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# Astragalus (a traditional Chinese medicine) for treating chronic kidney disease (Review)

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# TABLE OF CONTENTS




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[Intervention Review]

# Astragalus (a traditional Chinese medicine) for treating chronic kidney disease

Hong Wei Zhang[1], Zhi Xiu Lin[1], Chuanshan Xu[1], Connie Leung[2], Lai Sum Chan[1]

[1]School of Chinese Medicine, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong, China. [2]Medical Services Department, Yan Oi Tong, Hong Kong, China

**Contact:** Hong Wei Zhang, School of Chinese Medicine, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong, China. zhanghw@cuhk.edu.hk.

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## ABSTRACT

### Background

Astragalus (*Radix Astragali*, *huang qi*) is the dried root of *Astragalus membranaceus* (Fisch.) Bge. var. *mongholicus* (Bge.) Hsiao or *Astragalus membranaceus* (Fisch.) Bge. (Family Leguminosae). It is one of the most widely used herbs in traditional Chinese medicine for treating kidney diseases. Evidence is needed to help clinicians and patients make judgments about its use for managing chronic kidney disease (CKD).

### Objectives

This review evaluated the benefits and potential harms of Astragalus for the treatment of people with CKD.

### Search methods

We searched the Cochrane Renal Group's Specialised Register to 10 July 2014 through contact with the Trials' Search Co-ordinator using search terms relevant to this review. We also searched CINAHL, AMED, Current Controlled Trials, OpenSIGLE, and Chinese databases including CBM, CMCC, TCMLARS, Chinese Dissertation Database, CMAC and Index to Chinese Periodical Literature.

### Selection criteria

Randomised controlled trials (RCTs) and quasi-RCTs comparing Astragalus, used alone as a crude herb or an extract, with placebo, no treatment, or conventional interventions were eligible for inclusion.

### Data collection and analysis

Two authors independently extracted data and assessed risk of bias in the included studies. Meta-analyses were performed using relative risk (RR) for dichotomous outcomes and mean differences (MD) for continuous outcomes, with 95% confidence intervals (CI).

### Main results

We included 22 studies that involved 1323 participants, of whom 241 were receiving dialysis treatment. Risk of bias was assessed as high in six studies, and unclear in the remaining 16 studies. Study quality was low overall.

Our nominated primary outcomes of time to requirement for renal replacement therapy (RRT) or initiation of dialysis and all-cause mortality were not reported in any of the included studies.


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Results concerning the effects of Astragalus on kidney function were inconsistent. Astragalus significantly increased CrCl at end of treatment (4 studies, 306 participants: MD 5.75 mL/min, 95% CI 3.16 to 8.34; $I^2$ = 0%), decreased SCr (13 studies, 775 participants: MD -21.39 µmol/L, 95% CI -34.78 to -8; $I^2$ = 70%) and especially in those whose baseline SCr was < 133 µmol/L in particular (3 studies, 187 participants: MD -2.52 µmol/l, 95% CI -8.47 to 3.42; $I^2$ = 0%). Astragalus significantly decreased 24 hour proteinuria at end of treatment (10 studies, 640 participants; MD -0.53 g/24 h, 95% CI -0.79 to -0.26; $I^2$ = 90%); significantly increased haemoglobin levels overall (4 studies, 222 participants): MD 9.51 g/L, 95% CI 4.90 to 14.11; $I^2$ = 0%) and in haemodialysis patients in particular (3 studies, 142 participants: MD 11.20 g/L, 95% CI 5.81 to 16.59; $I^2$ = 0%). Astragalus significantly increased serum albumin (9 studies, 522 participants: MD 3.55 g/L, 95% CI 2.33 to 4.78; $I^2$ = 65%). This significant increase was seen in both dialysis (3 studies, 152 participants): MD 4.04 g/L, 95% CI 1.91 to 6.16; $I^2$ = 72%) and non-dialysis patients (6 studies, 370 participants: MD 3.24 g/L, 95% CI 1.70 to 4.77; $I^2$ = 61%). Astragalus significantly decreased systolic blood pressure (2 studies, 77 participants: MD -16.65 mm Hg, 95% CI -28.83 to -4.47; $I^2$ = 50%), and diastolic blood pressure (2 studies, 77 participants: MD -6.02 mm Hg, 95% CI -10.59 to -1.46; $I^2$ = 0%).

Six of 22 included studies reported no adverse effects were observed; while the remaining 16 studies did not report adverse effects.

**Authors' conclusions**

Although Astragalus as an adjunctive treatment to conventional therapies was found to offer some promising effects in reducing proteinuria and increasing haemoglobin and serum albumin, suboptimal methodological quality and poor reporting meant that definitive conclusions could not be made based on available evidence.

## PLAIN LANGUAGE SUMMARY

### Astragalus (a traditional Chinese medicine) for treating chronic kidney disease

Chronic kidney disease affects increasing numbers of people around the world, but as yet, effective strategies to control its progression have not been universally accepted. Astragalus is one of most widely used herbs for treating kidney disease. We conducted this review to evaluate the benefits and potential harms of Astragalus for the treatment of people with chronic kidney disease.

We searched the literature published up to July 204 and summarised 22 studies involving 1323 people with chronic kidney disease, including both on dialysis treatment or not.

Although we found some promising evidence suggesting that when given with conventional treatment, Astragalus may help to decrease the serum creatinine, reduce the amount of protein lost in urine and diminish the effects of some complications, such as anaemia and malnutrition, evidence quality was low. We found that errors and omissions in study methods and reporting were likely to have flawed results among the studies we assessed. Possible adverse effects associated with Astragalus injection should be noted, although we found no relevant reports from included studies.


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**Summary of findings for the main comparison. Astragalus and co-interventions compared with same co-interventions alone for people with CKD**

**Astragalus and conventional treatment versus conventional treatment alone for people with CKD**

**Patient or population:** patients with CKD
**Settings: h**ospitals in China
**Intervention:** Astragalus combined with co-interventions[1]

**Comparison**: conventional treatment

| Outcomes | Illustrative comparative risks* (95% CI) | | Relative effect (95% CI) | No of Participants (studies) | Quality of the evidence (GRADE) | Comments |
|---|---|---|---|---|---|---|
| | Assumed risk | Corresponding risk | | | | |
| | Control | Astragalus | | | | |
| **Time to requirement for RRT/initiation of dialysis** | See comment | See comment | Not estimable | 0 (0) | See comment | No study reported time to requirement for RRT or initiation of dialysis |
| **All-cause mortality** | See comment | See comment | Not estimable | 0 (0) | See comment | No study reported time to requirement for RRT therapy or initiation of dialysis |
| **Creatinine clearance (after treatment)** | Mean CrCl (after treatment) ranged from 38.3 to 86.3 mL/min | Mean CrCl (after treatment) was 5.75 higher (3.16 to 8.34 higher) | | 306 (4) | ⊕⊕⊖⊖ **low** | |
| **Serum creatinine (after treatment)** | Mean SCr (after treatment) ranged from 84 to 571.1 µmol/L | Mean SCr (after treatment) was 17.17 lower (5.35 to 28.98 lower) | | 841 (14) | ⊕⊕⊖⊖ **low** | |
| **24 h proteinuria (after treatment)** | Mean 24 h proteinuria (after treatment) ranged from 0.77 to 2.23 g/24 h | Mean 24 h proteinuria (after treatment) was 0.56 lower (0.3 to 0.81 lower) | | 706 (11) | ⊕⊕⊖⊖ **low** | |


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| | | | | | |
|---|---|---|---|---|---|
| **Albumin** | Mean albumin ranged from 26.08 to 34.76 g/L | Mean albumin was 3.56 higher (2.4 to 4.73 higher) | | 588 (10) | ⊕⊕⊝⊝ **low** |
| **Haemoglobin** | Mean Hb ranged from 72.7 to 90.65 g/L | Mean Hb was 9.51 higher (4.9 to 14.11 higher) | | 222 (4) | ⊕⊕⊕⊝ **moderate** |

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
Abbreviations: CI - confidence interval; RRT - renal replacement therapy

GRADE Working Group grades of evidence
**High quality:** Further research is very unlikely to change our confidence in the estimate of effect
**Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
**Low quality:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
**Very low quality:** We are very uncertain about the estimate

[1] Of 23 included studies, 17 investigated Astragalus injection, and 2 investigated Huang qi decoction for oral administration
CrCl - creatinine clearance; Hb -haemoglobin; SCr - serum creatinine


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# BACKGROUND

## Description of the condition

Chronic kidney disease (CKD) is characterised by gradual deterioration of kidney function caused by an array of medical conditions such as diabetes, hypertensive nephrosclerosis, glomerulonephritis and renovascular disease (Chertow 2005). According to the Kidney Disease Outcomes Quality Initiative (KDOQI) clinical guidelines, CKD can be defined as either kidney damage (indicated by markers such as abnormalities in urine or blood tests, or on imaging), or decreased glomerular filtration rate (GFR < 60 mL/min/1.73 $m^2$) with or without evidence of kidney damage, for three or more months, irrespective of the cause. Based on GFR levels, CKD can be further classified according to disease stage (Levey 2003):

- Stage 1: kidney damage with normal or increased GFR (≥ 90 mL/min/1.73 $m^2$)
- Stage 2: kidney damage with mild decreased GFR (60 to 89 mL/min/1.73 $m^2$)
- Stage 3: moderately decreased GFR (30 to 59 mL/min/1.73 $m^2$)
- Stage 4: severely decreased GFR (15 to 29 mL/min/1.73 $m^2$)
- Stage 5: kidney failure with GFR < 15 mL/min/1.73 $m^2$ or a need for dialysis.

Decreased kidney function is closely associated with a range of complications including hypertension, anaemia, malnutrition, bone disease, neuropathy, and reduced quality of life (NKF 2008). Moreover, it is an independent risk factor for cardiovascular diseases (Fried 2003; Mann 2001).

Incidence of CKD is widespread and imposes substantial burden on healthcare systems globally. The median prevalence of moderate-to-severe CKD (GFR < 60 mL/min/1.73 $m^2$) has been estimated at 7.2% in people aged 30 years and over, but escalates to 23.4% to 35.8% in people 64 years and over (Chen 2005; Zhang 2008). Both numbers of people with end-stage kidney disease (ESKD) who need dialysis or kidney transplantation and treatment resource costs have continued to increase (Moeller 2002; Lysaght 2002). Resource limitations mean that many people with ESKD in both economically developed and developing regions do not have access to dialysis or kidney transplantation (White 2008). Delaying progression to ESKD therefore benefits both patients and healthcare systems.

## Description of the intervention

Astragalus (*Radix Astragali*), known as *huang qi* in Chinese, is the dried root of *Astragalus membranaceus* (Fisch.) Bge. var. *mongholicus* (Bge.) Hsiao or *Astragalus membranaceus* (Fisch.) Bge. (Family Leguminosae). It is one of the most commonly prescribed herbs in traditional Chinese medicine.

Over thousands of years, traditional Chinese medicine has developed a unique theoretical system (such as yin-yang, five elements, Qi and meridians) that includes many different therapeutic and preventive methods (including Chinese herbal medicine, acupuncture and moxibustion, tuina therapy and qi-gong). According to traditional Chinese medicine theory, Astragalus reinforces the body's vital Qi, facilitates urination, promotes purulent discharge, and enhances soft tissue repair and growth (Chinese Pharmacopoeia Commission 2005). The diverse therapeutic functions of Astragalus mean that it is widely used by traditional Chinese medicine practitioners to treat a range variety of conditions including cardiovascular, cerebrovascular, kidney and digestive diseases (Xiong 2002).

The flavonoids, cyclolanostane-type saponins and polysaccharides are the main bioactive compounds in Astragalus (Lee 2005; Verotta 2001; Xu 2006; Yu 2007). Astragaloside IV, one of the cyclolanostane-type saponins, is used as a marker compound for quality control in the manufacture of Astragalus and its preparations (Luo 2004; Xia 2008). In modern Chinese medicine, Astragalus is used either alone or in combination with other herbs in oral decoction, pill or capsule forms. It is also manufactured in injectable form for intravenous and intramuscular administration.

## How the intervention might work

A number of clinical studies have shown that Astragalus can improve kidney function, reduce proteinuria, increase serum superoxide dismutase, decrease lipid peroxidation, decrease endothelin-1 and regulate cellular immunity in patients with moderate to severe CKD (Yang 1997; Zhou 2001; Zuo 2003). Pharmacological studies have also demonstrated that Astragalus may offer immunomodulatory (Kang 2004; Lee 2003), anti-inflammatory (Ryu 2008; Shon 2003), and renoprotective effects (Chen 2008). It may also ameliorate renal interstitial fibrosis (Zuo 2008), inhibit glomerular mesangial cell proliferation and interleukin-6 secretion (Bao 2005). These mechanisms may account for improvements in kidney function and CKD clinical symptoms that have been attributed to Astragalus.

## Why it is important to do this review

Although Astragalus is widely used in traditional Chinese medicine for people with CKD, no definitive conclusions about its effectiveness have been determined. Safety is an important factor, especially when extracts prepared from the crude herb are used as an injectable form. Although use is widespread in mainland China, Astragalus injection is generally not approved for use elsewhere. A previous review has demonstrated that Astragalus and its preparations had relatively fewer side effects compared with other herbal preparations (Xiong 2002). However, reported adverse reactions relating to Astragalus injection are evident; the most common are allergic reactions (Deng 2001; Zeng 2005).

This review was undertaken to assess the available evidence to determine effectiveness and adverse effects associated with Astragalus for the treatment of people with CKD.

# OBJECTIVES

This review evaluated the benefits and potential harms of Astragalus for the treatment of people with CKD.

# METHODS

## Criteria for considering studies for this review

### Types of studies

All randomised controlled trials (RCTs) and quasi-RCTs (RCTs in which allocation was obtained by alternation, use of alternate medical records, date of birth or other predictable methods) on the treatment of people with CKD using Astragalus were included. There was no restriction on publication status or language.


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### Types of participants

#### *Inclusion criteria*

We included adults and children with CKD at all stages. Where possible we used the KDOQI definition for CKD (NKF 2008); however, we also accepted definitions of CKD as described by the included studies.

#### *Exclusion criteria*

- Studies stating that participants had renal impairment, but did not provide baseline GFR, creatinine clearance (CrCl) or creatinine concentration, and where additional data could not be obtained from the report or after contacting the authors
- Patients who were kidney transplant recipients
- Patients with diabetic kidney disease and patients with primary nephrotic syndrome, which have been addressed in other reviews (Feng 2013; Liu 2007a).

### Types of interventions

- Treatment group participants needed to have received Astragalus or its extract as the treatment drug, regardless of formulation or route of administration.
- Control group participants received placebo, no treatment, or conventional treatment. Other herbal or complementary medicines lacking validated efficacy were not accepted as control interventions.
- Studies involving Astragalus as one of multiple active components in a compound preparation or as a part of a combined treatment regimen were not included in the review.
- Co-interventions were included where all randomised study arm participants received the same co-intervention.

### Types of outcome measures

#### *Primary outcomes*

1. Time to requirement for renal replacement therapy (RRT)/ initiation of dialysis
2. All-cause mortality.

#### *Secondary outcomes*

1. Kidney function measured by glomerular filtration rate (GFR), CrCl, or serum creatinine (SCr)
2. Quality of life measured by a validated scale
3. Proteinuria measured by 24 hour urinary protein excretion (UPE), protein/creatinine ratio (PCR) or albumin/creatinine ratio (ACR)
4. Blood pressure (systolic and diastolic)
5. Anaemia measured by haemoglobin (Hb) or haematocrit (HCT)
6. Nutritional status assessed by serum albumin, serum total cholesterol, oedema-free actual body weight, percent standard (NHANES II) body weight, normalised protein nitrogen appearance or dietary interviews and diaries
7. Bone disease measured by serum calcium and phosphorus or bone mineral density
8. Symptoms including skin pruritus, vomiting, measured by the visual analogue scale (VAS) or other scales
9. Adverse effects.

Primary and secondary outcome measurements were collected immediately after treatment and at the end of follow-up.

## Search methods for identification of studies

### Electronic searches

We searched the Cochrane Renal Group's Specialised Register to 10 July 2014 through contact with the Trials' Search Co-ordinator using search terms relevant to this review. The Cochrane Renal Group's Specialised Register contains studies identified from the following sources.

1. Monthly searches of the Cochrane Central Register of Controlled Trials CENTRAL
2. Weekly searches of MEDLINE OVID SP
3. Handsearching of renal-related journals and the proceedings of major renal conferences
4. Searching of the current year of EMBASE OVID SP
5. Weekly current awareness alerts for selected renal journals
6. Searches of the International Clinical Trials Register (ICTRP) Search Portal and ClinicalTrials.gov.

Studies contained in the Specialised Register are identified through search strategies for CENTRAL, MEDLINE, and EMBASE based on the scope of the Cochrane Renal Group. Details of these strategies, as well as a list of handsearched journals, conference proceedings and current awareness alerts, are available in the Specialised Register section of information about the Cochrane Renal Group.

We also searched:

1. CINAHL (Cumulative Index of Nursing and Allied Health, 1982 to 10 July 2014), AMED (Allied and Complementary Medicine Database, 19 January 2010), and CISCOM (Centralised Information Service for Complementary Medicine) were also searched using strategies adapted from that described for MEDLINE.
2. Current Controlled Trials (www.controlled-trials.com), and OpenSIGLE (System for Information on Grey Literature in Europe) were also searched for ongoing and grey literature
3. The following Chinese databases were searched to January 2011.
   a. CBM (Chinese BioMedical Literature Database)
   b. CMCC (Chinese Medical Current Contents)
   c. TCMLARS (Traditional Chinese Medical Literature Analysis and Retrieval System)
   d. Chinese Dissertation Database
   e. CMAC (China Medical Academic Conference)
   f. Index to Taiwan Periodical Literature.
4. Index to theses and ProQuest Dissertations and theses were searched for relevant studies reported in dissertations.

