for 12-18 months. Finally, decreased gradually until withdrawal. • Anticoagulation therapy • Best support care
Outcomes	• No improvement: minimal change in urine protein and serum albumin, symptoms of nephrotic syndrome still present, no improvement in kidney function • Relapse: proteinuria changed from negative to positive longer than 2 weeks within 3 months after complete remission • Adverse reactions
Notes	• Baseline declining kidney function: NS • Pathology: NS • Remission: described in detail • Relapse: described in detail • Mean follow-up: NS • Time to relapse: described in detail • Prepare method: not described in detail • Dosage: described in detail • Source of funding: none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	We interviewed the author by telephone, computer generated random numbers sequence was used.
Allocation concealment (selection bias)	High risk	The random number table was produced by themselves. Investigator knew the intervention group before eligible participants entered in the study.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Simple blinding was used, but the doctors and data analysts knew who took the Huangqi (25 g) and 15 g Hongzao.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NS
Incomplete outcome data (attrition bias) All outcomes	Low risk	The data all 60 patients were reported.
Selective reporting (reporting bias)	Low risk	All clinically relevant and reasonably expected outcomes were reported.
Other bias	Unclear risk	The study did not show any interest.

Zhou 2010

Methods	• Study design: parallel RCT
Participants	• Country: China

Zhou 2010 *(Continued)*

	• Primary nephrotic syndrome patients (34); relapsing nephrotic syndrome patients (12) (proteinuria > 3+ on dipstick; urinary protein-creatinine ratio > 0.2 g/mmol; > 40 mg/m^2/h or > 50 mg/kg/d); no infection in previous 4 weeks; no immunosuppressants • Number: treatment group (24); control group (22) • Age range: treatment group (1.5 to 6 years); control group (1.8 to 7 years) • Sex (M/F): treatment group (13/11); control group (11/9)

Interventions	Treatment group
	• Huangqi granules for 8 weeks
	  ○ When the patients were younger than 3 years, half packet of Huangqi granules was given to them twice a day. Otherwise, one packet of Huangqi granules was given to them twice a day
	• Given the same drugs as the control group
	Control group
	• Prednisone
	  ○ Initial dose 1.5 to 2.0 mg/kg/d
	  ○ Symptomatic and supportive treatments for 8 weeks

Outcomes	• Serum IFN-γ, IL-13,TGF-β1 expression level • Urine IFN-γ, IL-13,TGF-β1 expression level • Adverse effect: none • Effect • Infection rate • Relapse rate • Remission rate
Notes	• Baseline declining kidney function: NS • Pathology: NS • Remission: described in detail • Relapse: described in detail • Mean follow-up: NS • Time to relapse: NS • Prepare method: not described in detail • Dosage: described in detail • Source of funding: none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated random numbers sequence was used.
Allocation concealment (selection bias)	High risk	The random number table was produced by themselves. The participants involved in the clinical trial could not know the sequence before the patients entering in the study.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Blinding was not used in the study. The patients in control group and doctors knew they did not take the Huangqi granules.
Blinding of outcome assessment (detection bias)	Unclear risk	NS

Zhou 2010 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	The data all 46 patients were reported.
Selective reporting (reporting bias)	Low risk	All clinically relevant and reasonably expected outcomes were reported.
Other bias	Unclear risk	The study did not show any interest.

Zou 1997

Methods	• Study design: parallel RCT
Participants	• Country: China • Children with primary nephrotic syndrome (proteinuria > 3+ on dipstick; urinary protein-creatinine ratio > 0.2 g/mmol, > 40 mg/m^2/h or > 50 mg/kg/d) • Number: treatment group (15); control group (15) • Age: NS • Sex (M/F): NS
Interventions	Treatment group • Ciwujia with Huangqi mixture • Same drugs as the control group Control group • Prednisone ◦ Initial dose 1.5 to 2.0 mg/kg/d • Anticoagulation therapy and best support care
Outcomes	• Plasma endogenous cortisol level • Peripheral blood T lymphocyte subset • Relapsing rate
Notes	1. Baseline declining kidney function: NS 2. Pathology: NS 3. Remission: NS 4. Relapse: described in detail 5. Mean follow-up: NS 6. Time to relapse: NS 7. Prepare method: not described in detail 8. Dosage: NS 9. Source of funding: none

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated random numbers sequence was used.

Zou 1997 *(Continued)*

Allocation concealment (selection bias)	High risk	The random number table was produced by themselves. Investigator knew the intervention group before eligible participants entered in the study.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Blinding was not used in the study. The patients in control group and doctors knew they did not receive the traditional Chinese medicine.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	NS
Incomplete outcome data (attrition bias) All outcomes	Low risk	The data all 30 patients were reported.
Selective reporting (reporting bias)	Low risk	All clinically relevant and reasonably expected outcomes were reported.
Other bias	Unclear risk	The study did not show any interest.

NS: not stated

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

Study	Reason for exclusion
Bai 2004	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0564-3338406
Bai 2010	We telephoned the author in June 2011. The study was a retrospective study. The author summarized the past medical records. Telephone number: +86 13700201192
Bie 2006	We telephoned the author in August 2006. The study was not a double-blind RCT. The author summarized the past medical records. Telephone number: +86 0898-65343033
Cao 2009	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical records. Telephone number: +86 15633142939
Chang 2002b	The data is not in accord with the study description.
Chen 1998	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0917-8957075
Chen 1999	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical records.
Chen 2001a	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion.

Study	Reason for exclusion
	Telephone number: +86 0539-2254441
Chen 2001b	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 0396-5039693
Chen 2001c	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 13305521186
Chen 2002	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0731-4327001
Chen 2003	We telephoned the author in August 2006. The study was not a double-blind RCT. The author summarized the past medical records. Telephone number: +86 0595-22771677
Chen 2004	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the order of the patients came to hospital, odd number to one group and even number to another. Telephone number: +86 0731-4327001
Chen 2005	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 0595-86869356
Chen 2006a	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0662-3527122
Chen 2006b	The patients in the treatment group did not receive the Huangqi.
Chen 2006c	The patients in the treatment group received the danshen injection, but the control group did not receive.
Chen 2007	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Chen 2008a	The article is the review, not the RCT.
Chen 2008b	The patients were allocated into two groups according to the medical order.
Chen 2009a	The secondary nephrotic syndrome patients were not excluded in the study.
Chen 2009b	We telephoned the author in June 2011. The study was a retrospective study. The author summarized the past medical records. Telephone number: +86 0738-5212590
Chen 2010a	The treatment group did not use the Huangqi.

Study	Reason for exclusion
Chen 2010b	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Chen 2010c	The patients in the treatment group receive the dexamethasone, but the control group did not receive it. The intervention was not in accord with the criteria.
Chen 2010d	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 023—68755114
Chen 2011	We telephoned the author in June 2011. The study was a retrospective study. The author summarized the past medical data. Telephone number: +86 0319-2233383.
Cheng 2004	The patients in the treatment group did not receive the Huangqi.
Dai 2006	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0591-83947272
Deng 2003	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 020-81048142
Deng 2008	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical records. Telephone number: +86 0745-7622223
Ding 2008	The patients were allocated into two groups according to the medical order.
Dong 2001	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0551-2237306
Dong 2005	We telephoned the author in August 2006. The study was not a double-blind RCT. The author summarized medical records. Telephone number: +86 0432-2166109
Dong 2009	We telephoned the author in June 2011. The study was a retrospective study. The author summarized the past medical data. Telephone number: +86 0731-84917863.
Du 2006a	The treatment group used both Huangqi and danshen injection, and the control group did not use the danshen injection.
Du 2006b	The patients in the treatment group receive the Danshen injection.
Duan 2006	The patients were allocated into two groups according to the medical order.
Fan 2001	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 13103309866

Study	Reason for exclusion
Feng 2007	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Feng 2010	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical records. Telephone number: +86 0710-3440874
Fu 2008	The patients in the treatment group did not receive the Huangqi.
Gao 2001	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups as the patients wish. Telephone number: +86 0718-8295122
Gao 2002	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 0912-5641830
Gong 2007	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized medical records. Telephone number: +86 0519-88104931
Gong 2009	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0633-2252750
Gong 2010	The study was a retrospective study. The author summarized the past medical records.
Gu 1998	We telephoned the author in August 2006. The study was not a double-blind RCT. The author numbered the patients, odd numbers were assigned to one group and even numbers to the other. Telephone number: +86 010-66385849
Guo 1997	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0471-6921203
Guo 1999	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 0571-85827888
Guo 2006	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 0760-8802802
Guo 2008a	The patients were allocated into the two groups according to the medical order.
Guo 2008b	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Guo 2010	We telephoned the author in June 2011. The study was retrospective study. The author summarized the past medical records. Telephone number: +86 0827-7330108
Hao 2007	We telephoned the author in June 2011.

Study	Reason for exclusion
	The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 022-27432299
He 2008	The intervention was not in accord with the criteria.
He 2010	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Hong 2001	The study was not a double-blind RCT. The author divided patients into groups using random sampling.
Hu 2005	The patients did not receive the Huangqi in the treatment group.
Hu 2006a	The patients in the treatment group did not receive the Huangqi.
Hu 2006b	The study was not a RCT, the patients were not divided into two groups randomly.
Hu 2009	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Hua 2010	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Huang 2004a	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 020-81048142
Huang 2004b	The patients in the treatment group did not receive the Huangqi formulation.
Huang 2006	The patients in the treatment group did not receive the Huangqi.
Huang 2007	The patients in the treatment group did not receive the Huangqi.
Huang 2009a	The patients were allocated into two groups according to the medical order.
Huang 2009b	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Huang 2010	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Ji 2009	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical records. Telephone number: +86 0370-2701366
Jia 2010	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0313-7219062.
Jiang 1997	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the pathogenetic condition. Telephone number: +86 0519-8132511

Study	Reason for exclusion
Jiang 2001a	We telephoned the author in August 2006 in order to identify the randomisation procedure and other methodological issues, but the author refused further information. We couldn't determine whether it is an RCT. Telephone number: +86 0451-53740549
Jiang 2001b	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 023-85381656
Jiang 2001c	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0535-6691999
Jiang 2008a	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 13038228715
Jiang 2008b	We telephoned the author in June 2011. The study was a retrospective study. The author summarized the past medical records. Telephone number: +86 0459-5805065
Jin 2001	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0377- 63200081
Jin 2007	The study did not exclude the secondary nephrotic syndrome patients.
Kang 2005	The secondary nephrotic syndrome patients were not excluded in the study.
Kong 2009	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical records. Telephone number: +86 010-69314902
Lai 2006	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0798-8417496.
Lan 2005	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the patients' opinion. Telephone number: +86 13028500622
Lan 2007	The study did not exclude the secondary nephrotic syndrome patients.
Lei 2006	The patients in the treatment group received the losartan, but the patients in the control group did not receive it.
Li 1988	The study was a case report.
Li 1994	We telephoned the author in August 2006.

