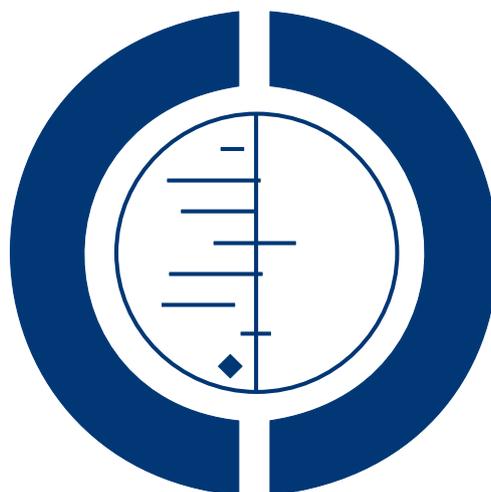


# Chinese herbal medicine for endometriosis (Review)

Flower A, Liu JP, Lewith G, Little P, Li Q



**THE COCHRANE  
COLLABORATION®**

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2012, Issue 5

<http://www.thecochranelibrary.com>

**WILEY**

## TABLE OF CONTENTS

HEADER . . . . .	1
ABSTRACT . . . . .	1
PLAIN LANGUAGE SUMMARY . . . . .	2
SUMMARY OF FINDINGS FOR THE MAIN COMPARISON . . . . .	3
BACKGROUND . . . . .	3
OBJECTIVES . . . . .	4
METHODS . . . . .	4
Figure 1. . . . .	6
Figure 2. . . . .	6
RESULTS . . . . .	8
DISCUSSION . . . . .	10
AUTHORS' CONCLUSIONS . . . . .	11
ACKNOWLEDGEMENTS . . . . .	11
REFERENCES . . . . .	12
CHARACTERISTICS OF STUDIES . . . . .	21
DATA AND ANALYSES . . . . .	32
Analysis 1.1. Comparison 1 CHM versus gestrinone, Outcome 1 Symptomatic relief. . . . .	34
Analysis 1.2. Comparison 1 CHM versus gestrinone, Outcome 2 Symptomatic relief rate (intention-to-treat). . . . .	34
Analysis 1.3. Comparison 1 CHM versus gestrinone, Outcome 3 Pregnant rate (accumulated from 3-24 months of follow-up). . . . .	35
Analysis 2.1. Comparison 2 CHM versus danazol, Outcome 1 Symptomatic relief. . . . .	36
Analysis 2.2. Comparison 2 CHM versus danazol, Outcome 2 Dysmenorrhea score. . . . .	37
Analysis 2.3. Comparison 2 CHM versus danazol, Outcome 3 Lumbosacral pain relief. . . . .	38
Analysis 2.4. Comparison 2 CHM versus danazol, Outcome 4 Rectal Irritation relief. . . . .	39
Analysis 2.5. Comparison 2 CHM versus danazol, Outcome 5 Tenderness of vaginal nodules in posterior fornix. . . . .	40
Analysis 2.6. Comparison 2 CHM versus danazol, Outcome 6 Adnexal masses disappearance or shrinkage. . . . .	41
Analysis 3.1. Comparison 3 CHM versus CHM, Outcome 1 Symptomatic relief. . . . .	42
Analysis 3.2. Comparison 3 CHM versus CHM, Outcome 2 Dysmenorrhea score. . . . .	42
Analysis 3.3. Comparison 3 CHM versus CHM, Outcome 3 Lumbosacral pain relief. . . . .	43
Analysis 3.4. Comparison 3 CHM versus CHM, Outcome 4 Rectal Irritation relief. . . . .	43
Analysis 3.5. Comparison 3 CHM versus CHM, Outcome 5 Tenderness of vaginal nodules in posterior fornix. . . . .	44
Analysis 3.6. Comparison 3 CHM versus CHM, Outcome 6 Adnexal masses disappearance or shrinkage. . . . .	44
APPENDICES . . . . .	44
WHAT'S NEW . . . . .	49
HISTORY . . . . .	50
CONTRIBUTIONS OF AUTHORS . . . . .	50
DECLARATIONS OF INTEREST . . . . .	50
SOURCES OF SUPPORT . . . . .	50
DIFFERENCES BETWEEN PROTOCOL AND REVIEW . . . . .	51
INDEX TERMS . . . . .	51