Appendix 1 presents the search strategies applied for this review.

### Searching other resources

Reference lists of nephrology textbooks, significant reviews and relevant studies were searched. Where necessary, we contacted study authors seeking information about unpublished or incomplete studies. Relevant responses and data were included in our analyses.


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## Data collection and analysis

### Selection of studies

The search strategy described was used to obtain titles and abstracts of studies that may be relevant to the review. Titles and abstracts were screened independently by two authors who discarded studies that were not applicable; however, studies and reviews that might include relevant data or information on studies were retained initially. Two authors independently assessed retrieved abstracts, and if necessary, the full text of these studies to determine which satisfied the inclusion criteria.

### Data extraction and management

Data extraction was carried out independently by the same authors using a pre-tested data extraction form. Where more than one publication of one study existed, reports were grouped together and the publication with the most complete data was used. Where relevant outcomes were only published in earlier versions, these data were used. Any discrepancies between published versions was to be highlighted. Any further information required from the original author was requested by written correspondence. Disagreements between authors were resolved by consensus and with a third author.

### Assessment of risk of bias in included studies

The following items were independently assessed by two authors using the risk of bias assessment tool (Higgins 2011) (see Appendix 2).

- 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 (all-cause mortality), results were expressed as risk ratio (RR) with 95% confidence intervals (CI). To determine applicability of the results to individual patients, a variety of numbers needed-to-treat were calculated for a range of assumed control risks.

Where continuous scales of measurement were used to assess the effects of treatment (kidney function, quality of life, proteinuria, blood pressure, anaemia, nutritional status, bone disease) the mean difference (MD) was used, or the standardised mean difference (SMD) if different scales were used.

### Unit of analysis issues

Outcomes analysis was conducted based on randomised participants. In the case of multiple intervention groups within a study, pair-wise comparisons relevant to the study's objective were made.

### Dealing with missing data

Where necessary, further information required from the original author was requested by written correspondence, and relevant information was included in the review. Evaluation of important numerical data such as screened, randomised patients as well as intention-to-treat, as-treated and per-protocol population was carefully performed. Attrition rates, such as drop-outs, losses to follow-up and withdrawals, were investigated. Issues of missing data and imputation methods were critically appraised (Higgins 2011).

### Assessment of heterogeneity

Heterogeneity was analysed using a $Chi^2$ test on N-1 degrees of freedom, with an alpha of 0.1 used for statistical significance and with the $I^2$ test (Higgins 2003). $I^2$ values of 25%, 50% and 75% correspond to low, medium and high levels of heterogeneity, respectively.

### Assessment of reporting biases

Reporting biases were interpreted using funnel plots (Higgins 2011).

### Data synthesis

Data were pooled using the random-effects model under the assumption that the effects being estimated were not identical across studies, but followed certain distribution patterns. The fixed-effect model was also analysed to ensure robustness of the model chosen and susceptibility to outliers (Higgins 2011).

### Subgroup analysis and investigation of heterogeneity

We conducted subgroup analyses to explore potential sources of heterogeneity based on risk of bias, serum creatinine level and Astragalus preparations. There were insufficient studies to conduct subgroup analyses on the use of Astragalus preparation. Adverse effects have been presented qualitatively.

### Sensitivity analysis

There were insufficient relevant included studies to conduct sensitivity analyses to evaluate whether limiting the definition of CKD according to KDOQI parameters, or if the apparent deficits in studies' sequence generation and blinding influenced effect estimates.

We evaluated evidence quality using the GRADE system. We also considered the quality of evidence, potential benefits and harms, study context and patients' values when interpreting the results.

# RESULTS

## Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; and Characteristics of studies awaiting classification.

### Results of the search

Our search identified 1773 records (Figure 1). After excluding 363 duplicate and 1173 irrelevant records, 241 studies were identified for assessment. The full-text of five records (Biao 1992; Chen 1999; Li 1999; Peng 1999; Yu 2002) were not available for assessment and have been listed as studies awaiting assessment. We reviewed


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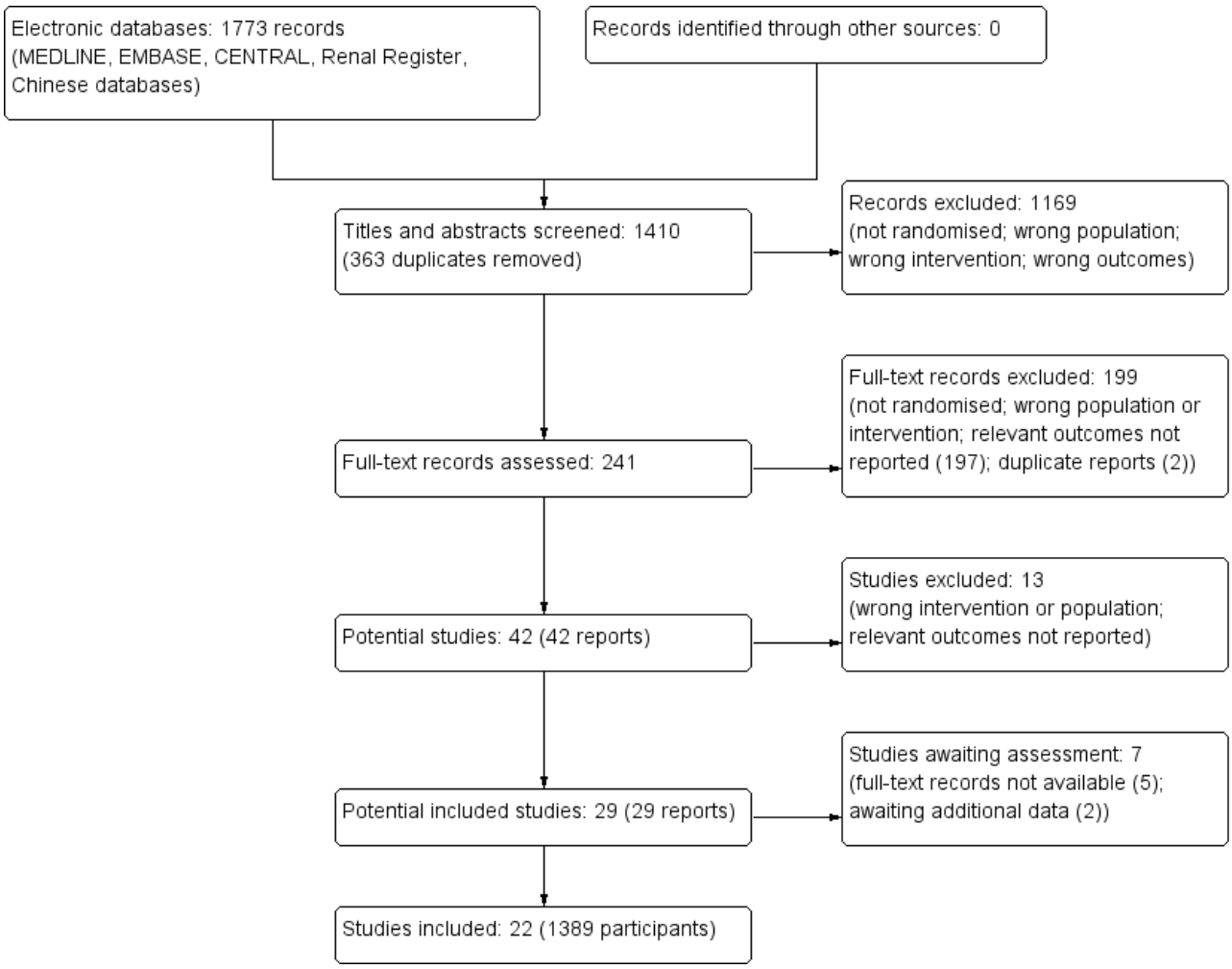
236 full-text studies for inclusion, and identified 37 eligible studies. A further two studies were listed as awaiting assessment after our attempts to contact authors for additional information were unsuccessful (Chen 2003; Cui 2005) and 13 studies were excluded (Chen 2004a; Cui 2000; Gao 2006; Huang 2004; Lu 1999; Qiu 2008; Qu 2008; Qun 1999; Wang 2004; Wei 2006; Zhang 2005; Zhu 2002; Zuo 2003). We included 22 studies in this review.

**Figure 1. Study selection flow diagram**




### Included studies

The 22 included studies involved 1323 participants and were conducted in China and published in Chinese (Bi 2007; Cheng 2001; Li 2006; Li 2008; Liu 2002; Miao 2002; Su 2007; Sun 1989; Tao 2001; Wang 2000; Wu 2008; Xu 2008; Yang 1997; Yang 2005; Yao 2004; Zeng 2009; Zhang 2001; Zhang 2003; Zhang 2006; Zhao 2010; Zhou 2001; Zhu 2003). With one exception, all studies were parallel arm studies; Tao 2001 included three study arms. Twenty one studies (1182 participants) reported participants' gender; 56% of participants were male. Study populations ranged from 29 to 90 participants.

CKD stage varied among participants. Four studies (181 participants) recruited patients on haemodialysis (Wang 2000; Yao 2004; Zhang 2006; Zhao 2010); one study recruited patients with chronic nephritis, including four people on continuous ambulatory peritoneal dialysis (CAPD) (Sun 1989); and one study recruited 56 participants with CKD who were receiving dialysis treatment or colon dialysis (Li 2008). In colon dialysis, the Chinese herbal medicine decoction was injected into the colon to help adsorb the toxins in the body through the colon mucous membrane.

Because most studies provided baseline SCr data only, we elected to categorise studies using a baseline of 133 µmol/L. This cut-off value was chosen because it is an established national criterion for abnormal kidney function in China. Four studies recruited participants with SCr < 133 µmol/L (Li 2006; Tao 2001; Zeng 2009; Zhang 2001), 10 studies involved participants with SCr > 133 µmol/L who were not receiving dialysis (Cheng 2001; Liu 2002; Miao 2002; Wu 2008; Xu 2008; Yang 1997; Yang 2005; Zhang 2003; Zhu 2003; Zhou 2001). CKD stage was not defined in two studies that did not provide baseline SCr, CrCl, or GFR data (Bi 2007; Su 2007).

The primary causes of CKD varied, but included chronic glomerulonephritis, diabetic nephropathy, IgA nephropathy and hypertensive nephropathy. Two studies specifically recruited CKD patients diagnosed with the Chinese medicine syndrome of Qi insufficiency (Su 2007; Zeng 2009). Participants in these two studies all had indications of kidney dysfunction, as well as symptoms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such as fatigue, lower back pain, oedema and weak pulse, which according to Chinese medicine theory can be summarised as Qi insufficiency syndrome. Administration of Chinese medicinal herbs was based on physicians' judgements.

All included studies compared Astragalus plus conventional treatment with the same conventional treatment. The main conventional treatments were dietary control, symptomatic and supportive treatments including maintaining water, electrolyte and acid-base balance, controlling blood pressure, treating anaemia, and controlling infection when necessary. Chinese herbal medicines (CHM) such as Panax notoginseng saponins injection and Jinshuibao capsules (Cordyceps mycelia extract) were also used. In the three-arm study by Tao 2001 that investigated Astragalus plus Panax notoginseng saponins plus CHM versus Astragalus plus CHM versus Panax notoginseng saponins plus CHM, only the Astragalus plus Panax notoginseng saponins plus CHM and Panax notoginseng saponins plus CHM comparison arms were included in this review. Panax notoginseng saponins plus CHM was regarded as the conventional treatment in two groups.

Of the 22 included studies, 16 investigated Astragalus injection (Huang qi injection) by IV infusion; one reported on Huang qi injection as a slow IV injection (Zhang 2006); one administered Huang qi in dialysis solution during maintenance haemodialysis (Yao 2004); and two administered Huang qi intramuscular injection at acupoints (Zeng 2009; Zhang 2003). Two studies investigated Huang qi decoction for oral administration (Sun 1989; Yang 1997). Huang qi injection is made from Astragalus using water extraction and ethanol precipitation, and is produced by 13 pharmaceutical manufacturers in China according to a national standard for registering Chinese patent medicines. Huang qi decoction is generally made by boiling Astragalus in water for 20 to 30 minutes. Decoction is a common method to administer Chinese medicinal herbs. In the included studies, Huang qi decoction was made by individual hospitals and no quality control measures were described. Huang qi 2 mL injection equates to 4 g of the raw herb (Chinese Pharmacopoeia Commission 2005).

Treatment duration ranged from two weeks to six months. With one exception, all included studies reported end-of-treatment outcome measures: Sun 1989 reported outcome measures at three months follow-up.

### Excluded studies

We excluded 13 studies: patients with nephrotic syndrome were included (Chen 2004a; Huang 2004; Zhang 2005); non-CKD patients included in control arm (Cui 2000); active treatment was used in conjunction with Astragalus (Gao 2006; Qiu 2008); TCM used as control (Lu 1999; Zhu 2003); Astragalus was not used (Wang 2004; Wei 2006); and relevant outcomes were not reported (Qu 2008; Qun 1999; Zhu 2002).

## Risk of bias in included studies

### Allocation

Only one included study reported use of a random number table (Zeng 2009). Random allocation was only briefly mentioned and detailed procedures were not provided in 20 studies. Entry sequencing was used to allocate participants in one study (Xu 2008).

None of the included studies reported allocation concealment procedures or methods.

### Blinding

None of the included studies described blinding personnel, participants or outcome assessors. It is possible that where personnel and participants were aware of the study's intervention design, especially in situations where multiple co-interventions were administered, behaviours were modified. Therefore, performance bias may exist. Lack of blinding of outcome assessors can induce detection bias, especially during assessment of subjective outcomes; however, we felt that it was unlikely that physiological outcome measurements, such as GFR, CrCl or SCr, were influenced by the absence of blinding among outcome assessors.

### Incomplete outcome data

None of the studies reported missing data during the study period. All studies conducted analyses based on initial treatment intent. This situation may be explained by most of the included studies having recruited hospital inpatients, among whom it may be more likely to ensure patients' full participation for the study duration. However, the possibility that studies applied intention-to-treat analyses could not be excluded.

### Selective reporting

Existence of selective reporting could not be determined because study protocols were unavailable, and few kidney function outcome measures were reported.

### Other potential sources of bias

We found evidence of SCr baseline value imbalance between treatment and control groups in one study (Cheng 2001). There were substantial differences in numbers of participants in the treatment and control groups in five studies (Li 2006; Li 2008; Zhang 2001; Zhang 2003; Zhou 2001).

Overall risk of bias was assessed as high in six studies (Cheng 2001; Li 2006; Li 2008; Zhang 2001; Zhang 2003; Zhou 2001), and unclear in 16 studies (Figure 2; Figure 3). Our assessment using the GRADE system found that overall quality was low for most outcome measures (Summary of findings for the main comparison).