Study	Reason for exclusion
	The study was not a double-blind RCT. The author divided patients into groups according to the pathogenetic condition. Telephone number: +86 0431-86816453
Li 1997	The study was not a RCT, there was no control group.
Li 1999a	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the pathogenetic condition. Telephone number: +86 0543-3201274
Li 1999b	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 13679015009
Li 2003a	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0411-83168514
Li 2003b	We telephoned the author in August 2006. The study was not a double-blind RCT. The author summarized medical records. Telephone number: +86 0932-6622418
Li 2004a	We telephoned the author in June 2011. The study was a retrospective study. Telephone number: +86 0734-8279011
Li 2004b	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0392-7256007
Li 2005	The patients in the treatment group received the lower molecular heparin, but the patients in the control group did not receive it.
Li 2006a	The patients in the treatment group did not receive the Huangqi.
Li 2006b	The patients in the treatment group did not receive the Huangqi.
Li 2006c	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the patient's opinion. Telephone number: +86 0736-2857719
Li 2006d	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0730-6222684
Li 2006e	We telephoned the author in June 2011. The study was a retrospective study. Telephone number: +86 0312-2322220-8076

Study	Reason for exclusion
Li 2007a	The patients in the treatment group did not use the Huangqi. The intervention was not in accord with the criteria.
Li 2007b	The secondary nephrotic syndrome patients were included in the study.
Li 2007c	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Li 2007d	We telephoned the author in June 2011. The study was not a double-blind RCT. Patients were divided into groups at their discretion. Telephone number: +86 029-33320873
Li 2007e	We telephoned the author in June 2011. The study was a retrospective study. The author summarized the past medical records. Telephone number: +86 0372-2957248
Li 2007g	The secondary nephrotic syndrome patients were not excluded in the study.
Li 2008a	The patients in the control group did not use the erigeron. The intervention was not in accord with the criteria.
Li 2008b	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Li 2008c	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Li 2008d	The patients were allocated into two groups according to the medical order.
Li 2008e	We telephoned the author in June 2011. The study was a retrospective study. The author summarized the past medical records. Telephone number: +86 0411-83168346
Li 2009	We telephoned the author in June 2011. The study was a retrospective study. The author summarized the past medical records. Telephone number: +86 0451-55653086
Li 2010a	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Li 2010b	We telephoned the author in June 2011. The study was a retrospective study. The author summarized the past medical records. Telephone number: +86 0875-5137574.
Li 2011a	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Li 2011b	We telephoned the author in June 2011. The study was a retrospective study. The author summarized the past medical records. Telephone number: +86 13907385605
Li 2011c	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical records. Telephone number: +86 13359757979

Study	Reason for exclusion
Liang 2005	The patients in the control group received the hormone, but the patients in the treatment group did not receive it.
Lin 2006	The outcomes reported in were not relevant to this review (L-10).
Lin 2007	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical records. Telephone number: +86 0714-6348622
Liu 1990	The study was not a RCT, there was no control group.
Liu 1994	Some patients did not receive the Huangqi.
Liu 1999a	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 0355-2024990
Liu 1999b	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the order of the patients came to hospital, odd number into one group and even number into another. Telephone number: +86 0539-8226999
Liu 2001a	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0554-3320706
Liu 2001b	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0931-7616126
Liu 2002	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0774-8282011
Liu 2003	The study was not a RCT, there was no control group.
Liu 2006	We telephoned the author in June 2011. The study was a retrospective study. Telephone number: +86 0710-3449468
Liu 2007a	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical records. Telephone number: +86 022-23051087
Liu 2007b	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical records. Telephone number: +86 0971-8247545
Liu 2008a	The patients were allocated into two groups according to the medical order.
Liu 2008b	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Liu 2008c	We telephoned the author in June 2011. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 13914564298

Study	Reason for exclusion
Liu 2008d	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical records. Telephone number: +86 0536-8652150
Liu 2008e	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical records. Telephone number: +86 0432-64661278
Liu 2009	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical records. Telephone number: +86 0993-2858573
Liu 2010a	The patients in the treatment group receive the sodium ferulate for Injection and Huangqi formulation, but the control group did not receive both. The intervention was not in accord with the criteria.
Liu 2010b	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the patients' opinion. Telephone number: +86 13973956628
Lu 2001	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the day of the patients came to hospital, odd numbered days to one group and even numbered days to the other. Telephone number: +86 0773-2838977
Lu 2004	The patients in the treatment group did not receive the Huangqi.
Lu 2007	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Lu 2010	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Luo 2002a	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 0579-4133053
Luo 2002b	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the order of the patients came to hospital, such as, 1-3 into one group and 4-6 into another. Telephone number: +86 0310-2115089
Luo 2009	The patients in the treatment group received tripterygium glycosides. The intervention was not in accord with the criteria.
Luo 2010	The intervention therapy was not equal in the two groups. The intervention was not in accord with the criteria.
Lv 2001	The patients in the treatment group received the nao ming injection, but the patients in the control group did not receive it.
Lv 2006	The patients in the treatment group received the sodium ferulate, but the patients in the control group did not receive it.

Study	Reason for exclusion
Lv 2007a	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Lv 2007b	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Ma 2006	The patients in the treatment group did not receive the Huangqi.
Ma 2007	The study was not a clinical trial.
Mao 2006	The patients in the treatment group received the five leaf gynostemma herb, but the patients in the control group did not receive it.
Min 2008a	The experimental group did not use the Huangqi. The intervention was not in accord with the criteria.
Min 2008b	The patients in the treatment group did not use the Huangqi. The intervention was not in accord with the criteria.
Mo 2004a	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0759-2387421
Mo 2004b	The secondary nephrotic syndrome patients were not excluded in the study.
Mo 2010	We telephoned the author in June 2011. The study was a retrospective study. The author summarized the past medical records. Telephone number: +86 0775-7222155
Ni 2007	The patient in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Ni 2009	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0731—28290022
Nie 1985	The study was not a RCT, there was no control group.
Ning 2002	The study is a retrospective study.
Niu 1999	We telephoned the author in August 2006. The study was not a double-blind RCT. The author summarized the past medical records. Telephone number: +86 0372-5119119
Ou 2003	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0731-4762681
Pang 2010	The patients were allocated into two groups according to the medical order.

Study	Reason for exclusion
Peng 2008	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Peng 2010	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Qi 1998	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0378-5956174
Qian 2002	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the pathogenetic condition. Telephone number: +86 0523-6361348
Qin 2009	The patients in the treatment group did not use the Huangqi. The intervention was not in accord with the criteria.
Qin 2010	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Qiu 2002	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0538-3212864
Qiu 2006	The study did not exclude the secondary nephrotic syndrome patients.
Qiu 2010	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Qu 2008	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical records. Telephone number: +86 0532-87895264
Ren 1999	The patients in the treatment group received the fu fang dan shen injection, but the patients in the control group did not receive it.
Shan 2002	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the time of the patients came to hospital, in one period of time patients we assigned to one group and the next period of time to the other. Telephone number: +8613333352318
Shen 2002	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0871-3638663.
Shen 2003	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 0745-2261533
Shen 2005	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other.

Study	Reason for exclusion
	Telephone number: +8613305756080
Shi 2001	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0573-88022799.
Shi 2003a	We telephoned the author in August 2006. The author had written protocol before commencing the study. In the protocol the author obtained serial numbers using a random numbers table, but did not strictly follow the protocol. Telephone number: +86 0756-2528723
Shi 2003b	The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other.
Shi 2004	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0313-8046904.
Shi 2007	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0731-84917778
Shi 2010	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0515-81608138
Song 1999a	The patients in the treatment group did not receive the Huangqi.
Song 1999b	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0373-2022300.
Song 2003	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 0539-5221030
Sun 2004a	We telephoned the author in August 2006. The study was not a double-blind RCT. The author summarized the past medical records. Telephone number: +86 0538-3159235
Sun 2004b	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number:+86 0718-8240995
Sun 2009a	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Sun 2009b	We telephoned the author in June 2006. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0313-4323450

Study	Reason for exclusion
Sun 2010	The patients were allocated into two groups by medical order.
Tan 2010	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0772-4362154.
Tang 2000a	The author divided patients into groups according to the order of the patients came to hospital, the experimental group number is twice as much as the control group.
Tang 2000b	The patients in the treatment group received dan shen injection, but the patients in the control group did not receive it.
Tang 2006	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0816-2222566.
Tang 2007	The patients in the treatment group received the tripterygium glycosides and Huangqi, but the control group did not receive both. The intervention was not in accord with the criteria.
Tong 2003	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0352-5556001.
Wan 2000	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 022-25868010.
Wang 1992	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 027-83662142.
Wang 1997	Not an RCT
Wang 1999	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 0451-82576141
Wang 2000a	We telephoned the author in August 2006. The author hadn't written the protocol beforehand. The author divided patients in groups by allocating when they came to hospital. Telephone number: +86 0311-87027951
Wang 2001a	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0351-4988999.
Wang 2001b	The patients in the control group received the CTX, but the patients in the treatment group did not receive it.
Wang 2001c	The treatment group did not use the hormone. The control group used the hormone.
Wang 2002a	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 0830-3165341

Study	Reason for exclusion
Wang 2002b	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 0854-8261502
Wang 2002c	Not randomised
Wang 2002d	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0351-4988999.
Wang 2002e	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 13975503269.
Wang 2002f	The study did not use the random sequence.
Wang 2003	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 027-85726187
Wang 2004a	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 0903-2050231
Wang 2004b	The patients in the treatment group received the losartan, but the patients in the control group did not receive it.
Wang 2006b	The patients were allocated into two groups by medical order.
Wang 2006c	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0854-8223218.
Wang 2007a	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Wang 2007b	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Wang 2008a	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 022-26220505
Wang 2008b	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0873-7653257.
Wang 2009a	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Wang 2010a	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Wang 2010b	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.

Study	Reason for exclusion
Wang 2010c	The diagnostic criteria were not according to the protocol.
Wang 2010d	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0530-5925757
Wang 2010e	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0396-2926207.
Wang 2011	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0717-6486471
Wei 1999	We couldn't determine who received Huangqi.
Wei 2000a	We couldn't determine who received Huangqi.
Wei 2000b	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0750-3509898.
Wei 2000c	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0772-2592557.
Wei 2000d	Some patients in the treatment group did not receive the Huangqi.
Wei 2002a	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0511-5345556
Wei 2002b	The study was not a double-blind RCT. The author divided patients into groups according to the order of the patients came to hospital.
Wei 2003	The patients in the control received warfarin sodium, but the patients in the control group did not receive it.
Wei 2004	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 0377-65973416
Wei 2005	The study was not a double-blind RCT. The author divided patients into groups according to the order of the patients came to hospital.
Wei 2009	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0776-5822395
Wen 2005	We telephoned the author in June 2011. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 13076877015.

Study	Reason for exclusion
Wen 2007	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Wu 1998b	The patients in the control group received the aspirin and dipyridamole, but the patients in the treatment group did not receive them.
Wu 1998c	The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital.
Wu 1999	We couldn't determine who received Huangqi.
Wu 2002	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 0571-63345410.
Wu 2005a	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the medical data. Telephone number: +86 0713-5282130.
Wu 2009a	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Wu 2009b	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0527-83552038.
Xi 2003	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0511-5345556.
Xiang 2007	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 15997643773
Xiao 2000	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the day the patients came to hospital, odd numbered days to one group and even numbered days to the other. Telephone number: +86 0536-8068883
Xie 2008	The Huangqi was not totally used in the treatment group. The intervention was not in accord with the criteria.
Xie 2010	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0716-8217707
Xiu 2002	We telephoned the author in August 2006. The study was not a double-blind RCT. The author summarized medical records. Telephone number: +86 0452-2739726.
Xu 1999	The patients in the treatment group received the β-sodium aescinate, but the patients in the control group did not receive it.

Study	Reason for exclusion
Xu 2000a	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized medical records. Telephone number: +86 023-63632756.
Xu 2002a	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical records. Telephone number: +86 0574-83870243.
Xu 2002b	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0752-3385263.
Xu 2004	The patients in the treatment group received the chuan qiong qin injection, but the patients in the control group did not receive it.
Xu 2006	The patients in the control group received the prednisone, but the patients in the treatment group did not receive it.
Xu 2008a	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0825-6621105.
Xu 2008b	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0431-85595114
Xu 2009	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0776-2513120
Xue 2004b	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0951-4091488.
Xue 2006	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 13839288161
Xue 2007	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 13610076366
Yan 2008	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0743-6612369
Yang 2000	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 0571-82621086-2347.

Study	Reason for exclusion
Yang 2002a	The patients in the control group received the dan shen, but the patients in the treatment group did not receive it.
Yang 2002b	We telephoned the author in June 2011. The study was not a RCT, the author summarized the past medical data. Telephone number: +86 0396-2922028.
Yang 2004	The patients in the control group received the aspirin, but the patients in the treatment group did not receive it.
Yang 2005	We telephoned the author in August 2006 in order to identify the randomisation procedure and other methodological issues, but the author refused further information. We couldn't determine whether it is an RCT. Telephone number: +86 0775-4200288
Yang 2006a	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the patients' wishes. Telephone number: +86 0351-2272164
Yang 2006b	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0762-3185586
Yang 2007	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Yang 2008	The secondary nephrotic syndrome patients were allocated in the study.
Yang 2010	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0370-2629955.
Yao 2010	The study did not exclude the secondary nephrotic syndrome.
Ye 1999	The patients in the control group received the persantin, but the patients in the treatment group did not receive it.
Ye 2002	We telephoned the author in August 2006 in order to identify the randomisation procedure and other methodological issues, but the author refused further information. We couldn't determine whether it is an RCT. Telephone number: +86 0576-6207776
Yi 2006	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0717-6486797.
Yin 2000	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized past medical data. Telephone number: +86 0530-5328667.
Yin 2009	We telephoned the author in June 2011.