[Intervention Review]

# Chinese herbal medicine for endometriosis

Andrew Flower<sup>1</sup>, Jian Ping Liu<sup>2</sup>, George Lewith<sup>3</sup>, Paul Little<sup>4</sup>, Qing Li<sup>2</sup>

<sup>1</sup>Complementary Medicine Research Unit, Dept Primary Medical Care, Southampton University, Ringmer, UK. <sup>2</sup>Centre for Evidence-Based Chinese Medicine, Beijing University of Chinese Medicine, Beijing, China. <sup>3</sup>Visiting Professor, University of Westminster, Complementary Medicine Research Unit, Southampton, UK. <sup>4</sup>Department of Primary Care and Population Sciences Division, Faculty of Medicine, Aldermoor Health Centre, University of Southampton, Southampton, UK

Contact address: Andrew Flower, Complementary Medicine Research Unit, Dept Primary Medical Care, Southampton University, Norlington Gate Farmhouse, Norlington Lane, Ringmer, Sussex, BN8 5SG, UK. [flower.power@which.net](mailto:flower.power@which.net).

**Editorial group:** Cochrane Menstrual Disorders and Subfertility Group.

**Publication status and date:** New search for studies and content updated (no change to conclusions), published in Issue 5, 2012.

**Review content assessed as up-to-date:** 31 October 2011.

**Citation:** Flower A, Liu JP, Lewith G, Little P, Li Q. Chinese herbal medicine for endometriosis. *Cochrane Database of Systematic Reviews* 2012, Issue 5. Art. No.: CD006568. DOI: 10.1002/14651858.CD006568.pub3.

Copyright © 2012 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

## ABSTRACT

### Background

Endometriosis is characterized by the presence of tissue that is morphologically and biologically similar to normal endometrium in locations outside the uterus. Surgical and hormonal treatment of endometriosis have unpleasant side effects and high rates of relapse. In China, treatment of endometriosis using Chinese herbal medicine (CHM) is routine and considerable research into the role of CHM in alleviating pain, promoting fertility, and preventing relapse has taken place.

This review is an update of a previous review published in the Cochrane Database of Systematic Reviews 2009, issue No 3.

### Objectives

To review the effectiveness and safety of CHM in alleviating endometriosis-related pain and infertility.

### Search methods

We searched the Menstrual Disorders and Subfertility Group Trials Register, Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library*) and the following English language electronic databases (from their inception to 31/10/2011): MEDLINE, EMBASE, AMED, CINAHL, and NLH.

We also searched Chinese language electronic databases: Chinese Biomedical Literature Database (CBM), China National Knowledge Infrastructure (CNKI), Chinese Sci & Tech Journals (VIP), Traditional Chinese Medical Literature Analysis and Retrieval System (TCMLARS), and Chinese Medical Current Contents (CMCC).

### Selection criteria

Randomised controlled trials (RCTs) involving CHM versus placebo, biomedical treatment, another CHM intervention; or CHM plus biomedical treatment versus biomedical treatment were selected. Only trials with confirmed randomisation procedures and laparoscopic diagnosis of endometriosis were included.

### Data collection and analysis

Risk of bias assessment, and data extraction and analysis were performed independently by three review authors. Data were combined for meta-analysis using relative risk (RR) for dichotomous data. A fixed-effect statistical model was used, where appropriate. Data not suitable for meta-analysis were presented as descriptive data.

---

Chinese herbal medicine for endometriosis (Review)

Copyright © 2012 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

## **Main results**

Two Chinese RCTs involving 158 women were included in this review. Both these trials described adequate methodology. Neither trial compared CHM with placebo treatment.

There was no evidence of a significant difference in rates of symptomatic relief between CHM and gestrinone administered subsequent to laparoscopic surgery (95.65% versus 93.87%; risk ratio (RR) 1.02, 95% confidence interval (CI) 0.93 to 1.12, one RCT). The intention-to-treat analysis also showed no significant difference between the groups (RR 1.04, 95% CI 0.91 to 1.18). There was no significant difference between the CHM and gestrinone groups with regard to the total pregnancy rate (69.6% versus 59.1%; RR 1.18, 95% CI 0.87 to 1.59, one RCT).