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

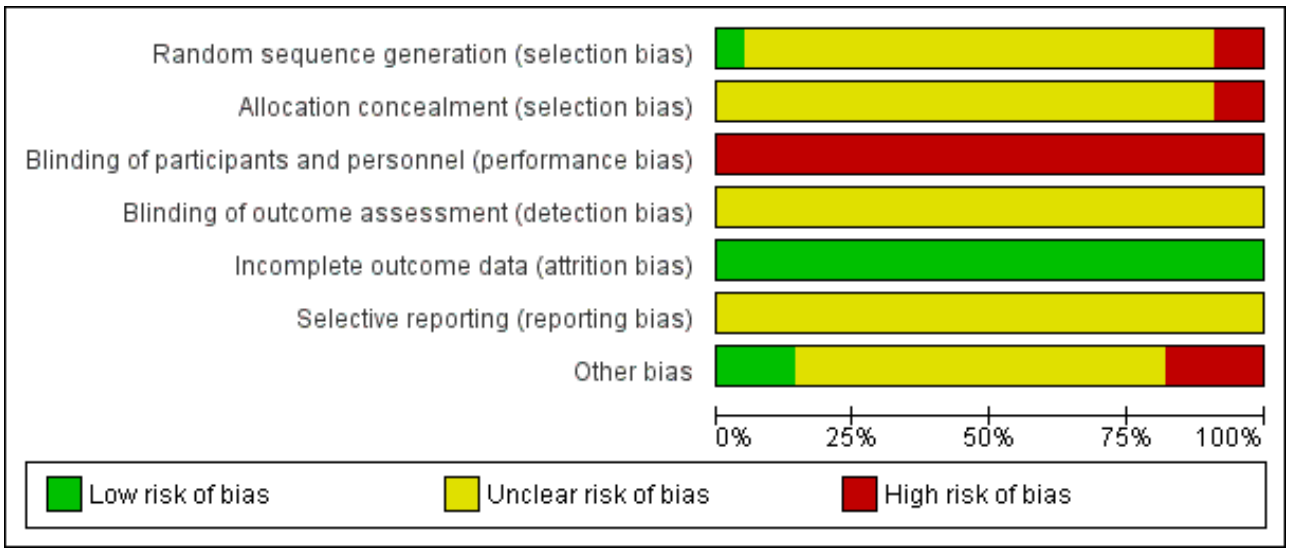



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**Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.**

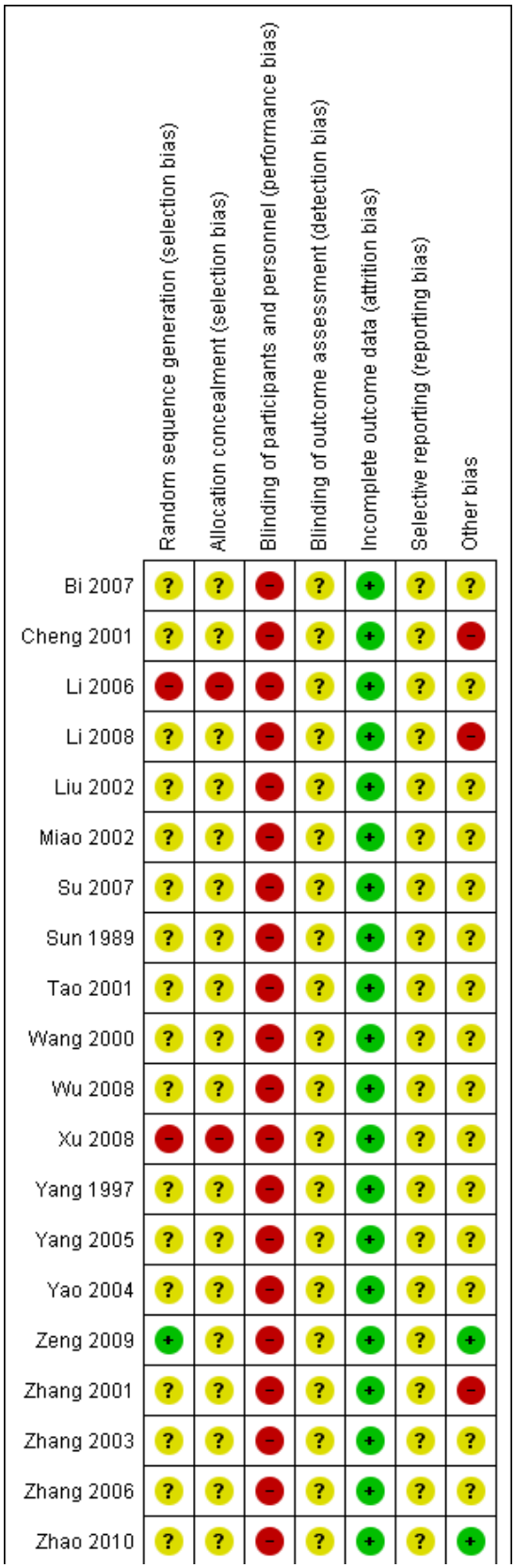



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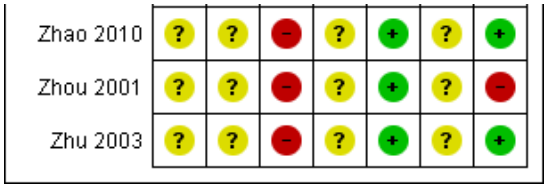
**Figure 3. (Continued)**




## Effects of interventions

See: **Summary of findings for the main comparison** Astragalus and co-interventions compared with same co-interventions alone for people with CKD

### Astragalus + conventional treatment versus conventional treatment

#### *Kidney function (measured by GFR, CrCl, or SCr)*

Astragalus significantly increased CrCl compared with control (Analysis 1.1 (4 studies, 306 participants): MD 5.75 mL/min, 95% CI 3.16 to 8.34; $I^2$ = 0%) at end of treatment. Xu 2008 reported no significant difference in GFR (Analysis 1.2 (1 study, 48 participants): MD 4.10 mL/min/1.73 $m^2$, 95% CI -2.38 to 10.58).

Pooled results indicated that compared with control, Astragalus significantly decreased SCr (Analysis 1.3.1 (13 studies, 775 participants): MD 21.39 µmol/L, 95% CI-34.78, -8.00; $I^2$ = 70%). Subgroup analysis indicated that Astragalus preparation significantly decreased SCr in people whose SCr levels were > 133 µmol/L (Analysis 1.3.2 (10 studies, 588 participants): MD -49.20 µmol/L, 95% CI -80.07 to -18.33; $I^2$ = 72%), but not in those whose baseline SCr was < 133 µmol/L (Analysis 1.3.3 (3 studies, 187 participants): MD -2.52 µmol/l, 95% CI -8.47 to 3.42; $I^2$ = 0%). Astragalus injection significantly decreased SCr levels (Analysis 1.3.4 (11 studies, 638 participants): MD -28.89 µmol/L, 95% CI -46.74 to -11.05; $I^2$ = 75%) while oral Astragalus decoction did not (Analysis 1.3.5 (2 studies, 137 participants): MD -7.83 µmol/L, 95% CI -17.19 to 1.54; $I^2$ = 0%).

In regard to long-term results, Sun 1989 reported that after three months follow-up Astragalus significantly increased CrCl (Analysis 1.4 (1 study, 86 participants): MD 48 mL/min, 95% CI 34.85 to 61.15) and significantly decreased SCr (Analysis 1.5 (1 study, 86 participants): MD 17 µmol/L, 95% CI 4.85 to 29.15).

#### *Proteinuria*

Astragalus significantly decreased 24 hour proteinuria at end of treatment (Analysis 1.6.1 (10 studies, 640 participants): MD -0.53 g/24 h, 95% CI -0.79 to -0.26; $I^2$ = 90%).

Sun 1989 reported that after three months follow-up Astragalus significantly decreased 24 hour proteinuria (Analysis 1.7 (1 study, 86 participants): MD -1.12 g/24 h, 95% CI -1.24 to -0.99) at three months follow-up.

#### *Blood pressure*

Astragalus significantly decreased systolic blood pressure (Analysis 1.8 (2 studies, 77 participants): MD -16.65 mm Hg, 95% CI -28.83 to -4.47; $I^2$ = 50%) and diastolic blood pressure (Analysis 1.9 (2 studies, 77 participants): MD -6.02 mm Hg, 95% CI -10.59 to -1.46; $I^2$ = 0%).

#### *Anaemia*

Overall, Astragalus significantly increased haemoglobin levels (Analysis 1.10.1 (4 studies, 222 participants): MD 9.51 g/L, 95% CI 4.90 to 14.11; $I^2$ = 0%).There was a significant increase in haemoglobin in patients on haemodialysis (Analysis 1.10.2 (3 studies, 142 participants): MD 11.20 g/L, 95% CI 5.81 to 16.59; $I^2$ = 0%) however Zhang 2003 reported no significant increase among people not receiving dialysis (Analysis 1.10.3 (1 study, 80 participants): MD 4.91 g/L; 95% CI -3.97 to 13.79).

Astragalus did not significantly change haematocrit (Analysis 1.11 (3 studies, 142 participants): MD 5.91%, 95% CI -0.99 to 12.81; $I^2$ = 94%). The difference in administration route of Astragalus injection and supportive co-interventions might contribute to the high heterogeneity to some degree. In Li 2008 and Wang 2000, Astragalus injection was administered as intra venous drip infusion; however, in Yao 2004, it was added into the dialysis fluid.

#### *Nutritional status*

Overall, Astragalus significantly increased albumin (Analysis 1.12.1 (9 studies, 522 participants): MD 3.55 g/L, 95% CI 2.33 to 4.78; $I^2$ = 65%). This significant increase was seen in both dialysis (Analysis 1.12.2 (3 studies, 152 participants): MD 4.04 g/L, 95% CI 1.91 to 6.16; $I^2$ = 72%) and non-dialysis patients (Analysis 1.12.3 (6 studies, 370 participants): MD 3.24 g/L, 95% CI 1.70 to 4.77; $I^2$ = 61%).

Astragalus did not significantly change total cholesterol (Analysis 1.13 (2 studies 138 participants): MD -0.34 mmol/L, 95% CI -1.51 to 0.83; $I^2$ = 78%).

#### *Adverse effects*

Six studies reported no adverse effects were observed; while the remaining 16 studies did not report adverse effects.

#### *Other outcomes*

The following outcomes were not reported by any of the included studies.

- Time to requirement of renal replacement therapy or initiation of dialysis (primary outcome)
- All-cause mortality (primary outcome)
- Quality of life measured by a validated scale (secondary outcome)
- Bone disease measured by serum calcium and phosphorus or bone mineral density (secondary outcome)
- Symptoms including skin pruritus, vomiting, measured by VAS scale or other scales (secondary outcome).

### Heterogeneity

Aside from CKD stage and Astragalus preparation type, other factors such as CKD aetiology, differences in participants' ages and dialysis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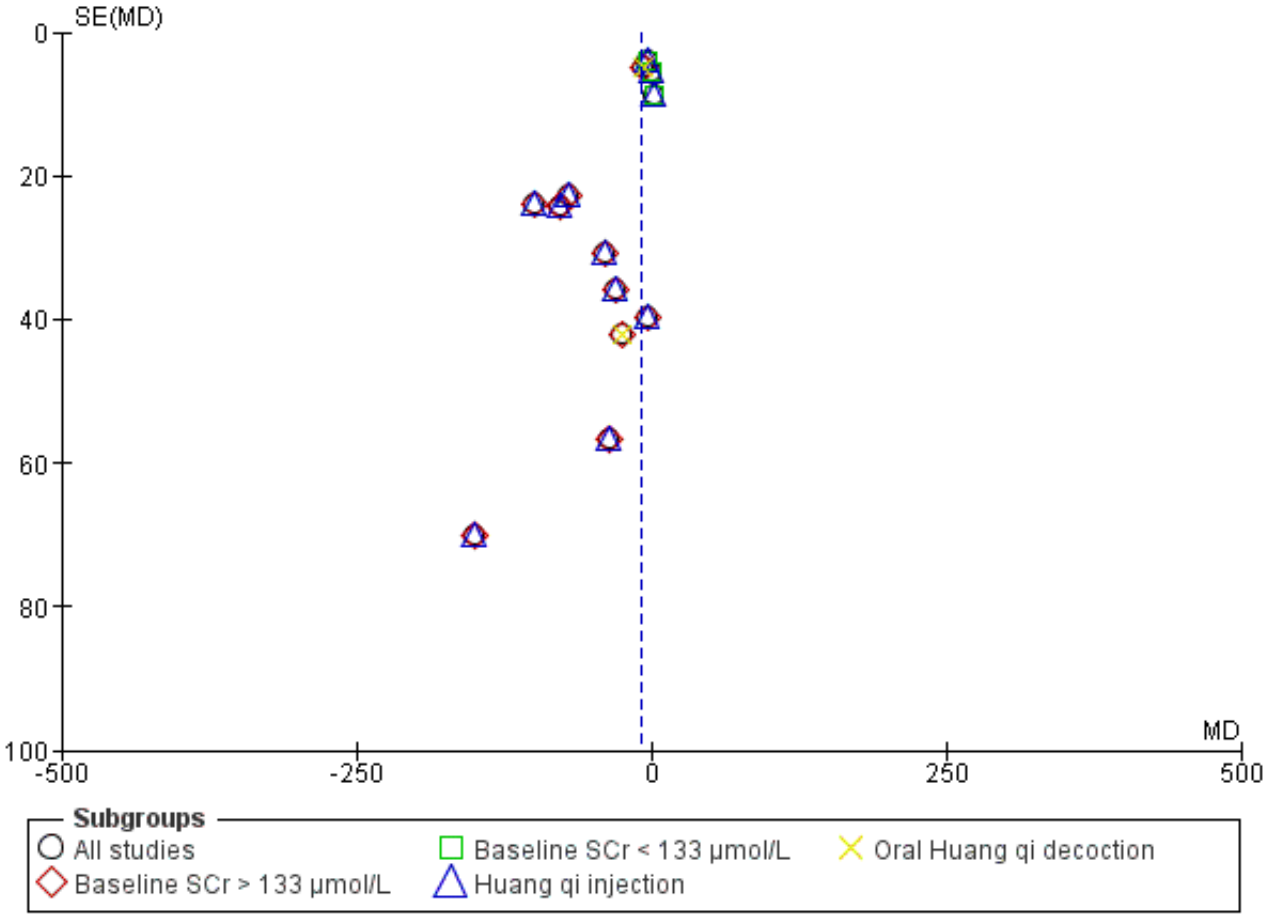
status may have contributed to the observed heterogeneity, which may have modified treatment outcomes. Asymmetry in the funnel plot suggested possibility of publication bias (Figure 4).

**Figure 4. Funnel plot: Astragalus + conventional treatment versus conventional treatment alone, outcome: 1.4 SCr: end of treatment (µmol/L)**




## DISCUSSION

### Summary of main results

This review included 22 studies that involved 1323 participants. All were conducted in hospitals in China. Participants were at various stages of CKD, and included those on dialysis. All studies included some form of conventional treatment in each group, and Astragalus was used in addition to this conventional treatment in the treatment arm of the studies.

We found some consistent evidence to suggest that Astragalus, as an adjunctive treatment to conventional medicine, may have positive effects in reducing 24 hour proteinuria, increasing haemoglobin and decreasing systolic and diastolic blood pressure and serum albumin.

Evidence concerning the effects of Astragalus on kidney function was inconsistent. Astragalus may have effect on increasing CrCl, and decreasing SCr in those patients with baseline SCr > 133 µmol/L but not < 133 µmol/L.

Overall, evidence was weakened by the potentially high risk of bias and poor reporting among the included studies.

### Overall completeness and applicability of evidence

Evidence about the potential benefits or harms of Astragalus for people with CKD is incomplete. None of the included studies presented data on our primary outcomes of time to requirement for renal replacement therapy or initiation of dialysis, all-cause mortality, or quality of life. Only data on kidney function measures were available. The effects of Astragalus in improving clinical symptoms such as fatigue, lower back and knee pain, loose stools and urination frequency were reported in some studies; however, most data were qualitative or measured using various self-defined scales.

Applicability may be limited; use of Astragalus injection is generally prohibited outside mainland China. This aspect poses questions on the global applicability of Astragalus for people with CKD.

Astragalus injection has been associated with some adverse effects, mainly allergic reactions and allergic shock (Liu 2007b). However, few included studies reported any adverse effects.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In traditional Chinese medicine practice, Astragalus is used to tonify Qi. In traditional Chinese medicine theory, Qi is one of the material elements of life activities in the human body. According to Chinese medicine treatment principles, disease caused by Qi insufficiency should be treated with Qi tonifying medications, and prescriptions usually vary for individual patients with CKD. In this review, only two studies recruited patients with Qi insufficiency syndrome using syndrome differentiation methods. One study focused on systemic lupus erythematosus nephritis and reported that treatment effects of Astragalus were superior among people with Qi insufficiency syndrome. However, a study that also included people with Qi insufficiency syndrome and damp-heat found no positive effects associated with Astragalus in reducing proteinuria; some participants in this study also developed mouth ulcers (Su 2007). From the perspective of Chinese medicine, Astragalus is unsuitable for people with damp-heat syndrome. Possible differences between the effects of Astragalus on people with or without Qi insufficiency syndrome requires further research.

### Quality of the evidence

Because most included studies were published before the introduction of trial reporting standards in China, study reporting was poor. Study quality was also suboptimal overall. Since no measures were applied to study participants, possible differences in co-interventions between treatment and control groups was likely to have introduced performance and detection bias. Furthermore, lack of reporting baseline characteristics made it difficult to accurately assess the appropriateness of random allocation and baseline comparability.

### Potential biases in the review process

We applied a comprehensive search strategy, rigid and clear inclusion criteria, systematic data collection and analysis to assess the effectiveness of Astragalus for people with CKD.

Although we found that all included studies reported positive results, funnel plot analysis results indicated potential for publication bias. We are therefore unsure that the published body of evidence available at the time this review was conducted was fully representative of all safety and efficacy effects observed in relation to Astragalus for the treatment of people with CKD.

### Agreements and disagreements with other studies or reviews

We found no other reviews that assessed Astragalaus for treating people with CKD.

## AUTHORS' CONCLUSIONS

### Implications for practice

The evidence suggested that when used with conventional treatment, Astragalus may be beneficial for people with chronic kidney disease to reduce proteinuria and alleviate some complications such as anaemia and malnutrition. However, this conclusion was limited by poor reporting and generally low study quality. Further studies are needed to inform more definitive conclusions.

### Implications for research

Further studies designed to incorporate scientifically rigorous methodology are required before conclusions can confidently be reached about the effects of Astragalus for the treatment of people with CKD. The following aspects should be considered when designing studies:

1. Describe clearly the method of random allocation and allocation concealment
2. Design a placebo control and ensure the blinding effect during the study
3. Calculate the sample size to ensure that the study is sufficiently powered
4. Consider the issue of Qi insufficiency syndrome during study design
5. Apply some long-term outcome measurements, such as the need for commencement of dialysis or kidney transplantation; all-cause mortality, and quality of life; and
6. Clearly report any adverse effects observed during the study.

The elaborated CONSORT statement for reporting randomised controlled trials of herbal medicines should also be consulted (Gagnier 2006).