Study	Reason for exclusion
	The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0539-5222878
Yu 2000	The patients in the treatment group did not receive the Huangqi.
Yu 2001	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 020-81048888.
Yu 2003	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized past medical data. Telephone number: +86 13660299035.
Yu 2005a	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0351-3365921.
Yu 2005b	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 029-87213310.
Yu 2005c	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0952-2013270.
Yu 2006	The patient in the treatment group did not receive the Huangqi.
Yu 2007	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Yu 2008	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Yu 2009	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0711-3222091
Yuan 2002	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0634-6279175.
Yuan 2006	The patients were allocated into two groups according to the medical order.
Yuan 2008a	The patients in the treatment group received the Huangqi and danshen injection, but the control group did not receive both. The intervention was not in accord with the criteria.
Yuan 2008b	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other.

Study	Reason for exclusion
	Telephone number: +86 0537-2253431
Yue 2006	The patients in the treatment group received the Ci Wu Jia, but the patients in the control group did not receive it.
Zang 2007	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Zeng 2008	We telephoned the author in June 2011. The study is a retrospective clinical analysis. The author summarized the past medical data. Telephone number: +86 0774-2036883
Zhang 1993	The study was not a RCT, there was no control group.
Zhang 1994	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0536-3272121
Zhang 1997	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. 0532-88555437
Zhang 1998	The intervention in the treatment group was not same.
Zhang 2001a	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 010-88276527
Zhang 2001b	The study is semi-randomised.
Zhang 2001c	The study did not use the random sequence.
Zhang 2002a	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 020-81081947.
Zhang 2002b	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 010-88276527
Zhang 2004	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 0558-2516001-2077
Zhang 2005a	We telephoned the author in August 2006. The study was not a double-blind RCT. Patients were divided into groups at the author's discretion. Telephone number: +86 0396-2959317
Zhang 2005b	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data.

Study	Reason for exclusion
	Telephone number: +86 0854-8261265.
Zhang 2006a	The patients in the treatment group received the bailing capsule, but the control group did not receive it.
Zhang 2006b	The patients in the treatment group did not receive the Huangqi.
Zhang 2007a	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Zhang 2007b	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Zhang 2007c	The inclusion criteria were in not accordance with the protocol.
Zhang 2007d	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Zhang 2007e	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the day of the patients came to the hospital, odd numbered days to one group and even numbered days to the other. Telephone number: +86 0393-4416620
Zhang 2008a	The study used the quasi-RCT.
Zhang 2008b	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.
Zhang 2008c	We telephoned the author in June 20116. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0759-2633663
Zhang 2008d	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the patients' opinion. Telephone number: +86 0516-83956312
Zhang 2008e	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0315-6612587
Zhang 2009a	The patients were allocated into two groups according to the medical order.
Zhang 2009b	The patients were allocated into two groups according to the medical order.
Zhang 2009c	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the day of the patients came to the hospital, odd numbered days to one group and even numbered days to the other. Telephone number: +86 13568150066
Zhang 2010a	The patients were allocated into the two groups according to the time sequence of seeing doctor.
Zhang 2010b	The patients in the treatment group did not receive the Huangqi. The intervention was not in accord with the criteria.

Study	Reason for exclusion
Zhang 2010c	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical records. Telephone number: +86 022-27285222
Zhang 2010d	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0758-7765408
Zhang 2010e	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the day of the patients came to the hospital, odd numbered days to one group and even numbered days to the other. Telephone number: +86 0530-8211111
Zhao 1999a	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized medical records. Telephone number: +86 0871-3211101.
Zhao 1999c	The inclusion criteria were not in accordance with the protocol.
Zhao 2001a	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the day of the patients came to the hospital, odd numbered days to one group and even numbered days to the other. Telephone number: +86 0536-8068883
Zhao 2001b	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0319-3286194.
Zhao 2001c	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized medical records. Telephone number: +86 0746-8413510.
Zhao 2010	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized medical records. Telephone number: +86 072-82433165.
Zhi 2010	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 010-68489948
Zhong 2002	We telephoned the author in August 2006. The study was not a double-blind RCT. The author summarized medical records. Telephone number: +86 0754-8258290.
Zhong 2006	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the pathogenetic condition. Telephone number: +86 0750-8860123
Zhong 2008	The patients in the treatment group did not receive the Huangqi.

Study	Reason for exclusion
Zhong 2009	The treatment group did not use the Huangqi.
Zhong 2011	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 15842672222
Zhou 2000	The control group did not receive the Danshen injection.
Zhou 2003	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0511-5345556.
Zhou 2004	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical record. Telephone number: +86 0518-83229682
Zhou 2006	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical record. Telephone number: +86 0790-6651018
Zhou 2007a	The intervention therapy was not equal in the two groups.
Zhou 2007b	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical record. Telephone number: +86 0739-8244825
Zhou 2008	The patients in the treatment group did not receive the Huangqi.
Zhou 2009a	The patients in the treatment group did not receive the Huangqi.
Zhou 2009c	We telephoned the author in June 2011. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 13396169118
Zhu 2001	The patients in the treatment group received the cordate houttuynia, but the control group did not receive it.
Zhu 2002	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the pathogenetic condition. Telephone number: +86 021-58670283
Zhu 2004	We telephoned the author in August 2006. The study was not a double-blind RCT. The author divided patients into groups according to the order the patients came to hospital, odd numbers were assigned to one group and even numbers into the other. Telephone number: +86 0511-5345556
Zhu 2006	The treatment group did not use the Huangqi.

Study	Reason for exclusion
Zhu 2010a	The treatment group used the Huangqi and shuxuetong injection. But the control group did not use the shuxuetong injection.
Zhu 2010b	We telephoned the author in June 2011. The study was not a double-blind RCT. The author summarized the past medical data. Telephone number: +86 0394-8279742

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

Li 2007f

Methods	• Randomisation mentioned, but not described in detail
Participants	• Country: China • Primary nephrotic syndrome patients (urinary protein > 3.5 g/24 h; plasma albumin < 30 g/dL; oedema and hypercholesterolaemia) • Number: treatment group (30); control group (28) • Age range: treatment group (5 to 42 years); control group (4 to 44 years) • Sex (M/F): treatment group (19/11); control group (17/11) • Exclusions: secondary nephrotic syndrome
Interventions	Treatment group • Simiao soup once a day • Drugs the control group received Control group • Prednisone • initial dose 1.0mg/kg/d. Dose was then reduced gradually 10% after 8 weeks. • When prednisone was ineffective or partially effective, CTX combined with methylprednisolone was used
Outcomes	• Plasma albumin • 24 hours urine protein • Blood cholesterol • Blood triglyceride • Effective rate
Notes	1. Baseline declining kidney function: NS 2. Remission: NS 3. Pathology: NS 4. Relapse: NS 5. Time to relapse: NS 6. Mean follow-up: 6 months 7. Dosage: described in detail 8. Prepare method: NS 9. Source of funding: none

Liu 1998

Methods	• Randomisation mentioned, but not described in detail
Participants	• Country: China • Primary nephrotic syndrome patients (urinary protein > 3.5g/24 h; plasma albumin < 30 g/dL; oedema and hypercholesterolaemia) • Number: treatment group (30); control group (28) • Age range: 14 to 67 years • Sex (M/F): 34/26 • Exclusions: secondary nephrotic syndrome

Interventions	Treatment group
	• Huangqi intravenous injection
	  ○ Dose: once a day
	• Drugs the control group received
	Control group
	• Prednisone
	  ○ Initial dose 1.0mg/kg/d
	• Tripterygium glycosides
	• Dipyridamole
	• Heparin

Outcomes	• Effective rate
Notes	• Baseline declining kidney function: NS • Remission: NS • Pathology: NS • Relapse: NS • Time to relapse: NS • Mean follow-up: NS • Dosage: described in detail • Prepare method: NS • Source of funding: none

Ma 2001

Methods	• Randomisation mentioned, but not described in detail
Participants	• Country: China • Primary nephrotic syndrome (urinary protein > 3.5g/24 h; plasma albumin < 30 g/dL; oedema and hypercholesterolaemia) • Number: treatment group (10); control group (10) • Age range: NS • Sex (M/F): NS • Exclusions: secondary nephrotic syndrome
Interventions	Treatment group • Huangqi with Yimucao decoction ○ Dose: twice a day • Drugs the control group received

Ma 2001 *(Continued)*

	Control group • Prednisone
Outcomes	• Plasma albumin • 24 hours urine protein • Blood cholesterol • oedema
Notes	• Baseline declining kidney function: NS • Remission: NS • Pathology: NS • Relapse: NS • Time to relapse: NS • Mean follow-up: NS • Dosage: described in detail • Prepare method: NS • Source of funding: none

Su 2000a

Methods	• Randomisation mentioned, but not described in detail
Participants	• Country: China • Primary nephrotic syndrome patients (24 h proteinuria > 0.1 g/kg; plasma albumin < 3 g%; hypercholesterolaemia >5.2mmol/L; oedema) • Number: treatment group (30); control group (30) • Age range: treatment group (3 to 14 years); control group (3.2 to 14 years) • Sex (M/F): treatment group (20/10); control group (21/9)
Interventions	Treatment group • Huangqi formulation ○ Dose: 3 to 5 times/d • Drugs the control group received Control group • Prednisone
Outcomes	• Effective rate • Relapse rate • Adverse effect
Notes	• Baseline declining kidney function: NS • Remission: NS • Pathology: NS • Relapse: described in detail • Time to relapse: NS • Mean follow-up: NS • Dosage: NS • Prepare method: NS • Source of funding: none

Tang 2005

Methods	• Randomisation mentioned, but not described in detail
Participants	• Country: China • Primary nephrotic syndrome patients (24 h proteinuria > 0.1g/kg; plasma albumin < 3 g%; hypercholesterolaemia > 5.2 mmol/L; oedema) • Number: treatment group (35); control group (41) • Age range: treatment group (2.8 to 13.8 years); control group (2.9 to 14.0 years) • Sex (M/F): treatment group (27/8); control group (30/11)

Interventions	Treatment group
	• Huangqi granules
	  ○ Dose: twice a day
	• Drugs the control group received
	Control group
	• Prednisone
	  ○ Dose: 2 mg/kg/d

Outcomes	• Immunoglobulin • Relapse rate • T cell
Notes	• Baseline declining kidney function: NS • Remission: NS • Pathology: NS • Relapse: described in detail • Time to relapse: described in detail • Mean follow-up: 12-24 months • Dosage: described in detail • Prepare method: NS • Source of funding: none

Wan 2009

Methods	• Randomisation mentioned, but not described in detail
Participants	• Country: China • Primary nephrotic syndrome patients (urinary protein > 3.5g /24 h; plasma albumin < 30 g/dL; oedema and hypercholesterolaemia) • Number: treatment group (50); control group (46) • Age range: 130 75 years • Sex (M/F): NS • Exclusions: secondary nephrotic syndrome
Interventions	Treatment group • Huangqi and Danggui ○ Dose: twice a day for 8 weeks • Drugs the control group received

Wan 2009 *(Continued)*

	Control group • Prednisone ○ Dose: 1 mg/kg/d
Outcomes	• Plasma albumin • 24 hours urine protein • Blood cholesterol • Blood triglyceride • Effective rate
Notes	• Baseline declining kidney function: NS • Remission: NS • Pathology: described in detail • Relapse: NS • Time to relapse: NS • Mean follow-up: NS • Dosage: described in detail • Prepare method: NS • Source of funding: none

Wang 2000b

Methods	• Randomisation mentioned, but not described in detail
Participants	• Country: China • Primary nephrotic syndrome patients (urinary protein > 3.5 g/24 h; plasma albumin < 30 g/dL; oedema and hypercholesterolaemia) • Number: treatment group (30); control group (28) • Average age: 38.3 years • Sex (M/F): 32/26 • Exclusions: secondary nephrotic syndrome
Interventions	Treatment group • Huangqi intravenous injection • Drugs the control group received Control group • Prednisone
Outcomes	• Plasma albumin • 24 urine albumin
Notes	• Baseline declining kidney function: NS • Remission: NS • Pathology: NS • Relapse: NS • Time to relapse: NS • Mean follow-up: NS • Dosage: described in detail • Prepare method: NS