CHM administered orally and then in conjunction with a herbal enema resulted in a greater proportion of women obtaining symptomatic relief than with danazol (RR 5.06, 95% CI 1.28 to 20.05; RR 5.63, 95% CI 1.47 to 21.54, respectively). Overall, 100% of women in all the groups showed some improvement in their symptoms.

Oral plus enema administration of CHM showed a greater reduction in average dysmenorrhoea pain scores than did danazol (mean difference (MD) -2.90, 95% CI -4.55 to -1.25;  $P < 0.01$ ). Combined oral and enema administration of CHM also showed a greater improvement measured as the disappearance or shrinkage of adnexal masses than with danazol (RR 1.70, 95% CI 1.04 to 2.78). For lumbosacral pain, rectal discomfort, or vaginal nodules tenderness, there was no significant difference between CHM and danazol.

## **Authors' conclusions**

Post-surgical administration of CHM may have comparable benefits to gestrinone but with fewer side effects. Oral CHM may have a better overall treatment effect than danazol; it may be more effective in relieving dysmenorrhoea and shrinking adnexal masses when used in conjunction with a CHM enema. However, more rigorous research is required to accurately assess the potential role of CHM in treating endometriosis.

## **PLAIN LANGUAGE SUMMARY**

### **Chinese herbs for endometriosis**

Endometriosis is a common gynaecological condition causing menstrual and pelvic pain. Treatment involves surgery and hormonal drugs, with potentially unpleasant side effects and high rates of reoccurrence of endometriosis. This review suggests that Chinese herbal medicine (CHM) may be useful in relieving endometriosis-related pain with fewer side effects than experienced with conventional treatment. However, the two trials included in this review are of poor methodological quality so these findings must be interpreted cautiously. Better quality randomised controlled trials are needed to investigate a possible role for CHM in the treatment of endometriosis.

## SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Study	Risk of bias	Number of participants	Comparisons	RR (95% CI)
Wu SZ 2006a	B-moderate	100	CHM (oral + enema) versus gestri- none	RR 1.02 (95% CI 0.93 to 1.12)
Wu SZ 2006b	B-moderate	58	CHM oral versus CHM oral+enema versus danazol	For 'symptomatic relief' CHM oral versus danazol RR 5.06 (95% CI 1.28 to 20.05) CHM oral+enema versus danazol RR 5.63 (95% CI 1.47 to 21.54)

## BACKGROUND

### Description of the condition

Endometriosis is a disease characterized by the presence of tissue that is morphologically and biologically similar to normal endometrium in ectopic locations outside the uterine cavity. Hormonally stimulated cyclical bleeding from the endometriotic deposit appears to contribute to the induction of a local inflammatory reaction and fibrous adhesion; and, in the case of deep implants in the ovary, leads to the formation of an endometrioma or chocolate cyst.

Endometriosis classically presents with severe dysmenorrhoea, pelvic pain, dyspareunia, menstrual irregularities, and infertility. Systemic symptoms may also occur, such as fatigue, increased incidence of allergies, and autoimmune disease (Ballweg 2004). Definitive diagnosis is usually made through laparoscopic investigation although recent research suggests that non-invasive symptom evaluation may have a greater positive prediction value (Ling 1999; Winkel 2003).

The precise prevalence of endometriosis is unclear but there is a broad consensus that between 5% to 15% of the female population will have signs and symptoms of the disease during their reproductive years (aged 15 to 50 years) (Eskenazi 1997; Stenchever 2001; Zondervan 2001).

Endometriosis is increasingly regarded as a complex, multi-factorial condition of uncertain aetiology where immunological (Ballweg 2004; Lebovic 2001; Sheng 1998), hormonal (Noble 1997), genetic (Bischoff 2004; Malinak 1980), environmental (Ballweg 2004; Ohtake 2003), and possibly even psychological (Low 1993; Strauss 1992) factors combine together to create a context for rogue endometrial cells to develop into a full-blown disease.