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## CHARACTERISTICS OF STUDIES

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

**Bi 2007**

| | |
|---|---|
| Methods | • Study design: parallel RCT<br>• Power calculation: no |
| Participants | • Country: Taiyuan, Shanxi Province, China<br>• Setting: hospital<br>• Patients aged ≥ 60 years; primary hypertension; continued hypertension (20/13.3 kPa) > 4 to 5 years before presentation of proteinuria; continued proteinuria or increased urine micro-albumin; retinal arteriosclerosis or retinal disease caused by arteriosclerosis<br>• Number: treatment group (40); control group (40)<br>• Mean age (range): 73.5 years (64 to 83)<br>• Sex (M/F): 45/35<br>• Exclusion criteria: cardiovascular, liver or haematological diseases; non-compliance |
| Interventions | Treatment group<br>• Astragalus<br>  ○ Huang qi: 20 mL in 250 mL liquid, IV, once/d<br>  ○ Treatment duration: 3 weeks<br>• Conventional treatment |


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**Bi 2007** *(Continued)*

| | |
|---|---|
| | Control group<br>• Conventional treatment<br>Conventional treatment<br>• Blood pressure and blood lipid control |
| Outcomes | • 24 hour urinary protein excretion |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Not reported |
| Allocation concealment (selection bias) | Unclear risk | Not reported |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Placebo control and blinding not described |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | No blinding of outcome assessment; however, physiological outcome measurements were unlikely to have been influenced by lack of blinding |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | No losses to follow-up. All participants were included in the analysis |
| Selective reporting (reporting bias) | Unclear risk | Limited outcome measures were reported; data were insufficient to enable assessment of risk of bias |
| Other bias | Unclear risk | Baseline data were not reported, although it was stated that there were no statistically significant differences in age, sex and other baseline characteristics between groups |

**Cheng 2001**

| | |
|---|---|
| Methods | • Study design: parallel RCT<br>• Power calculation: no |
| Participants | • Country: Hangzhou, Zhejiang Province, China<br>• Setting: hospital<br>• Patients with CKD<br>• Mean baseline SCr (μmol/L): treatment group (231.2); control group (318.9)<br>• Number: treatment group (30); control group (30)<br>• Mean age: 51.1 years<br>• Sex (M/F): 34/26<br>• Exclusion criteria: NS |


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**Cheng 2001** *(Continued)*

| | |
|---|---|
| Interventions | Treatment group<br>• Astragalus<br>  ○ Huang qi: 30 mL in 250 mL liquid, IV, once/d<br>  ○ Treatment duration: 20 days<br>• Conventional treatment<br>Control group<br>• Conventional treatment<br>Conventional treatment<br>• Dietary control<br>• Maintain water, electrolyte and acid-base balance, control blood pressure, and infection as required |
| Outcomes | • SCr<br>• 24 hour urinary protein excretion |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Not reported |
| Allocation concealment (selection bias) | Unclear risk | Not reported |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Placebo control and blinding not described |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | No blinding of outcome assessment; however, physiological outcome measurements were unlikely to have been influenced by lack of blinding |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | No losses to follow-up. All participants were included in the analysis |
| Selective reporting (reporting bias) | Unclear risk | Limited outcome measures were reported; data were insufficient to enable assessment of risk of bias |
| Other bias | High risk | A significant difference was found in the values of baseline SCr between treatment and control group participants |

**Li 2006**

| | |
|---|---|
| Methods | • Study design: parallel RCT<br>• Power calculation: no |
| Participants | • Country: Shijiazhuang, Hebei Province, China |


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**Li 2006** *(Continued)*

- Setting: hospital
- Patients with IgA nephropathy diagnosed by kidney biopsy in the past week
- Mean baseline SCr (μmol/L): treatment group (90.6); control group (95.8)
- Number: treatment group (47); control group (20)
- Mean age (range): 31.7 years (15 to 57)
- Sex (M/F): 41/26
- Exclusion criteria: secondary kidney diseased caused by systematic lupus erythematosus, diabetes mellitus, allergic purpura, or hepatitis B

| | |
|---|---|
| Interventions | Treatment group<br>• Astragalus<br>  ○ Huang qi: 40 mL in 250 mL 5% dextrose, IV, once/d<br>  ○ Treatment duration: 28 days<br>• Conventional treatment<br>Control group<br>• Conventional treatment<br>Conventional treatment<br>• Oral dipyridamole tablets 75 mg, three times daily; benazepril hydrochloride tablets 10 mg, once daily; or nifedipine controlled-release tablets 30 mg once daily |
| Outcomes | • SCr<br>• 24 hour urinary protein excretionAlbumin |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | High risk | Random allocation was indicated, but not described. There was a significant difference in participant numbers between groups, which was suggestive of suboptimal random allocation |
| Allocation concealment (selection bias) | High risk | Unsuccessful random allocation suggested |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Placebo control and blinding not described |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | No blinding of outcome assessment; however, physiological outcome measurements were unlikely to have been influenced by lack of blinding |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | No losses to follow-up. All participants were included in the analysis |
| Selective reporting (reporting bias) | Unclear risk | Limited outcome measures were reported; data were insufficient to enable assessment of risk of bias |


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**Li 2006** *(Continued)*

| | | |
|---|---|---|
| Other bias | Unclear risk | Baseline data were not reported, although it was stated that there were no statistically significant differences in baseline characteristics between groups |

**Li 2008**

| | |
|---|---|
| Methods | • Study design: parallel RCT<br>• Power calculation: no |
| Participants | • Country: Changchun, Jilin Province, China<br>• Setting: hosptial<br>• Patients with CKD + anaemia<br>• Mean baseline SCr (μmol/L): treatment group (593.4); control group (589.6)<br>• Number: treatment group (32); control group (24)<br>• Mean age (range): 41.7 years (21 to 71)<br>• Sex (M/F): 33/23<br>• Exclusion criteria: NS |
| Interventions | Treatment group<br>• Astragalus<br>  ○ Huang qi: 30 mL in 250 mL 5% dextrose (or 9% NaCl for patients with diabetic nephropathy) IV, once/d<br>  ○ Treatment duration: 2 months<br>• Conventional treatment<br>Control group<br>• Conventional treatment<br>Conventional treatment<br>• High quality, low protein diet<br>• Maintain water, electrolyte and acid-base balance<br>• Control blood pressure<br>• Haemodialysis or colon dialysis, and other symptomatic treatment<br>• Erythropoietin (EPO) 2000 U, 2 to 3 times/wk |
| Outcomes | • SCr<br>• Hb<br>• HCT |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Not reported |
| Allocation concealment (selection bias) | Unclear risk | Not reported |


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**Li 2008** *(Continued)*

| | | |
|---|---|---|
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Placebo control and blinding not described |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | No blinding of outcome assessment; however, physiological outcome measurements were unlikely to have been influenced by lack of blinding |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | No losses to follow-up. All participants were included in the analysis |
| Selective reporting (reporting bias) | Unclear risk | Limited outcome measures were reported; data were insufficient to enable assessment of risk of bias |
| Other bias | High risk | A significant difference in numbers of treatment and control group participants was suggestive of baseline imbalance. Baseline data were not reported |

**Liu 2002**

| | |
|---|---|
| Methods | • Study design: parallel RCT<br>• Power calculation: no |
| Participants | • Country: Shanghai, China<br>• Setting: hospital<br>• Patients with CKD<br>• Mean baseline SCr (μmol/L): treatment group (478.3); control group (462)<br>• Number: treatment group (24); control group (23)<br>• Mean age (range): 57.6 years (36 to 82)<br>• Sex (M/F): 31/16<br>• Exclusion criteria: NS |
| Interventions | Treatment group<br>• Astragalus<br>  ◦ Huang qi: 20 mL in 250 mL 5% dextrose or 9% NaCl, IV, once/d<br>  ◦ Treatment duration: 28 days<br>• Conventional treatment<br>Control group<br>• Conventional treatment<br>Conventional treatment<br>• High quality low protein and phosphorus diet<br>• Maintain water, electrolyte and acid-base balance<br>• Blood pressure and hyperglycaemia control |
| Outcomes | • SCr |
| Notes | |
| ***Risk of bias*** | |


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**Liu 2002** *(Continued)*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Not reported |
| Allocation concealment (selection bias) | Unclear risk | Not reported |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Placebo control and blinding not described |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | No blinding of outcome assessment; however, physiological outcome measurements were unlikely to have been influenced by lack of blinding |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | No losses to follow-up. All participants were included in the analysis |
| Selective reporting (reporting bias) | Unclear risk | Limited outcome measures were reported; data were insufficient to enable assessment of risk of bias |
| Other bias | Unclear risk | Baseline data were not reported, although it was stated that there were no statistically significant differences in age, sex and other baseline characteristics between groups |

**Miao 2002**

| | |
|---|---|
| Methods | • Study design: parallel RCT<br>• Power calculation: no |
| Participants | • Country: Jinan, Shandong Province, China<br>• Setting: hospital<br>• Patients with CKD<br>• Mean baseline SCr (μmol/L): treatment group (380.4); control group (377.2)<br>• Number: treatment group (); control group ()<br>• Mean age: 56.5 years<br>• Sex (M/F): 26/14<br>• Exclusion criteria: NS |
| Interventions | Treatment group<br>• Astragalus<br>  ○ Huang qi: 60 mL in 250 mL 5% dextrose, IV, once/d<br>  ○ Treatment duration: 1 month<br>• Conventional treatment<br>Control group<br>• Conventional treatment<br>Conventional treatment<br>• Low protein diet (0.6 to 0.8 g/kg/d) |


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**Miao 2002** *(Continued)*

| | |
|---|---|
| | • Compound amino acid, compound α-ketoacid, vitamin and iron supplements<br>• Decrease phosphorus absorption, correct elevated potassium and metabolic acidosis<br>• Restrict water and salt intake; correct hypovolaemia<br>• High retention enema with compound Chinese herbal medicine (including Da huang, Fu zi, Di ding, and fan xie ye) one to two hours, once/d |
| Outcomes | • SCr |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Not reported |
| Allocation concealment (selection bias) | Unclear risk | Not reported |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Placebo control and blinding not described |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | No blinding of outcome assessment; however, physiological outcome measurements were unlikely to have been influenced by lack of blinding |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | No losses to follow-up. All participants were included in the analysis |
| Selective reporting (reporting bias) | Unclear risk | Limited outcome measures were reported; data were insufficient to enable assessment of risk of bias |
| Other bias | Unclear risk | Baseline data were not reported, although it was stated that the groups were comparable |

**Su 2007**

| | |
|---|---|
| Methods | • Study design: parallel RCT<br>• Power calculation: no |
| Participants | • Country: Shanghai, China<br>• Setting: hospital<br>• Patients with SLE and kidney dysfunction; Qi insufficiency syndrome<br>• Number: treatment group (23); control group (20)<br>• Mean age (range): NS<br>• Sex (M/F): NS<br>• Exclusion criteria: severe heart, brain, or liver disease; kidney atrophy detected by ultrasound |
| Interventions | Treatment group<br>• Astragalus |


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**Su 2007** *(Continued)*

| | |
|---|---|
| | ◦ Huang qi: 20 mL in 250 mL 5% dextrose IV, once/d for 12 days, followed by 18 day break<br>◦ Treatment duration: 3 months<br>• Conventional treatment<br><br>Control group<br><br>• Conventional treatment<br><br>Conventional treatment<br><br>• Cyclophosphamide 0.8 g in 500 mL 5% dextrose IV, once/mo<br>• Prednisone with continued dose after the treatment of cyclophosphamide to the maintained dose of 5 mg/d |
| Outcomes | • 24 h proteinuria<br>• Albumin |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Not reported |
| Allocation concealment (selection bias) | Unclear risk | Not reported |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Placebo control and blinding not described |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | No blinding of outcome assessment; however, physiological outcome measurements were unlikely to have been influenced by lack of blinding |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | No losses to follow-up. All participants were included in the analysis |
| Selective reporting (reporting bias) | Unclear risk | Limited outcome measures were reported; data were insufficient to enable assessment of risk of bias |
| Other bias | Unclear risk | Baseline data were not reported, although it was stated that there were no statistically significant differences in baseline characteristics between groups |

**Sun 1989**

| | |
|---|---|
| Methods | • Study design: parallel RCT<br>• Power calculation: no |
| Participants | • Country: Nanjing, Jiangsu Province, China<br>• Setting: hospital<br>• Patients with chronic nephritis, including patients on CAPD |


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**Sun 1989** *(Continued)*

- Number: treatment group (41); control group (45)
- Mean age (range): 29 years (7 to 57)
- Sex (M/F): 37/69
- Exclusion criteria: NS

| | |
|---|---|
| Interventions | Treatment group<br>• Astragalus<br>  ○ Oral Huang qi decoction: 150 mL (prepared by boiling Astragalus 1.5 g/kg body weight with water), twice/d; then after 4 weeks, oral Huang qi solution 4 mL (from 4 g Huang qi), three times/d<br>  ○ Treatment duration: 2 months<br>• Conventional treatment<br>Control group<br>• Conventional treatment<br>Conventional treatment<br>• Low protein and low sodium diet (except CAPD patients) |
| Outcomes | • SCr<br>• CrCl<br>• 24 hour proteinuria<br>• Outcomes measured and end of treatment and at end of follow-up |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Not reported |
| Allocation concealment (selection bias) | Unclear risk | Not reported |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Placebo control and blinding not described |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | No blinding of outcome assessment; however, physiological outcome measurements were unlikely to have been influenced by lack of blinding |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | No losses to follow-up. All participants were included in the analysis |
| Selective reporting (reporting bias) | Unclear risk | Limited outcome measures were reported; data were insufficient to enable assessment of risk of bias |
| Other bias | Unclear risk | Participant baseline data not reported |


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**Tao 2001**

| | |
|---|---|
| Methods | • Study design: parallel RCT<br>• Power calculation: no |
| Participants | • Country: Nanjing, Jiangsu Province, China<br>• Setting: hospital<br>• Patients with chronic GN<br>• Number: treatment group 1 (30); treatment group 2 (30); control group (30)<br>• Mean age (range): 32 years (9 to 68)<br>• Sex (M/F): 52/38<br>• Exclusion criteria: NS |
| Interventions | Treatment group 1<br>• Astragalus<br>  ◦ Huang qi: injection 30 mL<br>• Panax notoginseng saponins: 0.4 g in 250 to 500 mL 5% dextrose for IV drip infusion, once/d<br>• CHM<br>• Treatment duration: 28 days<br>Treatment group 2<br>• Astragalus<br>  ◦ Huang qi: injection 30 mL<br>• CHM<br>• Treatment duration: 28 days<br>Control group<br>• Panax notoginseng saponins: 0.4 g in 250 to 500 mL 5% dextrose, IV, once/d<br>• CHM<br>• Treatment duration: 28 days<br>CHM<br>• Personalised Chinese herbal decoction |
| Outcomes | • SCr<br>• 24 hour urinary protein excretion<br>• TCH<br>• Albumin |
| Notes | • Only the Astragalus + Panax notoginseng saponins and Panax notoginseng saponins comparison was included in the meta-analysis |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Not reported |
| Allocation concealment (selection bias) | Unclear risk | Not reported |
| Blinding of participants and personnel (performance bias) | High risk | Placebo control and blinding not described |


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**Tao 2001** *(Continued)*

| | | |
|---|---|---|
| All outcomes | | |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | No blinding of outcome assessment; however, physiological outcome measurements were unlikely to have been influenced by lack of blinding |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | No losses to follow-up. All participants were included in the analysis |
| Selective reporting (reporting bias) | Unclear risk | Limited outcome measures were reported; data were insufficient to enable assessment of risk of bias |
| Other bias | Unclear risk | Administration of individualised Chinese herbal decoction as a co-intervention may have differed between treatment and control group participants. Participant baseline data were not reported, although it was stated that the groups were comparable |

**Wang 2000**

| | |
|---|---|
| Methods | • Study design: parallel RCT<br>• Power calculation: no |
| Participants | • Country: Shanghai, China<br>• Setting: hospital<br>• Patients on HD > 1 year<br>• Number: treatment group (30); control group (27)<br>• Mean age (range): 48.7 years (24 to 75)<br>• Sex (M/F): 35/22<br>• Exclusion criteria: NS |
| Interventions | Treatment group<br>• Astragalus<br>  ◦ Huang qi: 12 mL (24 g) in 100 mL 0.9% NaCl, IV, before the end of HD<br>  ◦ Treatment duration: 6 months<br>• HD<br>Control group<br>• HD<br>HD<br>• 4 hours/session, 3 times/wk |
| Outcomes | • Hb<br>• Albumin<br>• HCT |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|


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**Wang 2000** *(Continued)*

| | | |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Not reported |
| Allocation concealment (selection bias) | Unclear risk | Not reported |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Placebo control and blinding not described |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | No blinding of outcome assessment; however, physiological outcome measurements were unlikely to have been influenced by lack of blinding |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | No losses to follow-up. All participants were included in the analysis |
| Selective reporting (reporting bias) | Unclear risk | Limited outcome measures were reported; data were insufficient to enable assessment of risk of bias |
| Other bias | Unclear risk | Participant baseline characteristics were not reported |

**Wu 2008**

| | |
|---|---|
| Methods | • Study design: parallel RCT<br>• Power calculation: no |
| Participants | • Country: Shanghai, China<br>• Setting: hospital<br>• Non dialysis CKD patients; baseline mean CrCL 13.59 ± 7.38 mL/min<br>• Number: treatment group (30); control group (30)<br>• Mean age: 56.3 years<br>• Sex (M/F): 36/24<br>• Exclusion criteria: autoimmune disease; serious infection in the prevoius 2 weeks |
| Interventions | Treatment group<br>Astragalus<br>◦ Huang qi: 40 g, IV, once/d<br>◦ Treatment duration: 30 days<br>• Conventional treatment<br>Control group<br>• Conventional treatment<br>Conventional treatment<br>• Diet<br>• Maintain water, electrolyte and acid-base balance<br>• Control blood pressure and anaemia |
| Outcomes | • SCr |


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**Wu 2008** *(Continued)*

| | |
|---|---|
| | • Albumin |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Not reported |
| Allocation concealment (selection bias) | Unclear risk | Not reported |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Placebo control and blinding not described |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | No blinding of outcome assessment; however, physiological outcome measurements were unlikely to have been influenced by lack of blinding |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | No losses to follow-up. All participants were included in the analysis |
| Selective reporting (reporting bias) | Unclear risk | Limited outcome measures were reported; data were insufficient to enable assessment of risk of bias |
| Other bias | Unclear risk | Participant baseline data were not reported, although it was stated that data were comparable between groups |