Wang 2000b *(Continued)*

	• Source of funding: none

Wu 1998a

Methods	• Randomisation mentioned, but not described in detail
Participants	• Country: China • Primary nephrotic syndrome patients (urinary protein > 3.5 g/24 h; plasma albumin < 30 g/dL; oedema and hypercholesterolaemia) • Number: treatment group (60); control group (60) • Average age: treatment group (41.2 years); control group (44.1 years) • Sex (M/F): treatment group (32/28); control group (36/24) • Exclusions: secondary nephrotic syndrome

Interventions	Treatment group
	• Huangqi intravenous injection
	• Drugs the control group received
	Control group
	• Prednisone
	  ○ Dose: 60 mg/d
	• Dipyridamole
	  ○ Dose:150 mg/d
	• Benazepril
	  ○ Dose: 5 mg/d

Outcomes	• Plasma β2-microalbumin • Urine β2-microalbumin • Plasma albumin • Urine γ-GT • Urine Gal • Urine NAG • 24 urine albumin
Notes	• Baseline declining kidney function: NS • Remission: NS • Pathology: NS • Relapse: NS • Time to relapse: NS • Mean follow-up: NS • Dosage: described in detail • Prepare method: NS • Source of funding: none

Xue 2004a

Methods	• Randomisation mentioned, but not described in detail
Participants	• Country: China

Xue 2004a *(Continued)*

	• Primary nephrotic syndrome patients (urinary protein > 3.5 g/24 h; plasma albumin < 30 g/dL; oedema and hypercholesterolaemia) • Number: treatment group (25); control group (25) • Age range: 16 to 56 years • Sex (M/F): 26/24 • Exclusions: secondary nephrotic syndrome

Interventions	Treatment group
	• Huangqi with Danggui mixture
	• Drugs the control group received
	Control group
	• Prednisone
	  ○ Dose: 1 mg/kg/d
	• Dipyridamole
	  ○ Dose: 300 mg/d
	• 5 patients used CTX (100 mg/d)

Outcomes	• Plasma albumin • Plasma cholesterol • 24 urine albumin
Notes	• Baseline declining kidney function: NS • Remission: NS • Pathology: described in detail • Relapse: NS • Time to relapse: NS • Mean follow-up: 12 weeks • Dosage: described in detail • Prepare method: NS • Source of funding: none

Zhang 2010f

Methods	• Randomisation mentioned, but not described in detail
Participants	• Country: China • Primary nephrotic syndrome patients (urinary protein > 3.5 g/24 h, plasma albumin < 30 g/dL, oedema and hypercholesterolaemia) • Number: treatment group (55); control group (41) • Age range: treatment group (3-15 years); control group (4-16 years) • Sex (M/F): treatment group (31/24); control group (22/19) • Exclusions: secondary nephrotic syndrome
Interventions	Treatment group • Huangqi intravenous injection ○ Dose: 1-2 mL/kg/d • Drugs the control group received Control group • Prednisone

Zhang 2010f *(Continued)*

	○ Dose: 1.5-2.0 mg/kg/d • When prednisone was inefficacy or partial efficacy, CTX (3-4 mg/kg) was used
Outcomes	• Plasma albumin • Plasma protein • Plasma cholesterol • Plasma triglyceride • Effective rate • Time of oedema remission
Notes	• Baseline declining kidney function: NS • Remission: NS • Pathology: NS • Relapse: NS • Time to relapse: NS • Mean follow-up: NS • Dosage: NS • Prepare method: NS • Source of funding: none

Zhao 1999b

Methods	• Randomisation mentioned, but not described in detail.
Participants	• Country: China • Primary nephrotic syndrome (urinary protein > 3.5 g/24 h, plasma albumin < 30 g/dL, oedema and hypercholesterolaemia) • Number: treatment group (20); control group (20) • Age range: treatment group (15-50 years); control group (16-48 years) • Sex (M/F): treatment group (12/8); control group (13/7) • Exclusions: secondary nephrotic syndrome
Interventions	Treatment group • Huangqi intravenous injection ○ Dose: 20 mL • Drugs the control group received Control group • Prednisone ○ Dose: 1.0 mg/kg/d • When prednisone was inefficacy or partial efficacy, CTX 0.2 g was used
Outcomes	• Plasma albumin • Plasma protein • Effective rate
Notes	• Baseline declining kidney function: NS • Remission: NS • Pathology: NS • Relapse: NS • Time to relapse: NS

Zhao 1999b *(Continued)*

- Mean follow-up: NS
- Dosage: NS
- Prepare method: NS
- Source of funding: none

Zhao 2003

Methods	• Randomisation mentioned, but not described in detail.
Participants	• Country: China • Primary nephrotic syndrome (urinary protein > 3.5 g/24 h, plasma albumin < 30 g/dL, oedema and hypercholesterolaemia) • Number: treatment group (30); control group (30) • Age range: 14-76 years • Sex (M/F): 38/22 • Exclusions: secondary nephrotic syndrome

Interventions	Treatment group
	• Huangqi with Danggui mixture
	  ○ Dose 80-100 mL
	• Drugs the control group received
	Control group
	• Prednisone
	  ○ Dose: 1.0 mg/kg/d

Outcomes	• Plasma cholesterol • Plasma protein • 24 h urine protein
Notes	• Baseline declining kidney function: NS • Remission: NS • Pathology: NS • Relapse: NS • Time to relapse: NS • Mean follow-up: NS • Dosage: NS • Prepare method: NS • Source of funding: none

Zhou 2009b

Methods	• Randomisation mentioned, but not described in detail.
Participants	• Country: China • Primary nephrotic syndrome (urinary protein > 3.5 g/24 h, plasma albumin < 30 g/dL, oedema and hypercholesterolaemia) • Number: treatment group (42); control group (39) • Age range: treatment group (16-58 years); control group (19-61 years)

Zhou 2009b *(Continued)*

	• Sex (M/F): treatment group (24/18); control group (20/19) • Exclusions: secondary nephrotic syndrome
Interventions	Treatment group • Huangqi intravenous injection ○ Dose: 60 mL • Drugs the control group received Control group • Prednisone • Dose: 1 mg/kg/d
Outcomes	• Blood urea • Blood creatinine • Plasma protein • Plasma albumin • 24 h urine protein
Notes	• Baseline declining kidney function: NS • Remission: NS • Pathology: NS • Relapse: NS • Time to relapse: NS • Mean follow-up: NS • Dosage: NS • Prepare method: NS • Source of funding: none

Zou 2008

Methods	• Randomisation mentioned, but not described in detail.
Participants	• Country: China • Primary nephrotic syndrome (urinary protein > 3.5 g/24 h, plasma albumin < 30 g/dL, oedema and hypercholesterolaemia) • Number: 55 • Age range: 25-68 years • Sex (M/F): 26/29 • Exclusions: secondary nephrotic syndrome
Interventions	Treatment group • Chinese herbal mixture (Huangqi, etc) • Drugs the control group received Control group • Prednisone ○ Dose: 1 mg/kg/d
Outcomes	• Blood urea • Blood creatinine

Zou 2008 *(Continued)*	• Plasma protein • Plasma albumin • 24 h urine protein
Notes	• Baseline declining kidney function: NS • Remission: NS • Pathology: NS • Relapse: NS • Time to relapse: NS • Mean follow-up: NS • Dosage: NS • Prepare method: NS • Source of funding: none

CTX - cyclophosphamide

DATA AND ANALYSES

Comparison 1. Huangqi and Huangqi type formulations versus control drugs

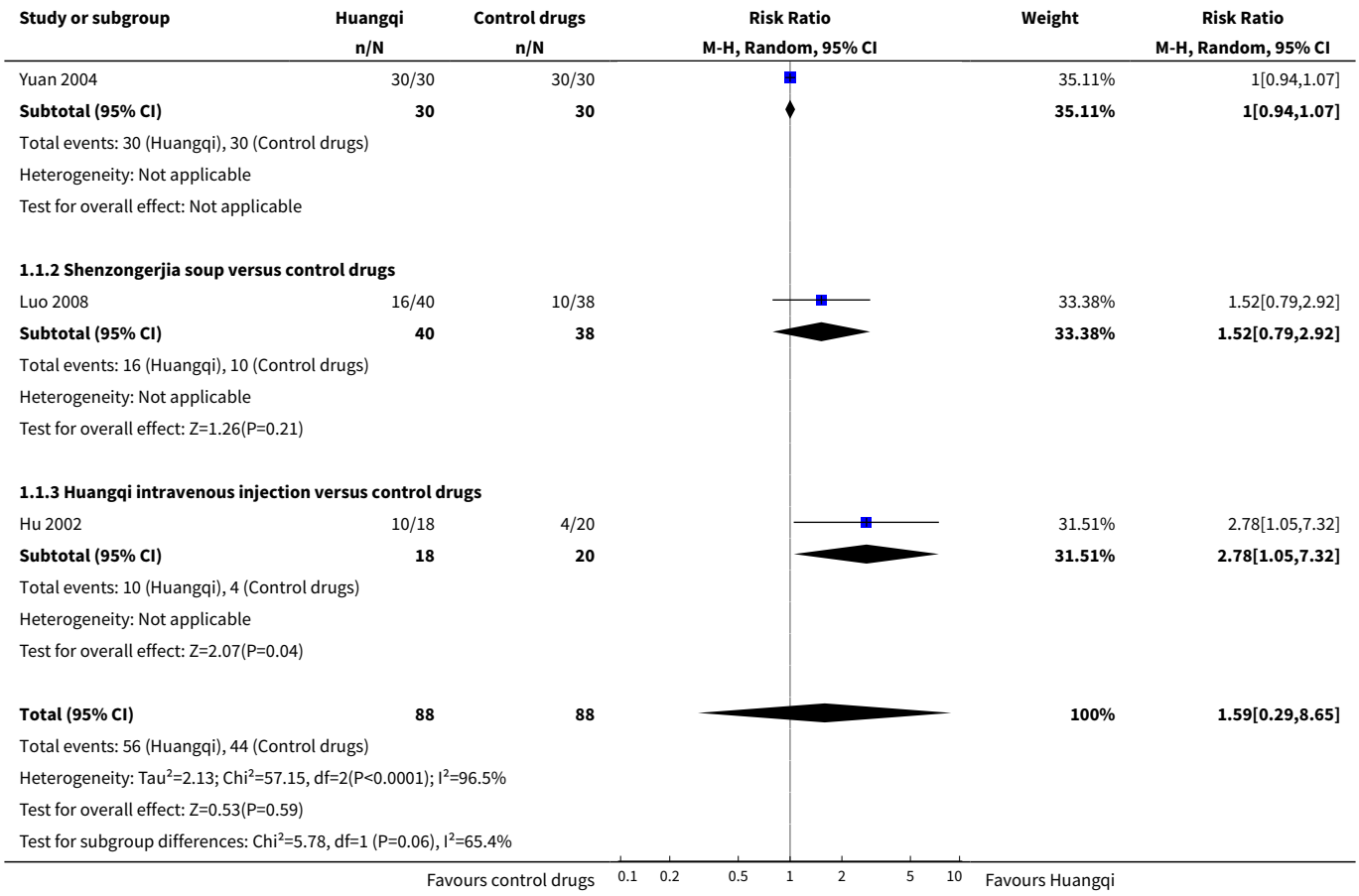
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Complete remission	3	176	Risk Ratio (M-H, Random, 95% CI)	1.59 [0.29, 8.65]
1.1 Huangqi with Hongzao mixture versus control drugs	1	60	Risk Ratio (M-H, Random, 95% CI)	1.0 [0.94, 1.07]
1.2 Shenzongerjia soup versus control drugs	1	78	Risk Ratio (M-H, Random, 95% CI)	1.52 [0.79, 2.92]
1.3 Huangqi intravenous injection versus control drugs	1	38	Risk Ratio (M-H, Random, 95% CI)	2.78 [1.05, 7.32]
2 Partial remission	2	116	Risk Ratio (M-H, Random, 95% CI)	1.22 [0.57, 2.58]
2.1 Huangqi intravenous injection versus control drugs	1	38	Risk Ratio (M-H, Random, 95% CI)	1.11 [0.38, 3.22]
2.2 Shenzongerjia soup versus control drugs	1	78	Risk Ratio (M-H, Random, 95% CI)	1.33 [0.46, 3.83]
3 Urine albumin excretion	3	176	Mean Difference (IV, Random, 95% CI)	-0.57 [-1.04, -0.10]
3.1 Shenzongerjia soup versus control drugs	1	78	Mean Difference (IV, Random, 95% CI)	-0.98 [-1.37, -0.59]
3.2 Huangqi oral solution versus control drugs	1	30	Mean Difference (IV, Random, 95% CI)	-0.59 [-0.98, -0.20]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.3 Shenkanglin decoction versus control drugs	1	68	Mean Difference (IV, Random, 95% CI)	-0.21 [-0.40, -0.02]
4 Plasma albumin	5	295	Mean Difference (IV, Random, 95% CI)	6.41 [4.24, 8.59]
4.1 Huangqi intravenous injection versus control drugs	2	119	Mean Difference (IV, Random, 95% CI)	8.28 [6.17, 10.39]
4.2 Huangqi oral solution versus control drugs	1	30	Mean Difference (IV, Random, 95% CI)	3.26 [1.02, 5.50]
4.3 Shenzongerjia soup versus control drugs	1	78	Mean Difference (IV, Random, 95% CI)	5.86 [3.04, 8.68]
4.4 Shenkanglin decoction versus control drugs	1	68	Mean Difference (IV, Random, 95% CI)	7.27 [4.21, 10.33]
5 Triglycerides	4	217	Mean Difference (IV, Random, 95% CI)	-0.33 [-0.63, -0.03]
5.1 Huangqi intravenous injection versus control drugs	2	119	Mean Difference (IV, Random, 95% CI)	-0.43 [-1.20, 0.34]
5.2 Huangqi with Danggui mixture versus control drugs	1	30	Mean Difference (IV, Random, 95% CI)	-0.11 [-0.49, 0.27]
5.3 Shenkanglin decoction versus control drugs	1	68	Mean Difference (IV, Random, 95% CI)	-0.52 [-0.89, -0.15]
6 Cholesterol	4	217	Mean Difference (IV, Random, 95% CI)	-1.70 [-2.26, -1.13]
6.1 Huangqi intravenous injection versus control drugs	2	119	Mean Difference (IV, Random, 95% CI)	-2.01 [-2.60, -1.43]
6.2 Huangqi with Danggui mixture versus control drugs	1	30	Mean Difference (IV, Random, 95% CI)	-0.85 [-1.70, -0.00]
6.3 Shenkanglin decoction versus control drugs	1	68	Mean Difference (IV, Random, 95% CI)	-1.91 [-2.82, 1.00]
7 Time to oedema remission	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
7.1 Huangqi oral solution versus control drugs	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
8 No improvement at 3 months	3	176	Risk Ratio (M-H, Random, 95% CI)	0.41 [0.20, 0.84]
8.1 Huangqi intravenous injection versus control drugs	1	38	Risk Ratio (M-H, Random, 95% CI)	0.22 [0.03, 1.73]