### Description of the intervention

The treatment of endometriosis can be broadly divided into medical or surgical management. Medical treatment ranges from symptomatic control with non-steroidal anti-inflammatory drugs (NSAIDs) and analgesics through to treatments that aim to suppress the normal ovarian production of estrogen by either hormonally simulating pregnancy (continuous oral contraceptives (COC) and progestins) or menopause (danazol and gonadotrophin-releasing hormone agonists (GnRH-a)). Surgical intervention can be either 'conservative', involving the removal of endometrial lesions or the severing of the nerve pathways responsible for the transmission of pelvic and uterine pain, or 'definitive', involving the removal of the uterus and ovaries.

Danazol, progestins, GnRH-a, and the COC have comparable short-term rates of success in alleviating the symptoms of endometriosis and in partially reducing the size of endometriosis-related lesions (GISG 1996; Moore 2004; Parazzini 2000; Prentice 2004; Selak 2007; Vercellini 1993). Unfortunately the benefits are poorly sustained over time with studies frequently reporting a high level of returning symptoms at six months post-treatment (Vercellini 1993). Even studies with more positive findings commonly demonstrate a return of symptoms in over a third of the women two to three years after stopping treatment (Biberoglu 1981; Dmowski 1998).

The short-term benefits of conventional medical treatment have to be balanced against the unpleasant and sometimes dangerous side effects resulting from these therapies. COC has been associated with increased thromboembolic risks (Anderson 2004). It is unsuitable for certain patient groups, such as women over the age of 35 years who smoke or who have a history of cardiovascular disease, and is obviously inappropriate for women trying to conceive. Danazol is associated with androgenic changes such as acne and weight gain, and menopausal symptoms such as flushing

and fatigue. Concerns raised have highlighted its potential role in raising low-density lipoprotein (LDL) cholesterol levels (Hughes 2004) and in possibly contributing to ovarian cancer (Cottreau 2003). GnRH-a tend to produce a more hypo-estrogenic state than danazol with more severe menopausal side effects such as hot flushes, insomnia, reduced libido, and vaginal dryness (Prentice 2004). Low estrogen levels can also cause serious osteoporosis and the long-term risks of add-back regimes using small amounts of progesterone and estrogen have not been adequately assessed as yet. Patients using progestin therapy reported a higher incidence of acne, fluid retention, bloating, and spotting. In addition, progestins are known to unfavourably reduce the level of high-density lipoproteins in the blood, which could potentially increase the risk of cardiovascular side effects such as thrombosis (Vasilakis 1999). The surgical management of endometriosis is also far from satisfactory. Two RCTs (Abbott 2004; Sutton 1994) and several observational studies (Abbott 2003; Fedele 2004; Wheeler 1983) demonstrate significant symptomatic relief after conservative laparoscopic surgery but in many cases these benefits were relatively short lived, with up to 44% of women experiencing a return of symptoms after one year (Lapp 2000). Surgery is also associated with the potential for serious side effects, with one study reporting that 2% to 3% of cases had post-operative bowel perforations with peritonitis (Koninckx 1996); an anonymous survey of 1951 gynaecologists revealed a significant number of unreported complications suggesting that the incidence of complications is higher than is commonly stated (Feste 1999).

In summary, current treatments all have high rates of reoccurrence and their short-term benefits have to be balanced with concerns over immediate and longer-term side effects.

### How the intervention might work

Chinese herbal medicine (CHM) is a system of medicine with an unbroken written tradition stretching back over two thousand years. Although endometriosis as a distinct entity did not exist in the classical tradition, the symptoms of dysmenorrhoea, dysuria, dyschezia, menorrhagia, and so on, were systematically differentiated and apparently well treated (Wu 1997). A common pattern underlying these conditions is the presence of what is known as stagnation of the blood and Qi (vital energy) causing localised obstructions and leading to pain. This is interestingly similar to the modern biomedical understanding of the central role that endometrial lesions play in the symptomatology of the disease.