**Xu 2008**

| | |
|---|---|
| Methods | • Study design: parallel RCT<br>• Power calculation: no |
| Participants | • Country: Shanghai, China<br>• Setting: hospital<br>• Patients with primary hypertension > 5 years before presentation of proteinuria; retinal atherosclerosis or arteriosclerotic retinopathy<br>• Number: treatment group (26); control group (22)<br>• Mean age (range): 63.5 years (52 to 71)<br>• Sex (M/F): 28/20<br>• Exclusion criteria: primary kidney disease; other secondary kidney disease |
| Interventions | Treatment group<br>• Astragalus<br>  ◦ Huang qi: 20 mL (40 g) in 250 mL 5% dextrose IV, once/d<br>  ◦ Treatment duration: 21 days<br>• Conventional treatment<br>Control group |


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**Xu 2008** *(Continued)*

| | |
|---|---|
| | • Conventional treatment<br><br>Conventional treatment<br><br>• High quality low protein and salt diet<br>• Oral telmisartan 80 mg and felodipine sustained release 5 mg, once/d<br>• Treatment of other symptoms |
| Outcomes | • GFR<br>• SBP<br>• DBP<br>• 24 hour urinary protein excretion |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | High risk | Randomisation achieved by sequencing by presentation at hospital |
| Allocation concealment (selection bias) | High risk | No allocation concealment |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Placebo control and blinding not described |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | No blinding of outcome assessment; however, physiological outcome measurements were unlikely to have been influenced by lack of blinding |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | No losses to follow-up. All participants were included in the analysis |
| Selective reporting (reporting bias) | Unclear risk | Limited outcome measures were reported; data were insufficient to enable assessment of risk of bias |
| Other bias | Unclear risk | Participant baseline data were not reported, although it was stated that there were no statistically significant differences in age, sex and other characteristics between groups |

**Yang 1997**

| | |
|---|---|
| Methods | • Study design: parallel RCT<br>• Power calculation: no |
| Participants | • Country: Qingzhou, Shandong Province, China<br>• Setting: hospital<br>• Patients with CKD, baseline mean SCr > 250 µmol/L, CrCl < 25.2 mL/min<br>• Number: treatment group (27); control group (24)<br>• Mean age: 38.2 years |


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**Yang 1997** *(Continued)*

- Sex (M/F): 27/24
- Exclusion criteria: NS

| | |
|---|---|
| Interventions | Treatment group<br>• Astragalus<br>  ○ Huang qi: 40 g decocted in water, administered orally, twice daily<br>  ○ Treatment duration: 2 months<br>• Conventional treatment<br>Control group<br>• Conventional treatment<br>Conventional treatment<br>• Captopril 25 mg, 3 times/d<br>• Symptomatic treatment, including increasing urine discharge and blood pressure control |
| Outcomes | • SCr |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Not reported |
| Allocation concealment (selection bias) | Unclear risk | Not reported |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Placebo control and blinding not described |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | No blinding of outcome assessment; however, physiological outcome measurements were unlikely to have been influenced by lack of blinding |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | No losses to follow-up. All participants were included in the analysis |
| Selective reporting (reporting bias) | Unclear risk | Limited outcome measures were reported; data were insufficient to enable assessment of risk of bias |
| Other bias | Unclear risk | Participants' baseline data were not reported |

**Yang 2005**

| | |
|---|---|
| Methods | • Study design: parallel RCT<br>• Power calculation: no |
| Participants | • Country: Guigang, Guangxi Province, China |


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**Yang 2005** *(Continued)*

- Setting: hospital
- Patients with CKD, baseline SCr 186 to 442 µmol/L, CrCL 50 to 20 mL/min
- Number: treatment group (30); control group (30)
- Mean age (range): 45.8 years (22 to 68)
- Sex (M/F): 34/26
- Exclusion criteria: NS

| | |
|---|---|
| Interventions | Treatment group<br>• Astragalus<br>  ○ Huang qi: 40 mL (80 g) in 250 mL 5% dextrose or 0.9% NaCl, IV, once/d<br>  ○ Treatment duration: 28 days<br>• Conventional treatment<br>Control group<br>• Conventional treatment<br>Conventional treatment<br>• High quality low protein (0.6 kg/d) diet<br>• Blood pressure, hyperglycaemia and infection control as required<br>• Maintain water, electrolyte and acid-base balance |
| Outcomes | • SCr |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Not reported |
| Allocation concealment (selection bias) | Unclear risk | Not reported |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Placebo control and blinding not described |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | No blinding of outcome assessment; however, physiological outcome measurements were unlikely to have been influenced by lack of blinding |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | No losses to follow-up. All participants were included in the analysis |
| Selective reporting (reporting bias) | Unclear risk | Limited outcome measures were reported; data were insufficient to enable assessment of risk of bias |
| Other bias | Unclear risk | Participant baseline data were not reported, although it was stated that there were no statistically significant differences in age, sex or other characteristics between groups |


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**Yao 2004**

| | |
|---|---|
| Methods | • Study design: parallel RCT<br>• Power calculation: no |
| Participants | • Country: Foshan, Guangdong Province, China<br>• Setting: hospital<br>• Patients with CKD undergoing HD, baseline SCr ≥ 442 µmol/L; anaemia, Hb < 70 g/L<br>• Number: treatment group (15); control group (14)<br>• Mean age (range): 46 years (21 to 69)<br>• Sex (M/F): 13/16<br>• Exclusion criteria: NS |
| Interventions | Treatment group<br>• Astragalus<br>  ○ Huang qi: 50 mL (100 g) in dialysis solution 2 to 3 times/wk<br>  ○ Treatment duration: 2 months<br>• Conventional treatment<br>Control group<br>• Conventional treatment<br>Conventional treatment<br>• HD 2 to 3 times/wk<br>• EPO 3000 U twice/wk<br>• Iron dextran tablet 150 mg/d |
| Outcomes | • Hb<br>• HCT<br>• SBP<br>• DBP |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Randomisation was stratified by haemoglobin level. The method to generate random numbers was not reported |
| Allocation concealment (selection bias) | Unclear risk | Not reported |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Placebo control and blinding not described |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | No blinding of outcome assessment; however, physiological outcome measurements were unlikely to have been influenced by lack of blinding |


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**Yao 2004** *(Continued)*

| | | |
|---|---|---|
| Incomplete outcome data (attrition bias) All outcomes | Low risk | No losses to follow-up. All participants were included in the analysis |
| Selective reporting (reporting bias) | Unclear risk | Limited outcome measures were reported; data were insufficient to enable assessment of risk of bias |
| Other bias | Unclear risk | Stratified randomisation reported, but baseline data were not reported |

**Zeng 2009**

| | |
|---|---|
| Methods | • Study design: parallel RCT<br>• Power calculation: no |
| Participants | • Country: Wuhan, Hubei Province, China<br>• Setting: hospital<br>• Patients with chronic GN; aged 20 to 27 years; Qi insufficiency syndrome of spleen and kidney (Pi Shen Qi Xu); proteinuria and 24 hour urinary protein excretion ≥ 150 mg; SBP 90 to 139 mm Hg, DBP 60 to 89 mm Hg; not received glucocorticoid, cytotoxic, ACEi or ARB therapies<br>• Number: treatment group (30); control group (30)<br>• Mean age: 35.2 years<br>• Sex (M/F): 33/27<br>• Exclusion criteria: CKD with CrCl < 80 mL/min or SCr > 134 µmol/L; serious oedema or skin rash; allergy to Astragalus; pregnant or lactating; cardiovascular disease, liver or haematopoietic system disease, or mental illness |
| Interventions | Treatment group<br>• Astragalus<br>  ○ Huang qi: 4 mL injected into acupoints of Zusanli (ST36) or Shenshu (BL23) on both sides of body on alternate days after deqi sensation was achieved, once/d<br>  ○ Treatment duration: 20 days<br>• Conventional treatment<br>Control group<br>• Conventional treatment<br>Conventional treatment<br>• High quality low protein and salt diet-<br>• 30 mL sulfotanshinone sodium in 100 mL 0.9% NaCl, IV, once/d<br>• Oral Jinshuibao capsule, three times/d<br>• Maintain water, electrolyte and acid-base balance; infection control as required |
| Outcomes | • SCr<br>• CrCl<br>• Albumin<br>• 24 hour urinary protein excretion |
| Notes | |
| ***Risk of bias*** | |


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**Zeng 2009** *(Continued)*

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | Random number table used |
| Allocation concealment (selection bias) | Unclear risk | Not reported |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Placebo control and blinding not described |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | No blinding of outcome assessment; however, physiological outcome measurements were unlikely to have been influenced by lack of blinding |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | No losses to follow-up. All participants were included in the analysis |
| Selective reporting (reporting bias) | Unclear risk | Limited outcome measures were reported; data were insufficient to enable assessment of risk of bias |
| Other bias | Low risk | Participants' baseline data were comparable; study appeared to be free of other sources of bias |

**Zhang 2001**

| | |
|---|---|
| Methods | • Study design: parallel RCT<br>• Power calculation: no |
| Participants | • Country: Pingdingshan, Henan Province, China<br>• Setting: hospital<br>• Patients with chronic GN<br>• Number: treatment group (43); control group (35)<br>• Mean age (range): NS<br>• Sex (M/F): 42/36<br>• Exclusion criteria: NS |
| Interventions | Treatment group<br>Astragalus<br>◦ Huang qi: 30 mL in 250 mL 5% dextrose, IV, once/d<br>◦ Treatment duration: 9 weeks active treatment, with 4 week intervals between each 3 week treatment block<br>• Conventional treatment<br>Control group<br>• Conventional treatment<br>Conventional treatment<br>• High quality low protein and phosphorus diet for participants with renal insufficiency |


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**Zhang 2001** *(Continued)*

| | |
|---|---|
| | • Blood pressure and infection control as required |
| Outcomes | • CrCl<br>• TCH |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Not reported |
| Allocation concealment (selection bias) | Unclear risk | Not reported |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Placebo control and blinding not described |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | No blinding of outcome assessment; however, physiological outcome measurements were unlikely to have been influenced by lack of blinding |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | No losses to follow-up. All participants were included in the analysis |
| Selective reporting (reporting bias) | Unclear risk | Limited outcome measures were reported; data were insufficient to enable assessment of risk of bias |
| Other bias | High risk | The large difference in the number of patients between treatment and control group may suggest baseline imbalance, and the baseline data were not present in the study. |

**Zhang 2003**

| | |
|---|---|
| Methods | • Study design: parallel RCT<br>• Power calculation: no |
| Participants | • Country: Tianjin, China<br>• Setting: hospital<br>• Patients with CKD, baseline SCr < 707 μmol/L, GFR > 10 mL/min<br>• Number: treatment group (43); control group (37)<br>• Mean age (range): 54.0 years (32 to 70)<br>• Sex (M/F): 49/31<br>• Exclusion criteria: HD or PD |
| Interventions | Treatment group<br>• Astragalus<br>o Huang qi 0.5 mL injected into acupoint Zusanli (ST36) or Shenshu (BL23) on both sides of body on alternate days after deqi sensation was achieved, once/d |


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**Zhang 2003** *(Continued)*

| | |
|---|---|
| | ○ Treatment duration: 30 days<br>• Conventional treatment<br><br>Control group<br><br>• Conventional treatment<br><br>Conventional treatment<br><br>• Low protein diet, high calorie diet<br>• Symptomatic treatment |
| Outcomes | • SCr<br>• CrCl<br>• Hb<br>• Albumin |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Not reported |
| Allocation concealment (selection bias) | Unclear risk | Not reported |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Placebo control and blinding not described |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | No blinding of outcome assessment; however, physiological outcome measurements were unlikely to have been influenced by lack of blinding |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | No losses to follow-up. All participants were included in the analysis |
| Selective reporting (reporting bias) | Unclear risk | Limited outcome measures were reported; data were insufficient to enable assessment of risk of bias |
| Other bias | Unclear risk | Participant baseline data were not reported, but it was stated that there were no statistically significant differences in age, sex and other baseline characteristics between groups. However, the numbers of treatment and control group participants differed |

**Zhang 2006**

| | |
|---|---|
| Methods | • Study design: parallel RCT<br>• Power calculation: no |
| Participants | • Country: Lishui, Zhejiang Province, China |


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**Zhang 2006** *(Continued)*

- Setting: hospital
- Patients on HD > 3 months
- Number: treatment group (30); control group (25)
- Mean age (range): 46.1 years (32 to 62)
- Sex (M/F): 32/23
- Exclusion criteria: history of infection, liver disease, angina pectoris, heart failure, or cancer; drinkers; smokers

| | |
|---|---|
| Interventions | Treatment group<br>• Astragalus<br>  ○ Huang qi: 20 mL in 20 mL 0.9% NaCl, slow IV infusion, 30 minutes before end of MHD<br>  ○ Treatment duration: 2 months<br>• Conventional treatment<br>Control group<br>• Conventional treatment<br>Conventional treatment<br>• HD for 4 to 5 hours, 2 to 3 times/wk<br>• Blood pressure and anaemia control<br>• Calcium supplements |
| Outcomes | • Albumin |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Not reported |
| Allocation concealment (selection bias) | Unclear risk | Not reported |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Placebo control and blinding not described |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | No blinding of outcome assessment; however, physiological outcome measurements were unlikely to have been influenced by lack of blinding |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | No losses to follow-up. All participants were included in the analysis |
| Selective reporting (reporting bias) | Unclear risk | Limited outcome measures were reported; data were insufficient to enable assessment of risk of bias |
| Other bias | Unclear risk | Baseline data were not present although it was stated that there was no statistically significant differences in age, sex and other baseline characteristics between groups |


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**Zhao 2010**

| | |
|---|---|
| Methods | • Study design: parallel RCT<br>• Power calculation: no |
| Participants | • Country: Jinzhong, Shanxi Province, China<br>• Setting: hospital<br>• Patients on HD 5 times, every 2 weeks; serum albumin < 30 g/L<br>• Number: treatment group (20); control group (20)<br>• Mean age (range): 48.8years (35 to 71)<br>• Sex (M/F): 21/19<br>• Exclusion criteria: infections, tumour or serious water electrolyte and acid-base imbalance |
| Interventions | Treatment group<br>• Astragalus<br>  ◦ Huang qi: 30 mL, IV, before MHD end, 10 x per month<br>  ◦ Treatment duration: 6 months<br>• Conventional treatment<br>Control group<br>• Conventional treatment<br>Conventional treatment<br>• High quality, low protein and salt diet<br>• HD for 4 to 5 hours, 5 times every 2 weeks<br>• Blood pressure and anaemia control as required |
| Outcomes | • Albumin |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Not reported |
| Allocation concealment (selection bias) | Unclear risk | Not reported |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Placebo control and blinding not described |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | No blinding of outcome assessment; however, physiological outcome measurements were unlikely to have been influenced by lack of blinding |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | No losses to follow up. All participants were included in the analysis |


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**Zhao 2010** *(Continued)*

| | | |
|---|---|---|
| Selective reporting (reporting bias) | Unclear risk | Limited outcome measures were reported; data were insufficient to enable assessment of risk of bias |
| Other bias | Low risk | Participant baseline data were reported. The study appeared to be free of other sources of bias |

**Zhou 2001**

| | |
|---|---|
| Methods | • Study design: parallel RCT<br>• Power calculation: no |
| Participants | • Country: Chongqing, China<br>• Setting: hospital<br>• CKD patients<br>• Mean baseline CrCl (mL/min): treatment group (43.7); control group (47.9)<br>• Number: treatment group (58); control group (30)<br>• Mean age (range): NS<br>• Sex (M/F): NS<br>• Exclusion criteria: patients receiving HD or PD |
| Interventions | Treatment group<br>• Astragalus<br>  ◦ Huang qi: 1 mL/kg in 250 mL 5% dextrose, IV, within 1.5 hours, once/d<br>  ◦ Treatment duration: 14 days<br>• Conventional treatment<br>Control group<br>• Conventional treatment<br>Conventional treatment<br>• Control diet and protein intake<br>• Symptomatic treatment |
| Outcomes | • CrCl<br>• 24 hour urinary protein excretion |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Not reported |
| Allocation concealment (selection bias) | Unclear risk | Not reported |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Placebo control and blinding not described |


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**Zhou 2001** *(Continued)*

| | | |
|---|---|---|
| Blinding of outcome assessment (detection bias) All outcomes | Unclear risk | No blinding of outcome assessment; however, physiological outcome measurements were unlikely to have been influenced by lack of blinding |
| Incomplete outcome data (attrition bias) All outcomes | Low risk | No losses to follow-up. All participants were included in the analysis |
| Selective reporting (reporting bias) | Unclear risk | Limited outcome measures were reported; data were insufficient to enable assessment of risk of bias |
| Other bias | High risk | a large difference in numbers of participants in the treatment and control groups may suggest baseline imbalance. Baseline data were not present in the study |