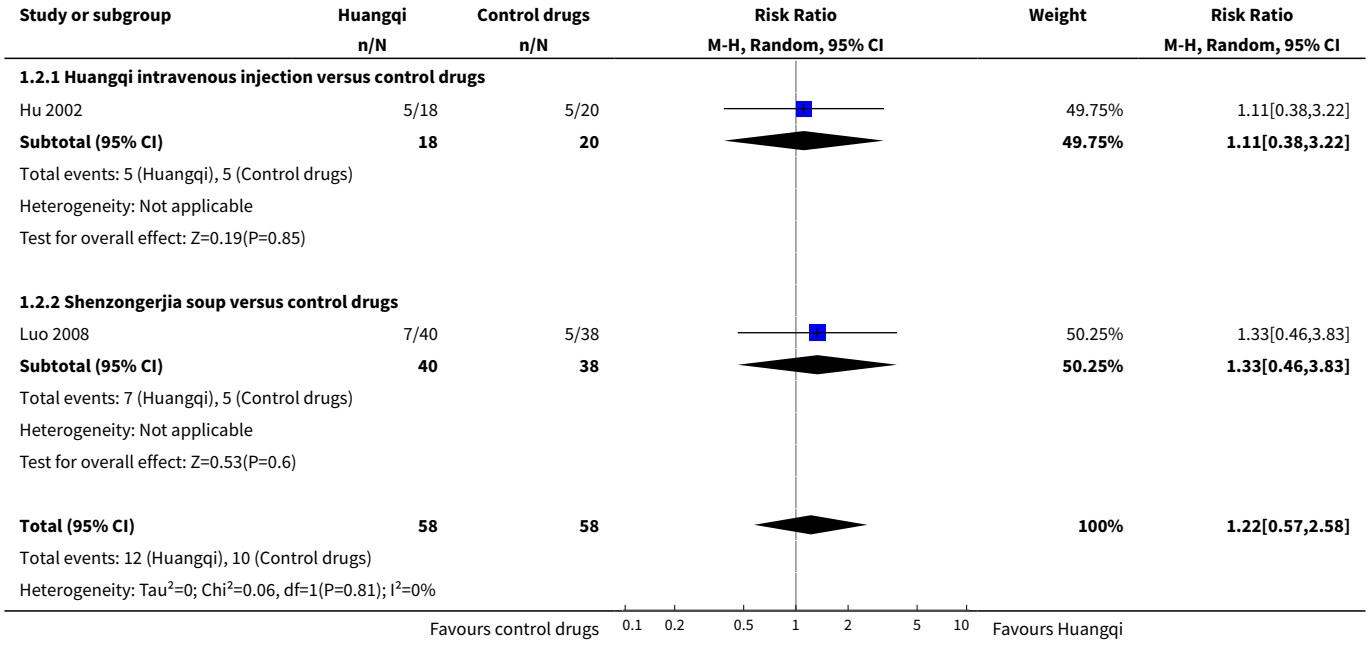
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.2 Huangqi with Hongzao mixture versus control drugs	1	60	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.3 Shenzongerjia soup versus control drugs	1	78	Risk Ratio (M-H, Random, 95% CI)	0.44 [0.20, 0.97]
9 Relapse	4		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
9.1 Huangqi granules versus control drugs (3 months)	1	46	Risk Ratio (M-H, Random, 95% CI)	0.20 [0.07, 0.59]
9.2 Huangqi with Hongzao mixture versus control drugs (12 months)	1	60	Risk Ratio (M-H, Random, 95% CI)	0.75 [0.18, 3.07]
9.3 Shenzongerjia soup versus control drugs (12 months)	1	78	Risk Ratio (M-H, Random, 95% CI)	0.43 [0.17, 1.13]
9.4 Huangqi with Hongzao mixture versus control drugs (24 months)	1	60	Risk Ratio (M-H, Random, 95% CI)	0.08 [0.00, 1.31]
9.5 Ciwujia with Huangqi mixture versus control drugs (36 months)	1	30	Risk Ratio (M-H, Random, 95% CI)	0.36 [0.15, 0.89]
10 Complications	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
10.1 Infection	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11 Adverse reactions	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
11.1 Cushing's syndrome	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.2 Steroid withdrawal syndrome	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.3 Respiratory tract infection	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
11.4 Upper gastrointestinal haemorrhage	1		Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]

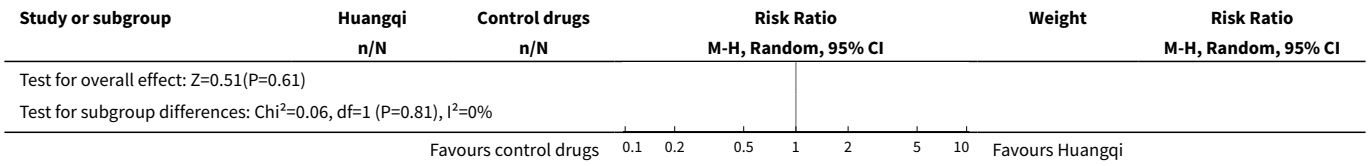
Analysis 1.1. Comparison 1 Huangqi and Huangqi type formulations versus control drugs, Outcome 1 Complete remission.

Study or subgroup	Huangqi n/N	Control drugs n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 Huangqi with Hongzao mixture versus control drugs					

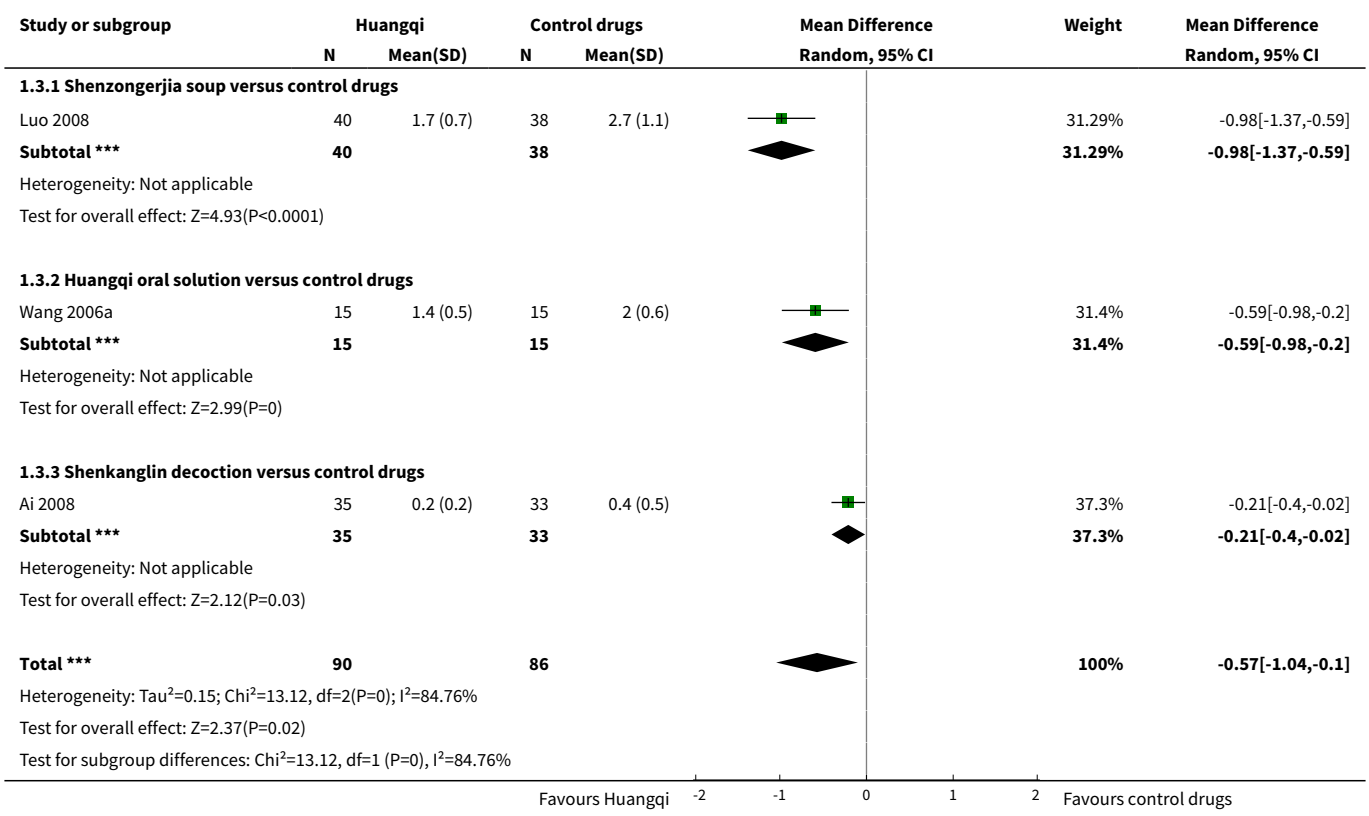


Analysis 1.2. Comparison 1 Huangqi and Huangqi type formulations versus control drugs, Outcome 2 Partial remission.