We have recently seen increasing integration of western medicine and CHM in China, and in the past 10 years the use of laparoscopic diagnosis has allowed some evaluation of the specific benefits of CHM in the treatment of endometriosis through a number of clinical trials. For example, one Chinese language review identified 13 randomised clinical trials on CHM treatment of endometriosis from Chinese literature published between 1994 and 2000 (Xu et al 2004). In these trials 1076 women were involved and Chi-

nese herbal medicines were applied either alone or in combination with biomedical drugs. The suggested mechanism of Chinese medicine for endometriosis may involve regulation of endocrine and immune systems, improvement of blood circulation, and anti-inflammatory activity (Huang 2006; Xu et al 2004).

Whilst herbs might contain phyto-steroids these are considerably less potent than synthetic steroids. There are no reports of any androgenic or cholesterol raising adverse effects from herbs used in the treatment of endometriosis.

### Why it is important to do this review

At present no other English language systematic review has been conducted to evaluate the results of these studies. We have reviewed the available Chinese and English language literature on the subject in an attempt to establish whether CHM has a valid role in the treatment of this common and disabling condition.

## OBJECTIVES

To review the effectiveness and safety of CHM in alleviating endometriosis-related pain and infertility.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

Published and unpublished randomised controlled trials (RCTs) were eligible for inclusion. We excluded non-randomised studies (for example studies with evidence of inadequate methods of sequence generation such as alternate days, patient numbers) as they are associated with a high risk of bias. If any crossover trials were found, it was planned to include only data from the first phase, as the crossover is not a valid design in this context.

#### Types of participants

Trials including women of reproductive age with a laparoscopically confirmed diagnosis of endometriosis were eligible for inclusion.

#### Types of interventions

Trials comparing the following interventions were eligible for inclusion:

CHM versus placebo;

CHM versus conventional biomedical treatment;  
CHM plus conventional biomedical treatment versus conventional biomedical treatment alone;  
One CHM strategy versus a different CHM strategy.

## Types of outcome measures

### Primary outcomes

- Relief of endometriosis-related pain (both in the long term and short term)

### Secondary outcomes

- Improvement in fertility rates (live birth or pregnancy)
- Reduction in the size and extent of endometrial cysts
- Improvement in quality of life scores
- Improvement of endometriosis-related symptoms apart from pain (e.g. fatigue)
  - Adverse effects resulting from the CHM intervention
  - Rates of reoccurrence

It was our intention to investigate long-term outcomes (and several of the studies we had to reject reported on recurrence rates) but using the trials that were eligible for inclusion we were not able to fulfil this objective in terms of symptomatic relief. [Wu SZ 2006a](#) did have a 24 month follow up but this was to assess pregnancy outcomes.

## Search methods for identification of studies

We searched for all published and unpublished RCTs of CHM for endometriosis, without language restriction and in consultation with the Menstrual Disorders and Subfertility Group (MDSG) Trials Search Co-ordinator:

### Electronic searches

We searched the following on the 31/10/11:

- (1) Menstrual Disorders and Subfertility Group Trials Register;
- (2) Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library*) using the keywords: endometriosis, Chinese herbal medicine;
- (3) MEDLINE, EMBASE, AMED, CINAHL, and NLH English language electronic databases (from inception to the present); for a detailed search string see [Appendix 1](#);

(4) Chinese language electronic databases Chinese Biomedical Literature Database (CBM), China National Knowledge Infrastructure (CNKI), Chinese Sci & Tech Journals (VIP), Traditional Chinese Medical Literature Analysis and Retrieval System (TCMLARS), and Chinese Medical Current Contents (CMCC) using the following terms: *Zigong Neimo Yiwei Zheng* (endometriosis), *Chuantong Yiyao* (traditional medicine), *Zhong Yao* (Chinese medicine), *Cao Yao* (herbal medicine), *Tiqu Yao* (plant extract), *Buchong Yiyao* (complementary medicine).

### Searching other resources

JPL searched the Chinese language databases to identify trials that could be considered for inclusion in this review. AF did the same in the English language databases. We handsearched reference lists of articles retrieved by the search.