**Zhu 2003**

| | |
|---|---|
| Methods | • Study design: parallel RCT<br>• Power calculation: no |
| Participants | • Country: Rucheng, Hunan Province, China<br>• Setting: hospital<br>• Patients with chronic GN<br>• Mean baseline SCr (μmol/L): treatment group (326); control group (312)<br>• Number: treatment group (24); control group (24)<br>• Mean age: 31.9 years<br>• Sex (M/F): 21/27<br>• Exclusion criteria: NS |
| Interventions | Treatment group<br>Astragalus<br>◦ Huang qi: 40 mL (80 g) in 250 mL 5% dextrose for IV drip infusion, once/d<br>◦ Treatment duration: 28 days<br>• Conventional treatment<br>Control group<br>• Conventional treatment<br>Conventional treatment<br>• Low protein, low phosphorus high quality diet<br>• Administer drug for gastrointestinal dialysis or α-ketoacid<br>• Maintain water, electrolyte and acid-base balance and control blood pressure |
| Outcomes | • SCr<br>• 24 hour urinary protein excretion |
| Notes | |

***Risk of bias***

| Bias | Authors' judgement | Support for judgement |
|---|---|---|


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**Zhu 2003** *(Continued)*

| | | |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | Not reported |
| Allocation concealment (selection bias) | Unclear risk | Not reported |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Placebo control and blinding not described |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | No blinding of outcome assessment; however, physiological outcome measurements were unlikely to have been influenced by lack of blinding |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | No losses to follow-up. All participants were included in the analysis |
| Selective reporting (reporting bias) | Unclear risk | Limited outcome measures were reported, but there was insufficient information to enable assessment of relevant risk of bias |
| Other bias | Low risk | Participant baseline data were reported. The study appeared to be free of other sources of bias |

ACEi - angiotensin-converting enzyme inhibitor; ARB - angiotensin II receptor blocker; CAPD - continuous ambulatory peritoneal dialysis; CHM - Chinese herbal medicine; CKD - chronic kidney disease; CrCl - creatinine clearance; DBP - diastolic blood pressure; EPO - erythropoietin; GN - glomerulonephritis; Hb - haemoglobin; HCT - haematocrit; HD - haemodialysis; IV - intravenous; NaCl - sodium chloride; RCT - randomised controlled trial; SCr - serum creatinine; TCH - total circulating haemoglobin; TCM - traditional Chinese medicine

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

| Study | Reason for exclusion |
|---|---|
| Chen 2004a | Included patients with nephrotic syndrome |
| Cui 2000 | People without kidney disease were recruited to the control group |
| Gao 2006 | Treatment group intervention was Huang qi injection combined with sodium ferulate |
| Huang 2004 | Patients with nephrotic syndrome were included |
| Lu 1999 | Traditional Chinese medicine was used as the control |
| Qiu 2008 | Huang qi and sodium ferulate administered together as the intervention in the treatment group |
| Qu 2008 | Relevant outcome not reported |
| Qun 1999 | Relevant outcome not reported |
| Wang 2004 | Intervention was not Astragalus preparation |
| Wei 2006 | Intervention was not Astragalus preparation |
| Zhang 2005 | Included patients with nephrotic syndrome |


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| Study | Reason for exclusion |
|---|---|
| Zhu 2002 | Relevant outcome not reported |
| Zuo 2003 | Herbal extract injection was used as control intervention |

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

**Biao 1992**

| | |
|---|---|
| Methods | Unknown |
| Participants | Unknown |
| Interventions | Unknown |
| Outcomes | Unknown |
| Notes | Full text unavailable |

**Chen 1999**

| | |
|---|---|
| Methods | Unknown |
| Participants | Unknown |
| Interventions | Unknown |
| Outcomes | Unknown |
| Notes | Full text unavailable |

**Chen 2003**

| | |
|---|---|
| Methods | RCT |
| Participants | CKD patients |
| Interventions | Astragalus + conventional treatment vs. conventional treatment |
| Outcomes | SCr<br>CrCl |
| Notes | Treatment duration data were not reported. The authors were contacted for clarification, but a response had not been received during the drafting of this review |


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**Cui 2005**

| | |
|---|---|
| Methods | Quasi-RCT |
| Participants | CKD patients |
| Interventions | Astragalus + conventional treatment vs. conventional treatment |
| Outcomes | SCr<br>CrCl<br>24 h proteinuria |
| Notes | There was lack of agreement between tabulated and narrative reporting identified in the study report. The authors were contacted for clarification, but a response had not been received during the drafting of this review |

**Li 1999**

| | |
|---|---|
| Methods | Unknown |
| Participants | Unknown |
| Interventions | Unknown |
| Outcomes | Unknown |
| Notes | Full text unavailable |

**Peng 1999**

| | |
|---|---|
| Methods | Unknown |
| Participants | Unknown |
| Interventions | Unknown |
| Outcomes | Unknown |
| Notes | Full text unavailable |

**Yu 2002**

| | |
|---|---|
| Methods | Unknown |
| Participants | Unknown |
| Interventions | Unknown |
| Outcomes | Unknown |


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**Yu 2002** *(Continued)*

| | |
|---|---|
| Notes | Full text unavailable |

## DATA AND ANALYSES

### Comparison 1. Astragalus + conventional treatment versus conventional treatment alone

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Creatinine clearance: end of treatment | 4 | 306 | Mean Difference (IV, Random, 95% CI) | 5.75 [3.16, 8.34] |
| 2 Glomerular filtration rate [ mL/min/1.73 $m^2$] | 1 | | Mean Difference (IV, Random, 95% CI) | Totals not selected |
| 3 Serum creatinine: end of treatment | 13 | | Mean Difference (IV, Random, 95% CI) | Subtotals only |
| 3.1 All studies | 13 | 775 | Mean Difference (IV, Random, 95% CI) | -21.39 [-34.78, -8.00] |
| 3.2 Baseline SCr > 133 µmol/L | 10 | 588 | Mean Difference (IV, Random, 95% CI) | -49.20 [-80.07, -18.33] |
| 3.3 Baseline SCr < 133 µmol/L | 3 | 187 | Mean Difference (IV, Random, 95% CI) | -2.52 [-8.47, 3.42] |
| 3.4 Huang qi injection | 11 | 638 | Mean Difference (IV, Random, 95% CI) | -28.89 [-46.74, -11.05] |
| 3.5 Oral Huang qi decoction | 2 | 137 | Mean Difference (IV, Random, 95% CI) | -7.83 [-17.19, 1.54] |
| 4 Creatinine clearance: end of follow-up | 1 | | Mean Difference (IV, Random, 95% CI) | Totals not selected |
| 5 Serum creatinine: end of follow-up | 1 | | Mean Difference (IV, Random, 95% CI) | Totals not selected |
| 6 Proteinuria: end of treatment | 10 | | Mean Difference (IV, Random, 95% CI) | Subtotals only |
| 6.1 All studies | 10 | 640 | Mean Difference (IV, Random, 95% CI) | -0.53 [-0.79, -0.26] |
| 7 Proteinuria: end of follow-up | 1 | | Mean Difference (IV, Random, 95% CI) | Totals not selected |
| 8 Systolic blood pressure | 2 | 77 | Mean Difference (IV, Random, 95% CI) | -16.65 [-28.83, -4.47] |
| 9 Diastolic blood pressure | 2 | 77 | Mean Difference (IV, Random, 95% CI) | -6.02 [-10.59, -1.46] |


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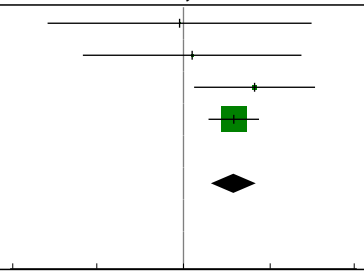
| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 10 Haemoglobin | 4 | | Mean Difference (IV, Random, 95% CI) | Subtotals only |
| 10.1 All studies | 4 | 222 | Mean Difference (IV, Random, 95% CI) | 9.51 [4.90, 14.11] |
| 10.2 Haemodialysis patients | 3 | 142 | Mean Difference (IV, Random, 95% CI) | 11.20 [5.81, 16.59] |
| 10.3 Non-dialysis patients | 1 | 80 | Mean Difference (IV, Random, 95% CI) | 4.91 [-3.97, 13.79] |
| 11 Haematocrit | 3 | | Mean Difference (IV, Random, 95% CI) | Subtotals only |
| 11.1 Haemodialysis patients | 3 | 142 | Mean Difference (IV, Random, 95% CI) | 5.91 [-0.99, 12.81] |
| 12 Albumin | 9 | | Mean Difference (IV, Random, 95% CI) | Subtotals only |
| 12.1 All studies | 9 | 522 | Mean Difference (IV, Random, 95% CI) | 3.55 [2.33, 4.78] |
| 12.2 Haemodialysis patients | 3 | 152 | Mean Difference (IV, Random, 95% CI) | 4.04 [1.91, 6.16] |
| 12.3 Non-dialysis patients | 6 | 370 | Mean Difference (IV, Random, 95% CI) | 3.24 [1.70, 4.77] |
| 13 Total cholesterol | 2 | 138 | Mean Difference (IV, Random, 95% CI) | -0.34 [-1.51, 0.83] |

**Analysis 1.1. Comparison 1 Astragalus + conventional treatment versus conventional treatment alone, Outcome 1 Creatinine clearance: end of treatment.**

| Study or subgroup | Astragalus N | Astragalus Mean(SD) | Control N | Control Mean(SD) | Mean Difference Random, 95% CI | Weight | Mean Difference Random, 95% CI |
|---|---|---|---|---|---|---|---|
| Zhou 2001 | 50 | 52.9 (37.1) | 38 | 53.3 (35.3) | | 2.89% | -0.45[-15.67,14.77] |
| Zhang 2001 | 42 | 92 (28.9) | 36 | 91 (27.8) | | 4.22% | 1[-11.6,13.6] |
| Zhang 2003 | 43 | 46.5 (19.4) | 37 | 38.3 (12) | | 13.78% | 8.2[1.23,15.17] |
| Zeng 2009 | 30 | 92.1 (5.6) | 30 | 86.3 (5.9) | | 79.11% | 5.8[2.89,8.71] |
| **Total *** ** | **165** | | **141** | | | **100%** | **5.75[3.16,8.34]** |

Heterogeneity: $Tau^2=0$; $Chi^2=1.66$, df=3(P=0.65); $I^2=0\%$

Test for overall effect: Z=4.35(P<0.0001)





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## Analysis 1.2. Comparison 1 Astragalus + conventional treatment versus conventional treatment alone, Outcome 2 Glomerular filtration rate [ mL/min/1.73 m²].

| Study or subgroup | Astragalus N | Astragalus Mean(SD) | Control N | Control Mean(SD) | Mean Difference Random, 95% CI | Mean Difference Random, 95% CI |
|---|---|---|---|---|---|---|
| Xu 2008 | 26 | 105.3 (12.4) | 22 | 101.2 (10.5) | | 4.1[-2.38,10.58] |

Favours control -20 -10 0 10 20 Favours Astragalus

## Analysis 1.3. Comparison 1 Astragalus + conventional treatment versus conventional treatment alone, Outcome 3 Serum creatinine: end of treatment.

| Study or subgroup | Astragalus N | Astragalus Mean(SD) | Control N | Control Mean(SD) | Mean Difference Random, 95% CI | Weight | Mean Difference Random, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.3.1 All studies** | | | | | | | |
| Cheng 2001 | 30 | 203.6 (60.4) | 30 | 303.1 (115.8) | | 5.78% | -99.55[-146.3,-52.8] |
| Li 2006 | 47 | 90.1 (21.2) | 20 | 90.9 (21) | | 17.24% | -0.88[-11.89,10.13] |
| Li 2008 | 32 | 421.2 (265.1) | 24 | 571.1 (254.3) | | 0.91% | -149.9[-286.97,-12.83] |
| Liu 2002 | 24 | 408.1 (124.1) | 23 | 438 (121.1) | | 3.07% | -29.9[-100.01,40.21] |
| Miao 2002 | 20 | 270.5 (220.9) | 20 | 306.5 (123.6) | | 1.36% | -35.98[-146.92,74.96] |
| Sun 1989 | 41 | 304.4 (21.2) | 45 | 312 (23.4) | | 17.79% | -7.6[-17.03,1.83] |
| Tao 2001 | 30 | 109 (40) | 30 | 107 (25) | | 14.89% | 2[-14.88,18.88] |
| Wu 2008 | 30 | 423.1 (113.1) | 30 | 462 (125) | | 3.93% | -38.9[-99.23,21.43] |
| Yang 1997 | 27 | 351.7 (137.3) | 24 | 376.9 (159.4) | | 2.34% | -25.2[-107.35,56.95] |
| Yang 2005 | 30 | 261.5 (86.5) | 30 | 338.6 (101.1) | | 5.63% | -77.1[-124.71,-29.49] |
| Zeng 2009 | 30 | 79.7 (15.5) | 30 | 84 (15.2) | | 18.31% | -4.3[-12.07,3.47] |
| Zhang 2003 | 43 | 398.2 (146.8) | 37 | 402.2 (198.6) | | 2.58% | -4[-81.59,73.59] |
| Zhu 2003 | 24 | 212 (76.5) | 24 | 282 (81) | | 6.17% | -70[-114.57,-25.43] |
| **Subtotal ***** | **408** | | **367** | | | **100%** | **-21.39[-34.78,-8]** |
| Heterogeneity: Tau²=239.12; Chi²=39.92, df=12(P<0.0001); I²=69.94% | | | | | | | |
| Test for overall effect: Z=3.13(P=0) | | | | | | | |
| **1.3.2 Baseline SCr > 133 µmol/L** | | | | | | | |
| Cheng 2001 | 30 | 203.6 (60.4) | 30 | 303.1 (115.8) | | 12.49% | -99.55[-146.3,-52.8] |
| Li 2008 | 32 | 421.2 (265.1) | 24 | 571.1 (254.3) | | 3.93% | -149.9[-286.97,-12.83] |
| Liu 2002 | 24 | 408.1 (124.1) | 23 | 438 (121.1) | | 9.2% | -29.9[-100.01,40.21] |
| Miao 2002 | 20 | 270.5 (220.9) | 20 | 306.5 (123.6) | | 5.37% | -35.98[-146.92,74.96] |
| Sun 1989 | 41 | 304.4 (21.2) | 45 | 312 (23.4) | | 17.22% | -7.6[-17.03,1.83] |
| Wu 2008 | 30 | 423.1 (113.1) | 30 | 462 (125) | | 10.49% | -38.9[-99.23,21.43] |
| Yang 1997 | 27 | 351.7 (137.3) | 24 | 376.9 (159.4) | | 7.81% | -25.2[-107.35,56.95] |
| Yang 2005 | 30 | 261.5 (86.5) | 30 | 338.6 (101.1) | | 12.36% | -77.1[-124.71,-29.49] |
| Zhang 2003 | 43 | 398.2 (146.8) | 37 | 402.2 (198.6) | | 8.31% | -4[-81.59,73.59] |

Favours Astragalus -500 -250 0 250 500 Favours control


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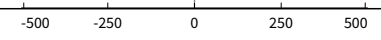
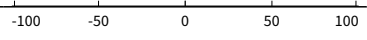
| Study or subgroup | Astragalus N | Astragalus Mean(SD) | Control N | Control Mean(SD) | Mean Difference Random, 95% CI | Weight | Mean Difference Random, 95% CI |
|---|---|---|---|---|---|---|---|
| Zhu 2003 | 24 | 212 (76.5) | 24 | 282 (81) | | 12.82% | -70[-114.57,-25.43] |
| **Subtotal ***** | **301** | | **287** | | | **100%** | **-49.2[-80.07,-18.33]** |
| Heterogeneity: $Tau^2$=1417.58; $Chi^2$=31.86, df=9(P=0); $I^2$=71.75% | | | | | | | |
| Test for overall effect: Z=3.12(P=0) | | | | | | | |
| **1.3.3 Baseline SCr < 133 µmol/L** | | | | | | | |
| Li 2006 | 47 | 90.1 (21.2) | 20 | 90.9 (21) | | 29.1% | -0.88[-11.89,10.13] |
| Tao 2001 | 30 | 109 (40) | 30 | 107 (25) | | 12.39% | 2[-14.88,18.88] |
| Zeng 2009 | 30 | 79.7 (15.5) | 30 | 84 (15.2) | | 58.5% | -4.3[-12.07,3.47] |
| **Subtotal ***** | **107** | | **80** | | | **100%** | **-2.52[-8.47,3.42]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=0.56, df=2(P=0.75); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=0.83(P=0.41) | | | | | | | |
| **1.3.4 Huang qi injection** | | | | | | | |
| Cheng 2001 | 30 | 203.6 (60.4) | 30 | 303.1 (115.8) | | 8.46% | -99.55[-146.3,-52.8] |
| Li 2006 | 47 | 90.1 (21.2) | 20 | 90.9 (21) | | 18.74% | -0.88[-11.89,10.13] |
| Li 2008 | 32 | 421.2 (265.1) | 24 | 571.1 (254.3) | | 1.56% | -149.9[-286.97,-12.83] |
| Liu 2002 | 24 | 408.1 (124.1) | 23 | 438 (121.1) | | 4.9% | -29.9[-100.01,40.21] |
| Miao 2002 | 20 | 270.5 (220.9) | 20 | 306.5 (123.6) | | 2.29% | -35.98[-146.92,74.96] |
| Tao 2001 | 30 | 109 (40) | 30 | 107 (25) | | 17.09% | 2[-14.88,18.88] |
| Wu 2008 | 30 | 423.1 (113.1) | 30 | 462 (125) | | 6.1% | -38.9[-99.23,21.43] |
| Yang 2005 | 30 | 261.5 (86.5) | 30 | 338.6 (101.1) | | 8.28% | -77.1[-124.71,-29.49] |
| Zeng 2009 | 30 | 79.7 (15.5) | 30 | 84 (15.2) | | 19.44% | -4.3[-12.07,3.47] |
| Zhang 2003 | 43 | 398.2 (146.8) | 37 | 402.2 (198.6) | | 4.19% | -4[-81.59,73.59] |
| Zhu 2003 | 24 | 212 (76.5) | 24 | 282 (81) | | 8.93% | -70[-114.57,-25.43] |
| **Subtotal ***** | **340** | | **298** | | | **100%** | **-28.89[-46.74,-11.05]** |
| Heterogeneity: $Tau^2$=410.64; $Chi^2$=39.73, df=10(P<0.0001); $I^2$=74.83% | | | | | | | |
| Test for overall effect: Z=3.17(P=0) | | | | | | | |
| **1.3.5 Oral Huang qi decoction** | | | | | | | |
| Sun 1989 | 41 | 304.4 (21.2) | 45 | 312 (23.4) | | 98.7% | -7.6[-17.03,1.83] |
| Yang 1997 | 27 | 351.7 (137.3) | 24 | 376.9 (159.4) | | 1.3% | -25.2[-107.35,56.95] |
| **Subtotal ***** | **68** | | **69** | | | **100%** | **-7.83[-17.19,1.54]** |
| Heterogeneity: $Tau^2$=0; $Chi^2$=0.17, df=1(P=0.68); $I^2$=0% | | | | | | | |
| Test for overall effect: Z=1.64(P=0.1) | | | | | | | |
| Test for subgroup differences: $Chi^2$=19.16, df=1 (P=0), $I^2$=79.13% | | | | | | | |