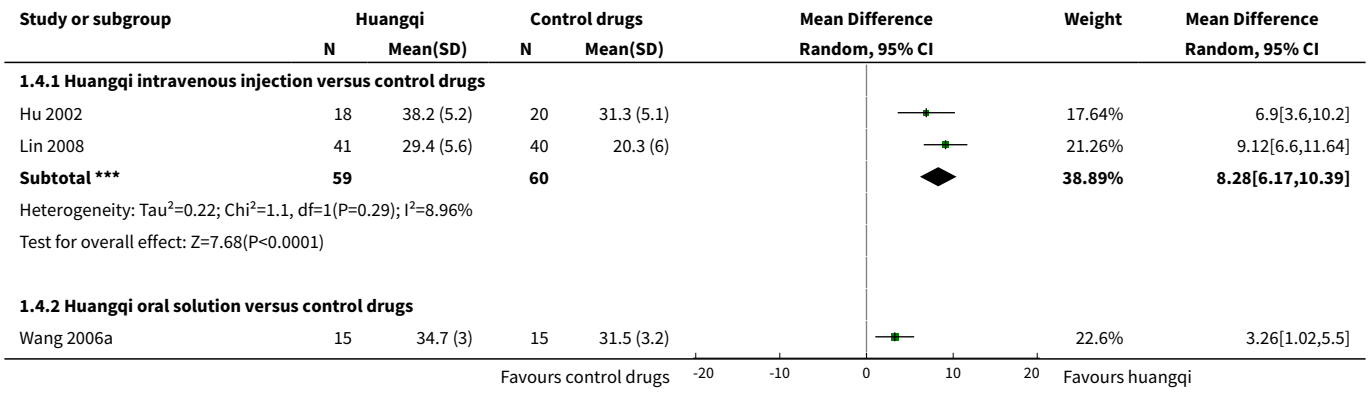


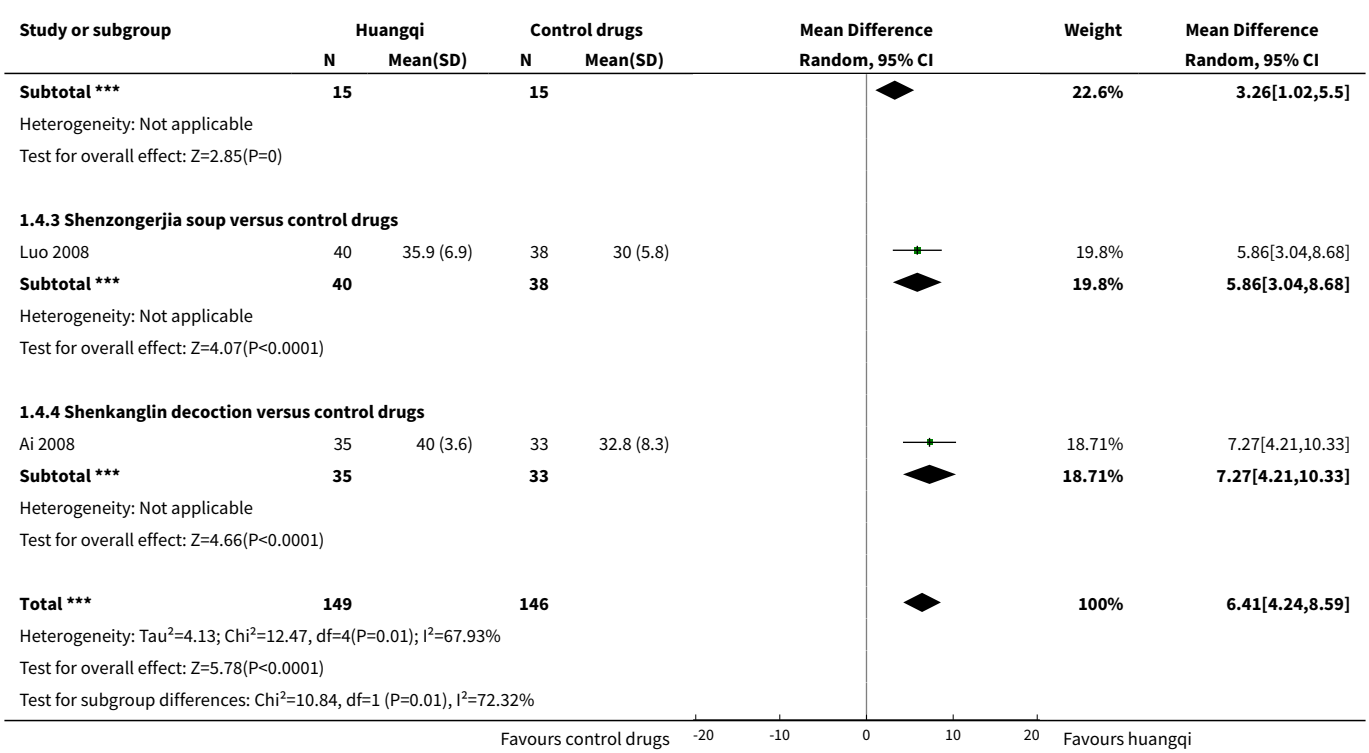


Analysis 1.3. Comparison 1 Huangqi and Huangqi type formulations versus control drugs, Outcome 3 Urine albumin excretion.

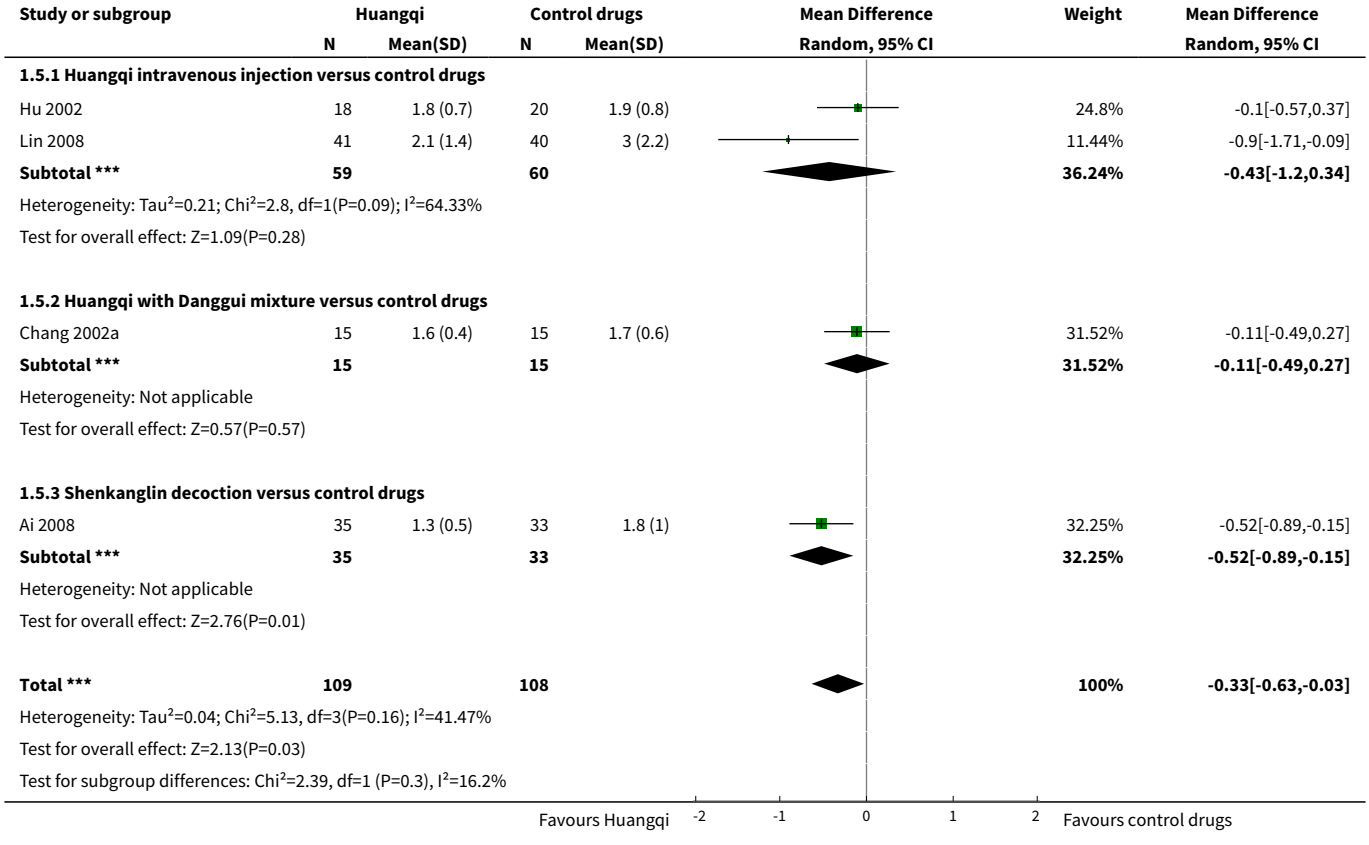


Analysis 1.4. Comparison 1 Huangqi and Huangqi type formulations versus control drugs, Outcome 4 Plasma albumin.

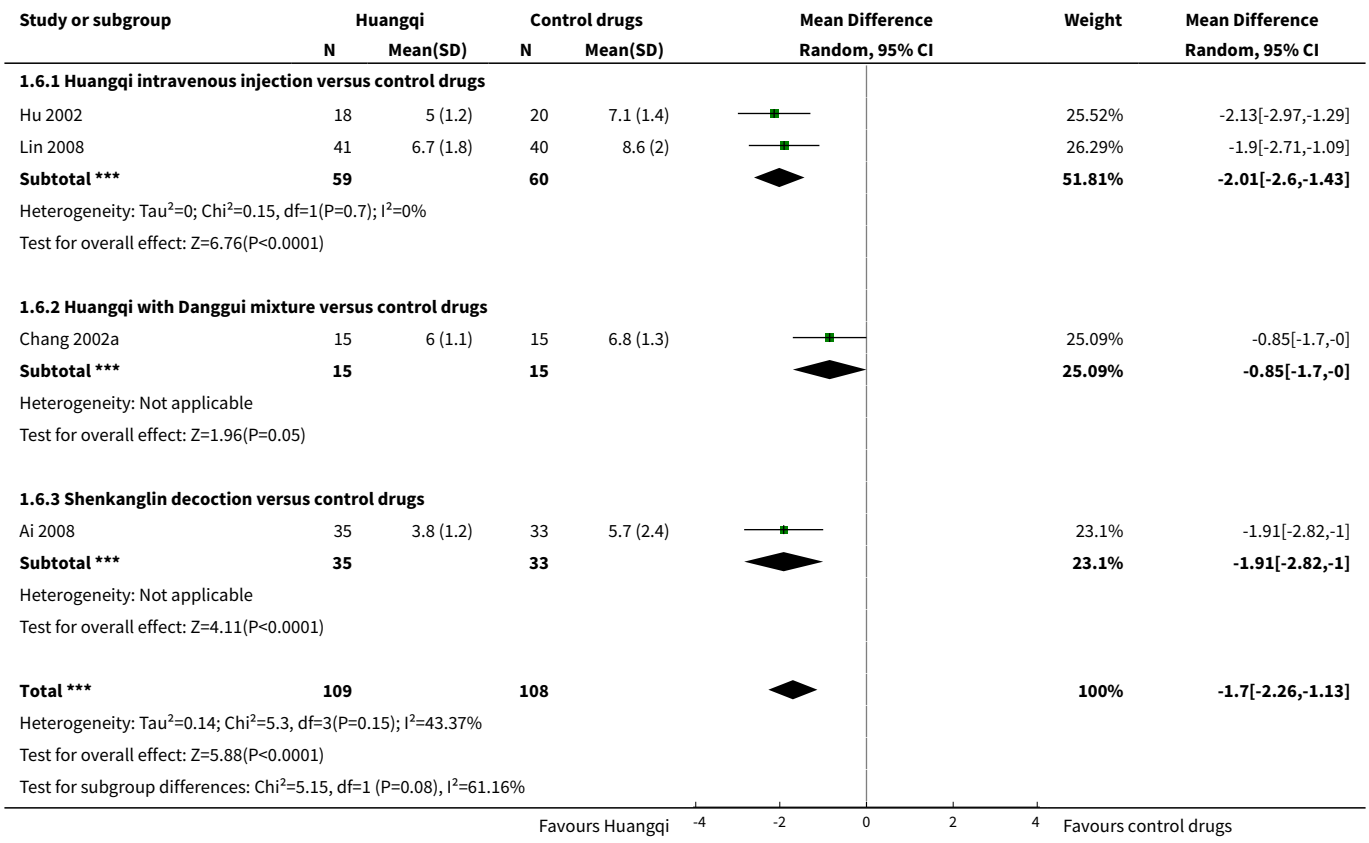




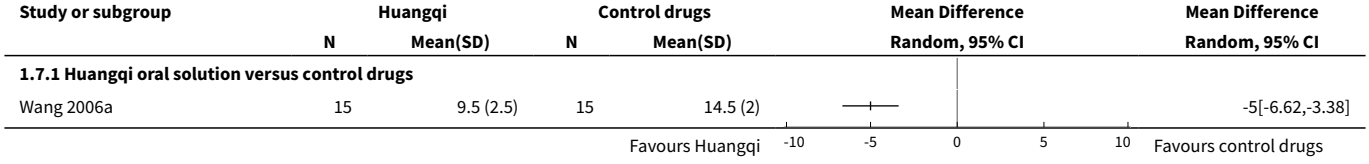
Analysis 1.5. Comparison 1 Huangqi and Huangqi type formulations versus control drugs, Outcome 5 Triglycerides.