## Data collection and analysis

### Selection of studies

AF and SC (in the UK) and JPL (in China) independently reviewed the studies retrieved by the search and identified those eligible for inclusion. Owing to some confusion over the term 'randomised' in Chinese research papers, the authors of all papers considered suitable for inclusion were telephoned by JPL to confirm that proper randomisation procedures had been applied. GL and PL acted in an advisory capacity during this process. Any differences of opinion were resolved through discussion.

### Data extraction and management

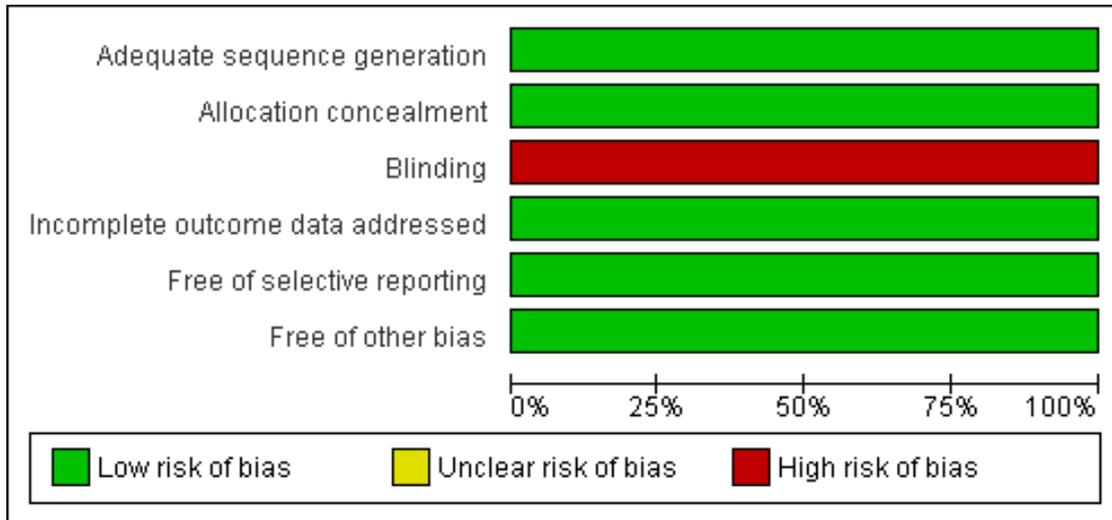
Two review authors independently extracted data from eligible studies, resolving any disagreements by discussion. Data extracted included study characteristics and outcome data.

### Assessment of risk of bias in included studies

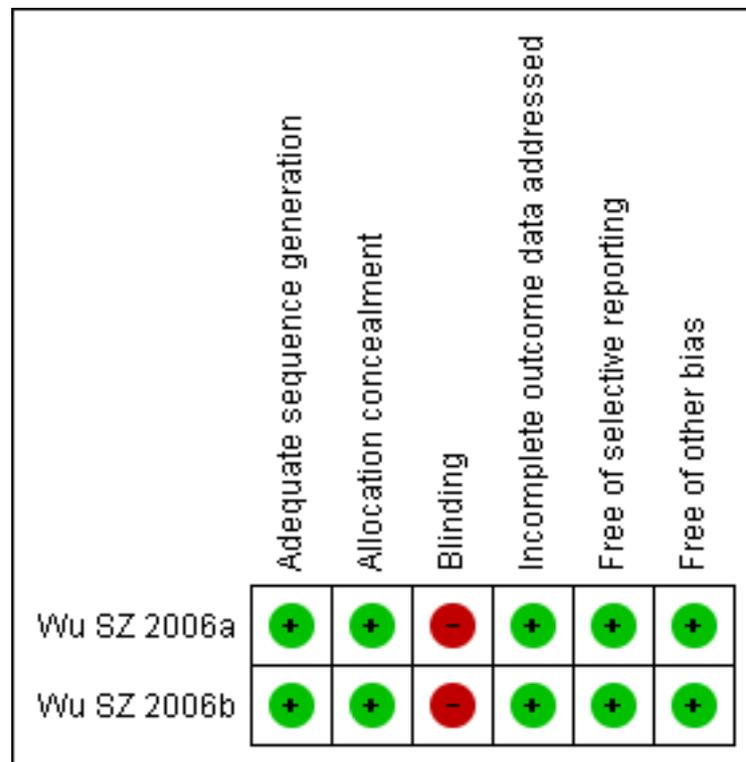
AF and SC (in the UK) and JPL (in China) independently reviewed the studies retrieved by the search and rated them using the Cochrane risk of bias assessment tool ([www.cochrane-handbook.org](http://www.cochrane-handbook.org)) to assess: selection bias (random sequence generation and allocation concealment); performance bias (blinding of participants and personnel); detection bias (blinding of outcome assessors); attrition bias (incomplete outcome data); reporting bias (selective reporting); and other sources of bias. Disagreements were resolved by discussion or by a third review author. GL and PL acted in an advisory capacity during this process.