## Analysis 1.4. Comparison 1 Astragalus + conventional treatment versus conventional treatment alone, Outcome 4 Creatinine clearance: end of follow-up.

| Study or subgroup | Astragalus N | Astragalus Mean(SD) | Control N | Control Mean(SD) | Mean Difference Random, 95% CI | Mean Difference Random, 95% CI |
|---|---|---|---|---|---|---|
| Sun 1989 | 41 | 102 (38) | 45 | 54 (21) | | 48[34.85,61.15] |





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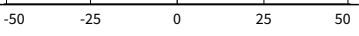
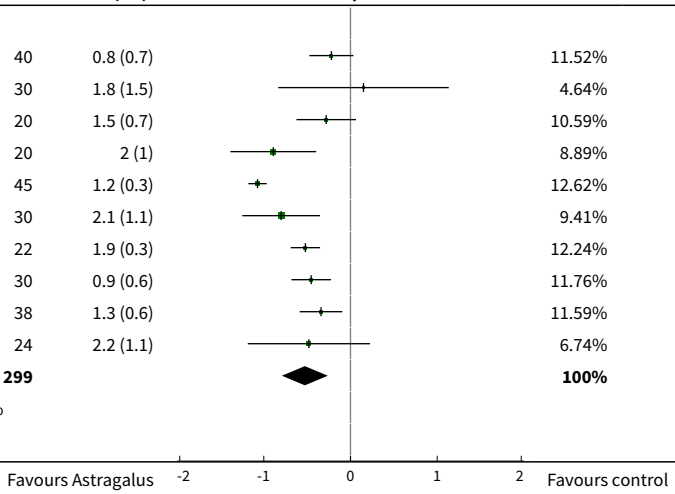
### Analysis 1.5. Comparison 1 Astragalus + conventional treatment versus conventional treatment alone, Outcome 5 Serum creatinine: end of follow-up.

| Study or subgroup | Astragalus N | Astragalus Mean(SD) | Control N | Control Mean(SD) | Mean Difference Random, 95% CI | Mean Difference Random, 95% CI |
|---|---|---|---|---|---|---|
| Sun 1989 | 41 | 297 (34.8) | 45 | 314 (20) | | -17[-29.15,-4.85] |




### Analysis 1.6. Comparison 1 Astragalus + conventional treatment versus conventional treatment alone, Outcome 6 Proteinuria: end of treatment.

| Study or subgroup | Astragalus N | Astragalus Mean(SD) | Control N | Control Mean(SD) | Mean Difference Random, 95% CI | Weight | Mean Difference Random, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.6.1 All studies** | | | | | | | |
| Bi 2007 | 40 | 0.6 (0.5) | 40 | 0.8 (0.7) | | 11.52% | -0.22[-0.47,0.03] |
| Cheng 2001 | 30 | 1.9 (2.3) | 30 | 1.8 (1.5) | | 4.64% | 0.15[-0.83,1.13] |
| Li 2006 | 47 | 1.2 (0.5) | 20 | 1.5 (0.7) | | 10.59% | -0.28[-0.62,0.06] |
| Su 2007 | 23 | 1.1 (0.6) | 20 | 2 (1) | | 8.89% | -0.89[-1.38,-0.4] |
| Sun 1989 | 41 | 0.1 (0.2) | 45 | 1.2 (0.3) | | 12.62% | -1.07[-1.18,-0.97] |
| Tao 2001 | 30 | 1.3 (0.6) | 30 | 2.1 (1.1) | | 9.41% | -0.8[-1.25,-0.35] |
| Xu 2008 | 26 | 1.3 (0.3) | 22 | 1.9 (0.3) | | 12.24% | -0.52[-0.69,-0.35] |
| Zeng 2009 | 30 | 0.4 (0.2) | 30 | 0.9 (0.6) | | 11.76% | -0.45[-0.68,-0.23] |
| Zhou 2001 | 50 | 0.9 (0.6) | 38 | 1.3 (0.6) | | 11.59% | -0.34[-0.59,-0.09] |
| Zhu 2003 | 24 | 1.7 (1.4) | 24 | 2.2 (1.1) | | 6.74% | -0.48[-1.18,0.22] |
| **Subtotal ***** | **341** | | **299** | | | **100%** | **-0.53[-0.79,-0.26]** |
| Heterogeneity: $Tau^2$=0.14; $Chi^2$=87.45, df=9(P<0.0001); $I^2$=89.71% | | | | | | | |
| Test for overall effect: Z=3.89(P<0.0001) | | | | | | | |



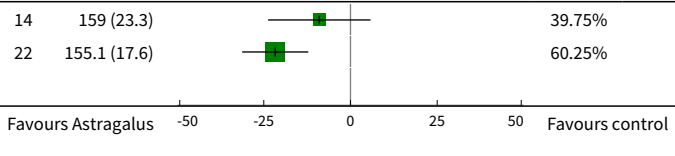

### Analysis 1.7. Comparison 1 Astragalus + conventional treatment versus conventional treatment alone, Outcome 7 Proteinuria: end of follow-up.

| Study or subgroup | Astragalus N | Astragalus Mean(SD) | Control N | Control Mean(SD) | Mean Difference Random, 95% CI | Mean Difference Random, 95% CI |
|---|---|---|---|---|---|---|
| Sun 1989 | 41 | 0.1 (0) | 45 | 1.2 (0.4) | | -1.12[-1.24,-0.99] |




### Analysis 1.8. Comparison 1 Astragalus + conventional treatment versus conventional treatment alone, Outcome 8 Systolic blood pressure.

| Study or subgroup | Astragalus N | Astragalus Mean(SD) | Control N | Control Mean(SD) | Mean Difference Random, 95% CI | Weight | Mean Difference Random, 95% CI |
|---|---|---|---|---|---|---|---|
| Yao 2004 | 15 | 150 (16.5) | 14 | 159 (23.3) | | 39.75% | -9[-23.77,5.77] |
| Xu 2008 | 26 | 133.4 (15.8) | 22 | 155.1 (17.6) | | 60.25% | -21.7[-31.24,-12.16] |





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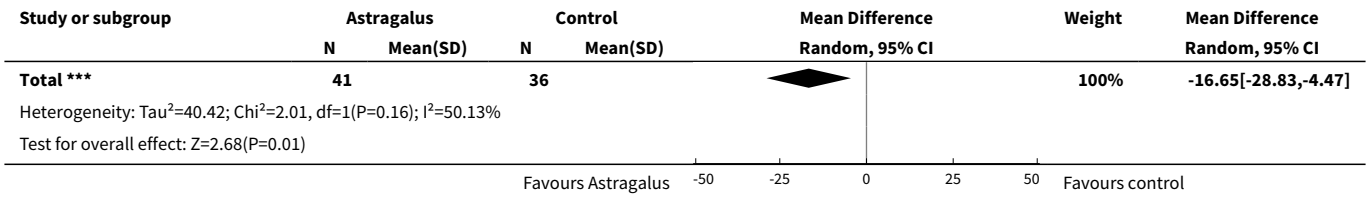
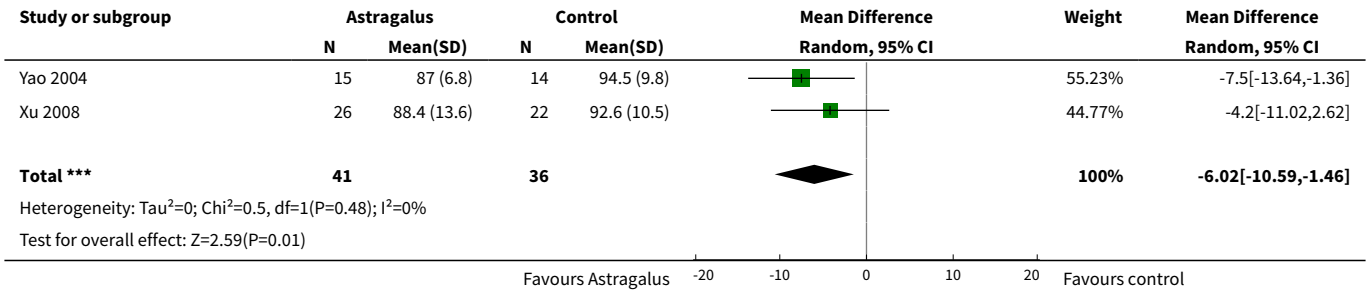
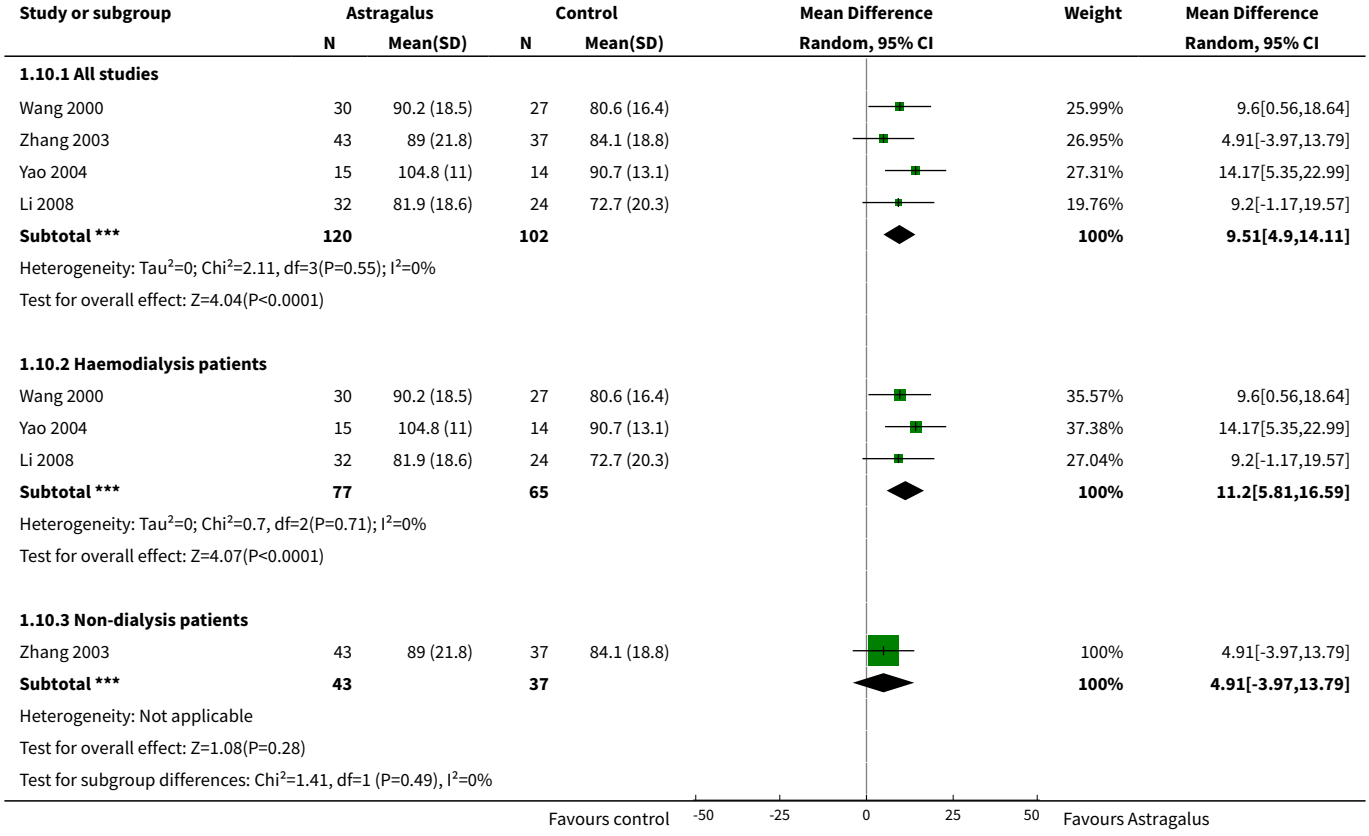



## Analysis 1.9. Comparison 1 Astragalus + conventional treatment versus conventional treatment alone, Outcome 9 Diastolic blood pressure.




## Analysis 1.10. Comparison 1 Astragalus + conventional treatment versus conventional treatment alone, Outcome 10 Haemoglobin.





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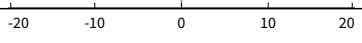
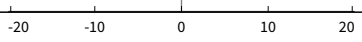
## Analysis 1.11. Comparison 1 Astragalus + conventional treatment versus conventional treatment alone, Outcome 11 Haematocrit.

| Study or subgroup | Astragalus N | Astragalus Mean(SD) | Control N | Control Mean(SD) | Mean Difference Random, 95% CI | Weight | Mean Difference Random, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.11.1 Haemodialysis patients** | | | | | | | |
| Wang 2000 | 30 | 24.3 (4.9) | 27 | 23.7 (4.1) | | 34.28% | 0.65[-1.68,2.98] |
| Yao 2004 | 15 | 30.9 (5) | 14 | 25 (5.7) | | 32.01% | 5.87[1.96,9.78] |
| Li 2008 | 32 | 35.8 (4.3) | 24 | 24.5 (5.9) | | 33.71% | 11.3[8.51,14.09] |
| **Subtotal ***** | **77** | | **65** | | | **100%** | **5.91[-0.99,12.81]** |
| Heterogeneity: $Tau^2$=34.7; $Chi^2$=33.05, df=2(P<0.0001); $I^2$=93.95% | | | | | | | |
| Test for overall effect: Z=1.68(P=0.09) | | | | | | | |




## Analysis 1.12. Comparison 1 Astragalus + conventional treatment versus conventional treatment alone, Outcome 12 Albumin.

| Study or subgroup | Astragalus N | Astragalus Mean(SD) | Control N | Control Mean(SD) | Mean Difference Random, 95% CI | Weight | Mean Difference Random, 95% CI |
|---|---|---|---|---|---|---|---|
| **1.12.1 All studies** | | | | | | | |
| Wang 2000 | 30 | 37.1 (4) | 27 | 34.8 (3.8) | | 12.54% | 2.34[0.33,4.35] |
| Tao 2001 | 30 | 33 (12) | 30 | 29 (13) | | 3.12% | 4[-2.33,10.33] |
| Zhang 2003 | 43 | 28.8 (3.3) | 37 | 27.9 (3.4) | | 14.93% | 0.9[-0.57,2.37] |
| Li 2006 | 47 | 35 (2.9) | 20 | 31.4 (2.2) | | 15.7% | 3.62[2.33,4.91] |
| Zhang 2006 | 30 | 37.1 (4) | 25 | 31.1 (3) | | 13.25% | 6.01[4.16,7.86] |
| Su 2007 | 23 | 34.8 (5.7) | 20 | 30 (7.2) | | 6.43% | 4.78[0.85,8.71] |
| Wu 2008 | 30 | 36.9 (4.3) | 30 | 34.1 (4.3) | | 11.89% | 2.8[0.63,4.97] |
| Zeng 2009 | 30 | 43.9 (5.5) | 30 | 38.2 (5.9) | | 9.27% | 5.65[2.77,8.53] |
| Zhao 2010 | 20 | 29.8 (3.2) | 20 | 26.1 (3.1) | | 12.86% | 3.67[1.73,5.61] |
| **Subtotal ***** | **283** | | **239** | | | **100%** | **3.55[2.33,4.78]** |
| Heterogeneity: $Tau^2$=2.05; $Chi^2$=23.16, df=8(P=0); $I^2$=65.46% | | | | | | | |
| Test for overall effect: Z=5.69(P<0.0001) | | | | | | | |
| **1.12.2 Haemodialysis patients** | | | | | | | |
| Wang 2000 | 30 | 37.1 (4) | 27 | 34.8 (3.8) | | 32.57% | 2.34[0.33,4.35] |
| Zhang 2006 | 30 | 37.1 (4) | 25 | 31.1 (3) | | 34.16% | 6.01[4.16,7.86] |
| Zhao 2010 | 20 | 29.8 (3.2) | 20 | 26.1 (3.1) | | 33.28% | 3.67[1.73,5.61] |
| **Subtotal ***** | **80** | | **72** | | | **100%** | **4.04[1.91,6.16]** |
| Heterogeneity: $Tau^2$=2.54; $Chi^2$=7.22, df=2(P=0.03); $I^2$=72.3% | | | | | | | |
| Test for overall effect: Z=3.73(P=0) | | | | | | | |
| **1.12.3 Non-dialysis patients** | | | | | | | |
| Tao 2001 | 30 | 33 (12) | 30 | 29 (13) | | 4.95% | 4[-2.33,10.33] |
| Zhang 2003 | 43 | 28.8 (3.3) | 37 | 27.9 (3.4) | | 24.55% | 0.9[-0.57,2.37] |
| Li 2006 | 47 | 35 (2.9) | 20 | 31.4 (2.2) | | 25.89% | 3.62[2.33,4.91] |
| Su 2007 | 23 | 34.8 (5.7) | 20 | 30 (7.2) | | 10.29% | 4.78[0.85,8.71] |
| Wu 2008 | 30 | 36.9 (4.3) | 30 | 34.1 (4.3) | | 19.36% | 2.8[0.63,4.97] |
| Zeng 2009 | 30 | 43.9 (5.5) | 30 | 38.2 (5.9) | | 14.96% | 5.65[2.77,8.53] |
| **Subtotal ***** | **203** | | **167** | | | **100%** | **3.24[1.7,4.77]** |
| Heterogeneity: $Tau^2$=1.93; $Chi^2$=12.87, df=5(P=0.02); $I^2$=61.15% | | | | | | | |