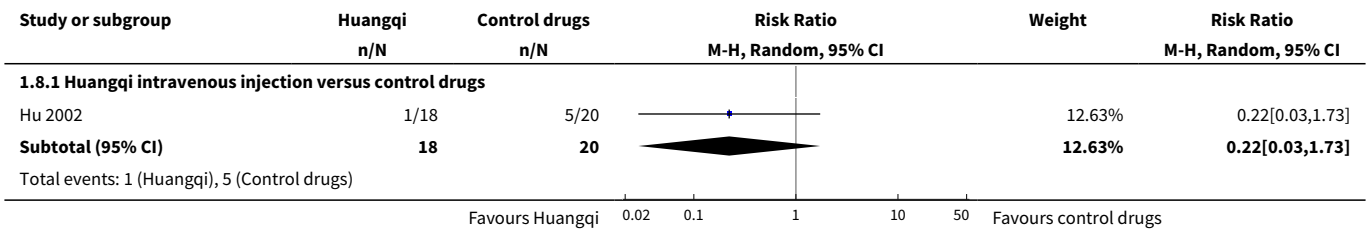
Analysis 1.6. Comparison 1 Huangqi and Huangqi type formulations versus control drugs, Outcome 6 Cholesterol.

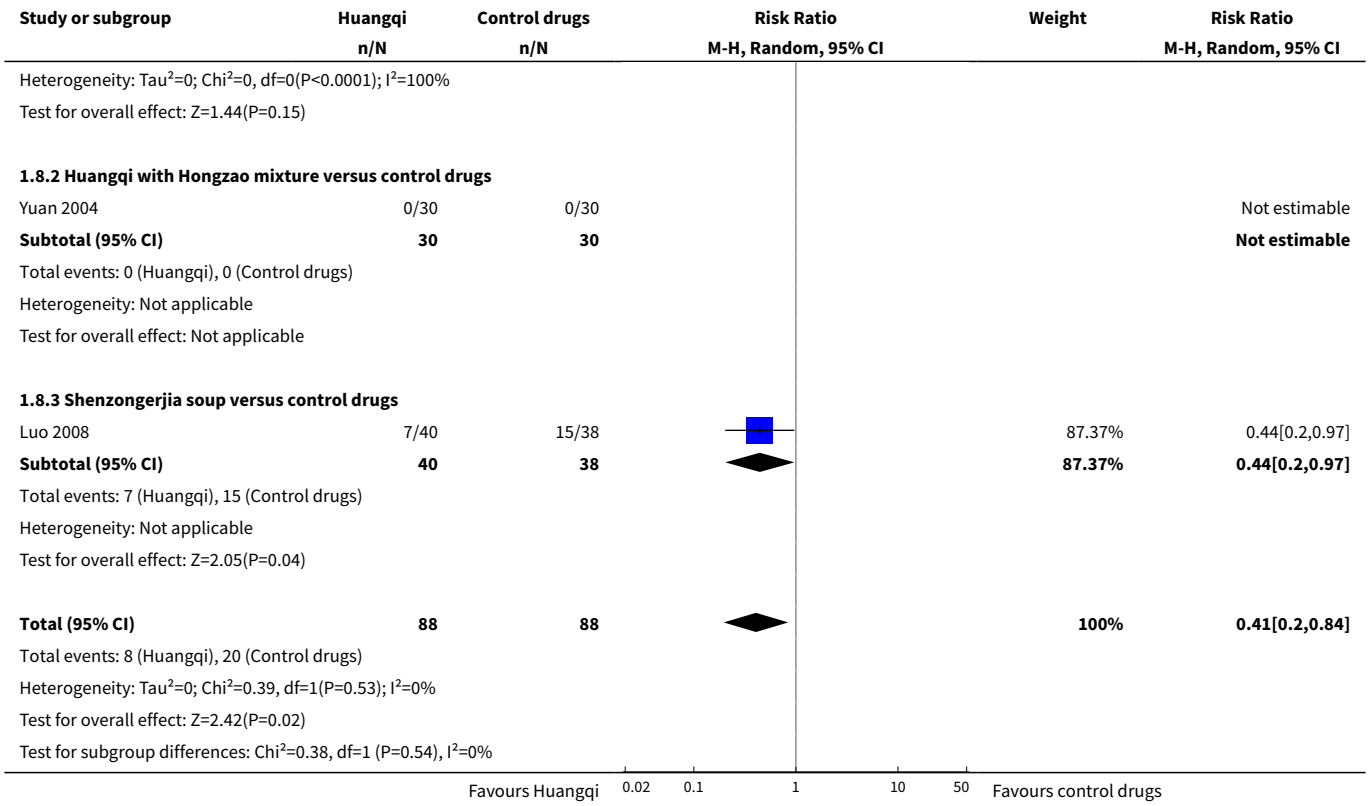


Analysis 1.7. Comparison 1 Huangqi and Huangqi type formulations versus control drugs, Outcome 7 Time to oedema remission.

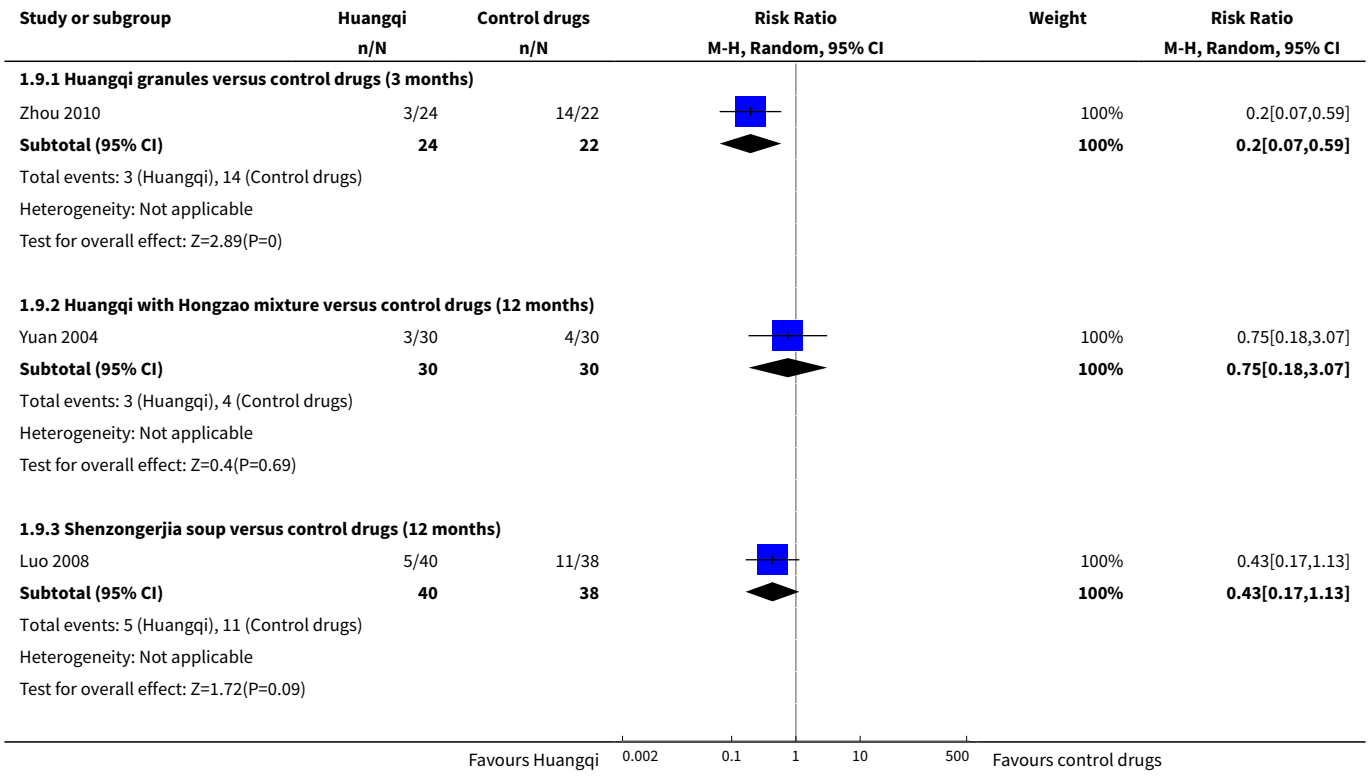


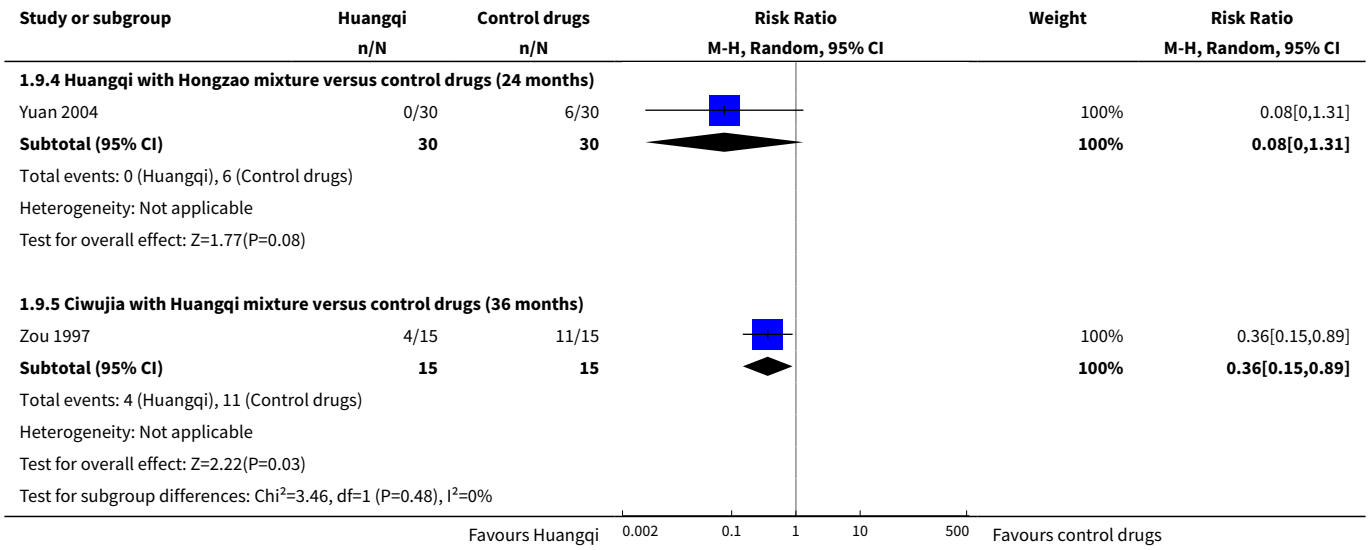
Analysis 1.8. Comparison 1 Huangqi and Huangqi type formulations versus control drugs, Outcome 8 No improvement at 3 months.