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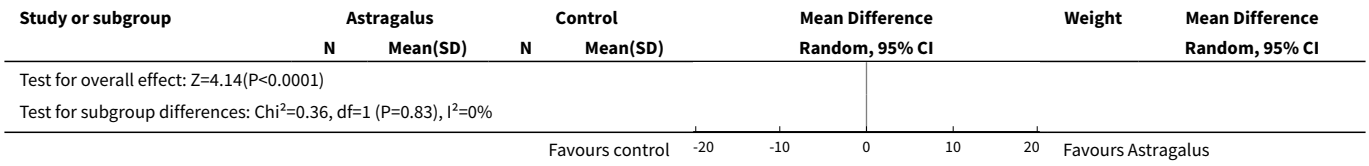
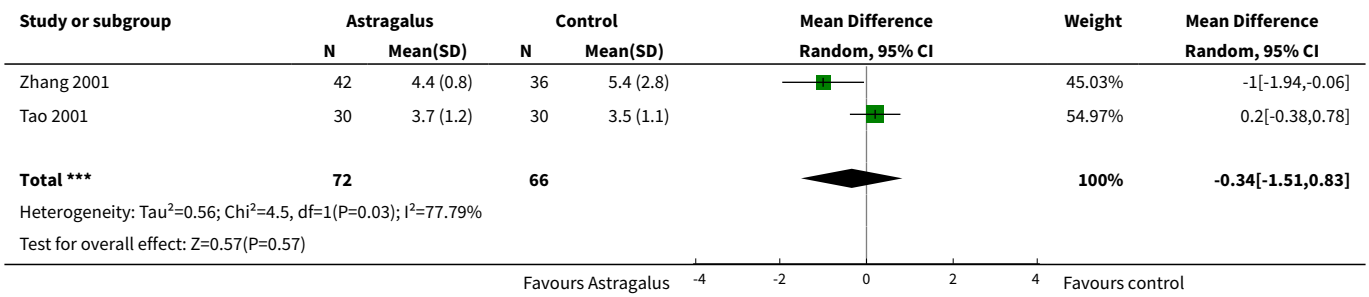



**Analysis 1.13. Comparison 1 Astragalus + conventional treatment versus conventional treatment alone, Outcome 13 Total cholesterol.**




## APPENDICES

### Appendix 1. Electronic search strategies

| Database | Search terms |
|---|---|
| CENTRAL | 1. dialysis:ti,ab,kw<br>2. (hemodialysis or haemodialysis):ti,ab,kw<br>3. (hemofiltration or haemofiltration):ti,ab,kw<br>4. (hemodiafiltration or haemodiafiltration):ti,ab,kw<br>5. (PD or CAPD or CCPD or APD):ti,ab,kw<br>6. ("end stage renal" or "end stage kidney" or "endstage renal" or "endstage kidney"):ti,ab,kw<br>7. (ESRF or ESKF or ESRD or ESKD):ti,ab,kw<br>8. ("chronic kidney" or "chronic renal"):ti,ab,kw<br>9. (CKF or CKD or CRF or CRD):ti,ab,kw<br>10.renal next insufficiency:ti,ab,kw<br>11.MeSH descriptor Renal Insufficiency, Chronic explode all trees<br>12.kidney diseases:kw<br>13.kidney failure:kw<br>14.ur*emi*:ti,ab,kw<br>15.(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14)<br>16.astragalus:ti,ab,kw<br>17.radix astragali:ti,ab,kw<br>18."huang qi":ti,ab,kw<br>19.huangqi:ti,ab,kw<br>20.(#16 OR #17 OR #18 OR #19)<br>21.(#15 AND #20) |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*(Continued)*

| | |
|---|---|
| MEDLINE | 1. exp Renal Dialysis/<br>2. (hemodialysis or haemodialysis).tw.<br>3. (hemofiltration or haemofiltration).tw.<br>4. (hemodiafiltration or haemodiafiltration).tw.<br>5. dialysis.tw.<br>6. (PD or CAPD or CCPD or APD).tw.<br>7. Renal Insufficiency/<br>8. exp Renal Insufficiency, Chronic/<br>9. Kidney Diseases/<br>10.Uremia/<br>11.(end-stage renal or end-stage kidney or endstage renal or endstage kidney).tw.<br>12.(ESRF or ESKF or ESRD or ESKD).tw.<br>13.(chronic kidney or chronic renal).tw.<br>14.(CKF or CKD or CRF or CRD).tw.<br>15.ur?emi$.tw.<br>16.or/1-15<br>17.exp Astragalus Plant/<br>18.astragalus.tw.<br>19.radix astragali.tw.<br>20.huang qi.tw.<br>21.huangqi.tw.<br>22.or/17-21<br>23.and/16,22 |
| EMBASE | 1. exp Renal Replacement Therapy/<br>2. (hemodialysis or haemodialysis).tw.<br>3. (hemofiltration or haemofiltration).tw.<br>4. (hemodiafiltration or haemodiafiltration).tw.<br>5. dialysis.tw.<br>6. (PD or CAPD or CCPD or APD).tw.<br>7. Kidney Disease/<br>8. Kidney Failure/<br>9. Chronic Kidney failure/<br>10.Chronic Kidney Disease/<br>11.Uremia/<br>12.(end-stage renal or end-stage kidney or endstage renal or endstage kidney).tw.<br>13.(ESRF or ESKF or ESRD or ESKD).tw.<br>14.(chronic kidney or chronic renal).tw.<br>15.(CKF or CKD or CRF or CRD).tw.<br>16.ur?emi$.tw.<br>17.or/1-16<br>18.Astragalus Plant/<br>19.Astragalus Membranaceus/<br>20.Astragalus Extract/<br>21.Astragalus Membranaceus Extract/<br>22.huang qi/<br>23.huangqi/<br>24.astragalus.tw.<br>25.radix astragali.tw.<br>26.huang qi.tw.<br>27.huangqi.tw. |


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(Continued)

| | |
|---|---|
| | 28.or/18-27<br>29.and/17,28 |
| AMED | 1. Hemodialysis/<br>2. dialysis.tw.<br>3. (hemodialysis or haemodialysis).tw.<br>4. (hemofiltration or haemofiltration).tw.<br>5. (hemodiafiltration or haemodiafiltration).tw.<br>6. (PD or CAPD or CCPD or APD).tw.<br>7. Kidney Disease/<br>8. Kidney Failure Chronic/<br>9. (end-stage renal or end-stage kidney or endstage renal or endstage kidney).tw.<br>10.(ESRF or ESKF or ESRD or ESKD).tw.<br>11.(chronic kidney or chronic renal).tw.<br>12.(CKF or CKD or CRF or CRD).tw.<br>13.ur?emi$.tw.<br>14.or/1-13<br>15.Astragalus/<br>16.astragalus.tw.<br>17.radix astragali.tw.<br>18.huang qi.tw.<br>19.huangqi.tw.<br>20.or/15-19<br>21.and/14,20 |
| CINAHL | S7 S3 AND S6<br><br>S6 S4 OR S5<br><br>S5 TI renal OR TI kidney* OR TI nephr* OR TI glomerul*<br><br>S4 (MH "Renal Insufficiency, Chronic+") OR (MH "Renal Insufficiency+")<br>OR (MH "Kidney Diseases+")<br><br>S3 S1 OR S2<br><br>S2 AB astragal* OR AB "huang qi" OR AB huangqi<br><br>S1 TI astragal* OR TI "huang qi" OR TI huangqi |
| CBM | 1. huangqi (Astragalus)<br>2. shen bing (Kidney disease) or shen shuai (kidney failure) or shen gong neng shuai jie (kidney function failure) or shen gong neng bu quan (kidney fucntion insufficiency) or niao du zheng (uremia) or dan zhi xue zheng (azotemia)<br>3. 1 and 2<br>4. lin chuang guan cha (clinical observation) or lin chuang yan jiu (clinical research) or liao xiao guan cha (effectiveness observation) or liao xiao yan jiu (effectiveness research) or lin chuang bao gao (clinical report) or lin chuang shi yan (clinical trial) or lin chuang ying yong (clinical application) or lin chuang ping gu (clinical assessment)<br>5. dui zhao (control) or dui bi (contrast) or bi jiao (compare) or fen zu (group)<br>6. sui ji (random) or mang fa (blindness) or dan mang (single-blindness) or shuang mang (double-blindness) or san mang (triple blinding) or an wei ji (placebo)<br>7. 4 or 5 or 6<br>8. 3 and 7<br>9. limit 8 to human |


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(Continued)

| | |
|---|---|
| | 10.tang niao bing shen bing (diabetic nephropathy) or shen bing zong he zheng (nephrotic syndrome). title<br>11.9 not 10 |
| CMCC | 1. huangqi (Astragalus).title or abstract or keyword<br>2. shen bing (Kidney disease) or shen shuai (kidney failure) or shen gong neng shuai jie (kidney function failure) or shen gong neng bu quan (kidney fucntion insufficiency) or niao du zheng (uremia) or dan zhi xue zheng (azotemia)<br>3. 1 and 2<br>4. 3 not animal<br>5. tang niao bing shen bing (diabetic nephropathy) or shen bing zong he zheng (nephrotic syndrome). title<br>6. 4 not 5 |
| TCMLARS | 1. huangqi (Astragalus)<br>2. shen bing (Kidney disease) or shen shuai (kidney failure) or shen gong neng shuai jie (kidney function failure) or shen gong neng bu quan (kidney fucntion insufficiency) or niao du zheng (uremia) or dan zhi xue zheng (azotemia)<br>3. 1 and 2<br>4. lin chuang guan cha (clinical observation) or lin chuang yan jiu (clinical research) or liao xiao guan cha (effectiveness observation) or liao xiao yan jiu (effectiveness research) or lin chuang bao gao (clinical report) or lin chuang shi yan (clinical trial) or lin chuang ying yong (clinical application) or lin chuang ping gu (clinical assessment)<br>5. dui zhao (control) or dui bi (contrast) or bi jiao (compare) or fen zu (group)<br>6. sui ji (random) or mang fa (blindness) or dan mang (single-blindness) or shuang mang (double-blindness) or san mang (triple blinding) or an wei ji (placebo)<br>7. 4 or 5 or 6<br>8. 3 and 7<br>9. limit 8 to human<br>10.tang niao bing shen bing (diabetic nephropathy) or shen bing zong he zheng (nephrotic syndrome). title<br>11.9 not 10 |
| Chinese Dissertation Database | 1. huangqi (Astragalus)<br>2. shen bing (Kidney disease) or shen shuai (kidney failure) or shen gong neng shuai jie (kidney function failure) or shen gong neng bu quan (kidney fucntion insufficiency) or niao du zheng (uremia) or dan zhi xue zheng (azotemia)<br>3. 1 and 2 |
| CMAC | 1. huangqi (Astragalus).title or abstract or keyword<br>2. shen bing (Kidney disease) or shen shuai (kidney failure) or shen gong neng shuai jie (kidney function failure) or shen gong neng bu quan (kidney fucntion insufficiency) or niao du zheng (uremia) or dan zhi xue zheng (azotemia)<br>3. 1 and 2<br>4. 3 not animal<br>5. tang niao bing shen bing (diabetic nephropathy) or shen bing zong he zheng (nephrotic syndrome). title6. 4 not 5 |
| Index to Taiwan Periodical literature system | 1. huangqi (Astragalus) |

## Appendix 2. Risk of bias assessment tool


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| Potential source of bias | Assessment criteria |
|---|---|
| **Random sequence generation**<br><br>Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence | *Low risk of bias:* Random number table; computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots; minimization (minimization may be implemented without a random element, and this is considered to be equivalent to being random). |
| | *High risk of bias:* Sequence generated by odd or even date of birth; date (or day) of admission; sequence generated by hospital or clinic record number; allocation by judgement of the clinician; by preference of the participant; based on the results of a laboratory test or a series of tests; by availability of the intervention. |
| | *Unclear:* Insufficient information about the sequence generation process to permit judgement. |
| **Allocation concealment**<br><br>Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment | *Low risk of bias:* Randomisation method described that would not allow investigator/participant to know or influence intervention group before eligible participant entered in the study (e.g. central allocation, including telephone, web-based, and pharmacy-controlled, randomisation; sequentially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes). |
| | *High risk of bias:* Using an open random allocation schedule (e.g. a list of random numbers); assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or non-opaque or not sequentially numbered); alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure. |
| | *Unclear*: Randomisation stated but no information on method used is available. |
| **Blinding of participants and personnel**<br><br>Performance bias due to knowledge of the allocated interventions by participants and personnel during the study | *Low risk of bias*: No blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding; blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken. |
| | *High risk of bias*: No blinding or incomplete blinding, and the outcome is likely to be influenced by lack of blinding; blinding of key study participants and personnel attempted, but likely that the blinding could have been broken, and the outcome is likely to be influenced by lack of blinding. |
| | *Unclear*: Insufficient information to permit judgement |
| **Blinding of outcome assessment**<br><br>Detection bias due to knowledge of the allocated interventions by outcome assessors. | *Low risk of bias:* No blinding of outcome assessment, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding; blinding of outcome assessment ensured, and unlikely that the blinding could have been broken. |
| | *High risk of bias:* No blinding of outcome assessment, and the outcome measurement is likely to be influenced by lack of blinding; blinding of outcome assessment, but likely that the blinding could have been broken, and the outcome measurement is likely to be influenced by lack of blinding. |
| | *Unclear:* Insufficient information to permit judgement |
| **Incomplete outcome data**<br><br>Attrition bias due to amount, nature or handling of incomplete outcome data. | *Low risk of bias:* No missing outcome data; reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias); missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size; missing data have been imputed using appropriate methods. |
| | *High risk of bias:* Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to |


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(Continued)

| | |
|---|---|
| | induce clinically relevant bias in intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size; 'as-treated' analysis done with substantial departure of the intervention received from that assigned at randomisation; potentially inappropriate application of simple imputation. |
| | *Unclear:* Insufficient information to permit judgement |
| **Selective reporting**<br><br>Reporting bias due to selective outcome reporting | *Low risk of bias:* The study protocol is available and all of the study's pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way; the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon). |
| | *High risk of bias:* Not all of the study's pre-specified primary outcomes have been reported; one or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. subscales) that were not pre-specified; one or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect); one or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis; the study report fails to include results for a key outcome that would be expected to have been reported for such a study. |
| | *Unclear:* Insufficient information to permit judgement |
| **Other bias**<br><br>Bias due to problems not covered elsewhere in the table | *Low risk of bias:* The study appears to be free of other sources of bias. |
| | *High risk of bias:* Had a potential source of bias related to the specific study design used; stopped early due to some data-dependent process (including a formal-stopping rule); had extreme baseline imbalance; has been claimed to have been fraudulent; had some other problem. |
| | *Unclear:* Insufficient information to assess whether an important risk of bias exists; insufficient rationale or evidence that an identified problem will introduce bias. |

## CONTRIBUTIONS OF AUTHORS

1. Draft the protocol: HWZ, ZXL
2. Study selection: HWZ, CSX
3. Extract data from studies: HWZ, CSX
4. Enter data into RevMan/check data entry: HWZ, CSX
5. Carry out the analysis: HWZ, CSX, ZXL
6. Interpret the analysis: HWZ, CSX, ZXL, CL, LSC
7. Draft the final review: HWZ, ZXL
8. Disagreement resolution: ZXL
9. Update the review: HWZ, CSX, ZXL

## DECLARATIONS OF INTEREST

None known.

## SOURCES OF SUPPORT

### Internal sources

- School of Chinese Medicine, The Chinese University of Hong Kong, Hong Kong.
- Medical Services Department, Yan Oi Tong, Hong Kong.

### External sources

- No sources of support supplied


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## DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We used progression of CKD, defined as CrCl increase or serum creatinine (SCr) decrease over 20% from baseline as the primary outcome in the protocol, because many trials conducted in China reported this outcome measure following the Guideline for Clinical Research on Developing New Chinese Medicine endorsed by the State Administration of Chinese Medicine.

## INDEX TERMS

### Medical Subject Headings (MeSH)

Astragalus propinquus [*chemistry]; Creatinine [blood]; Drugs, Chinese Herbal [adverse effects] [*therapeutic use]; Randomized Controlled Trials as Topic; Renal Dialysis; Renal Insufficiency, Chronic [blood] [*drug therapy]

### MeSH check words

Humans


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