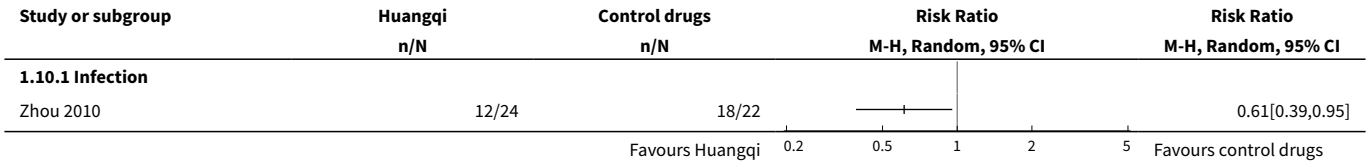


Analysis 1.9. Comparison 1 Huangqi and Huangqi type formulations versus control drugs, Outcome 9 Relapse.

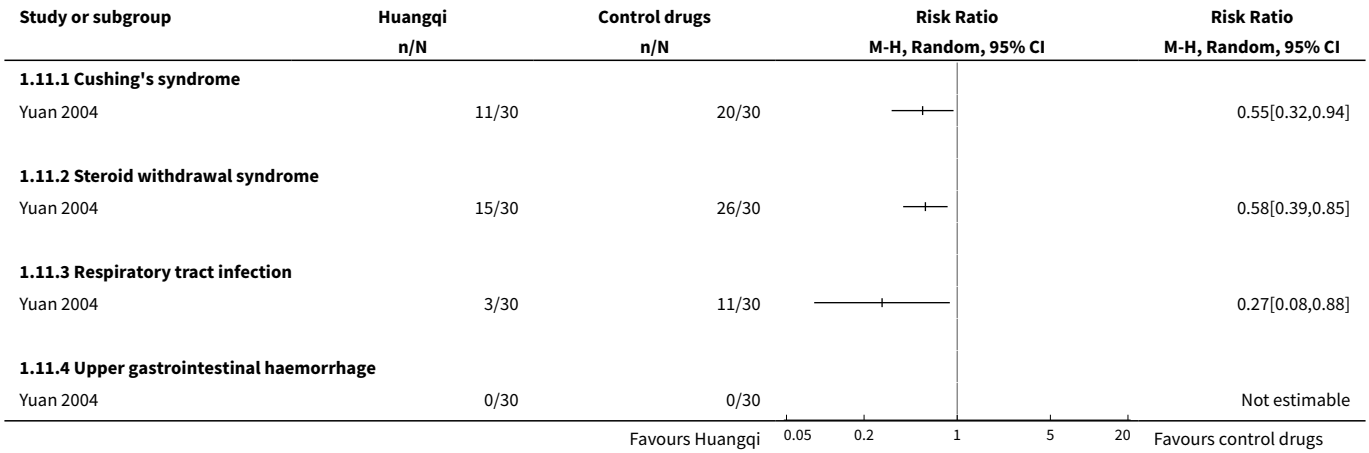




Analysis 1.10. Comparison 1 Huangqi and Huangqi type formulations versus control drugs, Outcome 10 Complications.



Analysis 1.11. Comparison 1 Huangqi and Huangqi type formulations versus control drugs, Outcome 11 Adverse reactions.



ADDITIONAL TABLES

Table 1. Preparation and composition of the herbal medicines in the included studies

Study ID	Herbs (composition)	Preparation
Chang 2002a	Huangqi with Danggui mixture: Huangqi and Danggui	1. 1 kg Huangqi and 1 kg Danggui soaked in 5 L water for 30 min 2. Decocted for 45 min to get filtrate 3. Added 3 L water to the residue and decocted for 45 min 4. Mixed the 2 filtrates and decocted to 2 L
Hu 2002	Huangqi intravenous injection: Huangqi	Produced by Chengdu Didao Jiuhong pharmaceutical factory
Yuan 2004	Huangqi with Hongzao mixture: Huangqi and Hongzao	Not described in detail
Wang 2006a	Huangqi oral solution: Huangqi	Produced by Jiangshu Yangzi Jiang pharmaceutical factory
Zhou 2010	Huangqi granules: Huangqi	Produced by Sichuan Baili pharmaceutical factory
Luo 2008	Shenzongerjia soup: Huangqi, Taizishen, Fulin, fried Baishu, Shudi, Guiban, Biejia, Danshen, Chuanqiong, Fangfeng, Chantui, Jiangchan, Dilong, Yimucao, Bai maogeng	Not described in detail
Ai 2008	Shenkanglin decoction: Huangqi, Shendi, Shanyu, Huaishan, Zexie, Fulin, Taizishen, Zhimu, Danshen, Shanlizhi, Xiuhuazhen	Not described in detail
Lin 2008	Huangqi intravenous injection: Huangqi	Produced by Chengdu Didao Jiuhong pharmaceutical factory
Zou 1997	Ci Wu Jia with Huangqi mixture: Ci Wu Jia and Huangqi	Not described in detail

APPENDICES

Appendix 1. Electronic search strategies

Database	Search terms
CENTRAL	#1. MeSH descriptor Nephrotic Syndrome explode all trees
	#2. MeSH descriptor Nephrosis, Lipoid explode all trees
	#3. MeSH descriptor Glomerulonephritis, Membranous explode all trees
	#4. MeSH descriptor Glomerulosclerosis, Focal explode all trees
	#5. MeSH descriptor Glomerulonephritis, Membranoproliferative explode all trees
	#6. minimal change disease
	#7. (MCD or MPGN or FSGS)

(Continued)

	#8. nephrotic syndrome
	#9. lipoid nephrosis
	#10. membrano* and glomerul*
	#11. focal near glomerul*
	#12. minimal change glomerul*
	#13. (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12)
	#14. MeSH descriptor Huangqi Plant explode all trees
	#15. MeSH descriptor Fabaceae explode all trees
	#16. MeSH descriptor Drugs, Chinese Herbal explode all trees
	#17. MeSH descriptor Phytotherapy explode all trees
	#18. MeSH descriptor Plants, Medicinal explode all trees
	#19. MeSH descriptor Plant Roots explode all trees
	#20. MeSH descriptor Plant Extracts explode all trees
	#21. astragal*
	#22. hedysarum polybotrys
	#23. huangqi or (huang next qi)
	#24. milkvetch or (milk next vetch)
	#25. (#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24)
	#26. (#13 AND #25)
MEDLINE	1. Nephrotic Syndrome/
	2. Nephrosis, Lipoid/
	3. Glomerulonephritis, Membranous/
	4. Glomerulosclerosis, Focal/
	5. Glomerulonephritis, Membranoproliferative/
	6. minimal change disease.tw.
	7. (MCD or MPGN or FSGS).tw.
	8. nephrotic syndrome$.tw.
	9. lipoid nephrosis.tw.
	10. membrano$ glomerul$.tw.
	11. (focal adj2 glomerul$).tw.
	12. minimal change glomerul$.tw.
	13. or/1-12
	14. exp Huangqi Plant/

(Continued)

	15. Fabaceae/
	16. Drugs, Chinese Herbal/
	17. Phytotherapy/
	18. Plants, Medicinal/
	19. Plant Roots/
	20. Plant Extracts/
	21. astragal$.tw.
	22. hedysarum polybotrys.tw.
	23. (huangqi or huang qi).tw.
	24. (milk vetch or milkvetch).tw.
	25. or/14-24
	26. 13 and 25
EMBASE	1. Nephrotic Syndrome/
	2. Lipoid Nephrosis/
	3. Membranous Glomerulonephritis/
	4. Minimal Change Glomerulonephritis/
	5. Membranoproliferative Glomerulonephritis/
	6. Focal Glomerulonephritis/
	7. minimal change disease.tw.
	8. (MCD or MPGN or FSGS).tw.
	9. nephrotic syndrome$.tw.
	10. lipoid nephrosis.tw.
	11. membrano$ glomerul$.tw.
	12. (focal adj2 glomerul$).tw.
	13. minimal change glomerul$.tw.
	14. or/1-13
	15. Huangqi plant/
	16. Huangqi Membranaceus/
	17. Huangqi Membranaceus Extract/
	18. Huangqi mongholicus extract/
	19. Chinese Medicine/ or Herbal Medicine/
	20. Chinese Drug/
	21. Medicinal Plant/
	22. Plant Root/

(Continued)

	23. Plant Extract/
	24. Phytotherapy/
	25. astragal$.tw.
	26. hedysarum polybotrys.tw.
	27. (huangqi or huang qi).tw.
	28. (milkvetch or milk vetch).tw.
	29. or/15-28
	30. and/14,29

Appendix 2. Risk of bias checklist

Randomisation

- High risk: Methods of allocation that appeared to be biased, for instance, coin tossing, sequence of seeing doctor, alternation, assignment based on date of birth, case record number and date of presentation or draw straws will be considered inadequate if it took place in front of the participants.
- Unclear risk: Randomisation stated but no information on method used is available.
- Low risk: Random method was described using one of the following approaches: random number tables, computer-generated random numbers.

Allocation concealment

- High risk: The randomisation number and schedule must be concealed from all care providers, ward physicians, and other research personnel before entering the study by using random number tables, computer-generated random numbers, opaque and sealed envelopes, or similar.
- Unclear risk: Did not report the method of allocation concealment.
- Low risk: Concealed allocation that reported an approach that did not fall into one of the categories in high risk.

Blinding

- Blinding of investigators: Yes/no/not stated
- Blinding of participants: Yes/no/not stated
- Blinding of outcome assessor: Yes/no/not stated
- Blinding of data analysis: Yes/no/not stated
- Blinding of manuscript writers: Yes/no/not stated

When considering the risk of bias from lack of blinding it is important to consider specifically:

1. who was and was not blinded
2. risk of bias in actual outcomes due to lack of blinding during the study (e.g. due to co-intervention or differential behaviour)
3. risk of bias in outcome assessments (considering how subjective or objective an outcome is).

Incomplete outcome data

- High risk: A difference in the proportion of incomplete outcome data across groups is of concern if the availability of outcome data is determined by the participants' true outcomes. For example, if participants with poorer clinical outcomes are more likely to drop out due to adverse effects, and this happens mainly in the experimental group, then the effect estimate will be biased in favour of the experimental intervention.
- Unclear risk: The numbers randomised into each intervention group are not clearly reported.
- Low risk: To conclude that there are no missing outcome data, review authors should be confident that the participants included in the analysis are exactly those who were randomised into the trial. Participants randomised but subsequently found not to be eligible need not always be considered as having missing outcome data.

Selective outcome reporting

- Low risk: Pre-defined or clinically relevant and reasonably expected outcomes were reported.
- Unclear risk: Not all pre-defined or clinically relevant and reasonably expected outcomes were reported, or they were not reported fully, or it is unclear whether data on these outcomes were recorded.
- High risk: One or more clinically relevant and reasonably expected outcomes was not reported, and the data on these outcomes were likely to have been recorded.

Other potential threats to validity

- Design-specific risks of bias
- Early stopping
- Baseline imbalance
- Blocked randomisation in unblinded trials
- Differential diagnostic activity
- others: The conduct of the study is affected by interim results. There is deviation from the study protocol in a way that does not reflect clinical practice. There is pre-randomization administration of an intervention that could enhance or diminish the effect of a subsequent, randomised, intervention. Inappropriate administration of an intervention. Occurrence of 'null bias' due to interventions being insufficiently well delivered or overly wide inclusion criteria for participants. An insensitive instrument is used to measure outcomes. Inappropriate influence of funders.

WHAT'S NEW

Date	Event	Description
18 March 2013	New citation required and conclusions have changed	Six new studies added; new interventions and outcomes available
18 March 2013	New search has been performed	Review methodology updated, risk of bias has replaced quality assessment checklist

HISTORY

Protocol first published: Issue 1, 2007
Review first published: Issue 2, 2008

Date	Event	Description
13 May 2009	Amended	Contact details updated.
12 May 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

FM, YW and TW were responsible for development of protocol and review, FM and ZRZ was responsible for searching for references and data extraction, interviewing the authors of trials. All five authors contributed to quality assessment of the trials.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- Chinese Cochrane Center, Chinese Centre of Evidence-Based Medicine, West China Hospital of Sichuan University, China.

External sources

- China Medical Board of New York, USA.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Risk of bias assessment tool has replaced the quality assessment checklist.

INDEX TERMS

Medical Subject Headings (MeSH)

*Phytotherapy; Albumins [metabolism]; Chemistry, Pharmaceutical; Drugs, Chinese Herbal [adverse effects] [*therapeutic use]; Nephrotic Syndrome [blood] [*drug therapy]; Recurrence

MeSH check words

Adult; Child; Humans