See [Figure 1](#); [Figure 2](#)

**Figure 1. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.**



**Figure 2. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.**



Trials were assessed to determine how successfully selection, performance, detection, attrition, reporting and other biases were minimized.

**To minimize bias related to random sequence generation and allocation concealment (selection bias)**

- A clear and acceptable method of randomisation
- Quality of allocation concealment

**To minimize bias related to blinding (performance and detection bias)**

- Were the participants blinded?
- Were the outcome assessors blinded to the assignment status?

**To minimize bias related to incomplete outcome data (attrition bias)**

- A record of the number of randomised participants excluded or lost to follow up
- A record of treatment compliance
- An intention-to-treat analysis

**To minimize selective reporting (reporting bias)**

- Were the outcome measures used clearly defined and clearly and consistently reported?

**To minimize other bias**

- Comparable treatment and control groups at entry
- Confirmation that the care programmes, apart from the trial options, were identical

For each domain of bias, we assigned one of the following three judgements: low risk of bias, unclear risk of bias, or high risk of bias.

**Measures of treatment effect**

For dichotomous data we used the numbers of events in the control and intervention groups of each study to calculate risk ratios (RRs) and 95% confidence intervals (CIs).

For continuous data (for example quality of life), if all studies reported exactly the same outcomes we planned to calculate mean difference (MDs) between treatment groups; or, if similar outcomes were reported on different scales, to calculate the standardised mean difference (SMD). However, no continuous data were reported by the included studies.

**Unit of analysis issues**

Analysis was per woman randomised.

**Dealing with missing data**

The data were analysed on an intention-to-treat basis as far as possible and attempts were made to obtain missing data from the original trialists. Where data were unobtainable, it was planned that only the available data would be analysed.

**Assessment of heterogeneity**

We considered whether the clinical and methodological characteristics of the included studies were sufficiently similar for meta-analysis to provide a clinically meaningful summary. If pooling was undertaken we planned to assess statistical heterogeneity by the measure of the  $I^2$  statistic. An  $I^2$  measurement greater than 50% would be taken to indicate substantial heterogeneity (Higgins 2003; Higgins 2008). If we detected substantial heterogeneity, we planned to explore possible explanations in sensitivity analyses and to take any statistical heterogeneity into account when interpreting the results, especially if there was any variation in the direction of effect.

Only two trials (testing CHM against different conventional biomedical interventions) were eligible for this review so no assessment of statistical heterogeneity was undertaken (Higgins 2003).

**Assessment of reporting biases**

In view of the difficulty of detecting and correcting for publication bias and other reporting biases, the authors aimed to minimize their potential impact by ensuring a comprehensive search for eligible studies and by being alert for duplication of data. If there were 10 or more studies in an analysis, it was planned to use a funnel plot to explore the possibility of small study effects (a tendency for estimates of the intervention effect to be more beneficial in smaller studies).

**Data synthesis**

If the studies were sufficiently similar, we planned to combine the data using fixed-effect models in the following comparisons:

- CHM versus placebo;
- CHM versus conventional biomedical treatment;
- CHM plus conventional biomedical treatment versus conventional biomedical treatment alone;
- CHM strategy versus another CHM strategy.

Only two trials (testing CHM against different conventional medical interventions) were eligible for this review so no meta-analysis was undertaken (Higgins 2003).

**Subgroup analysis and investigation of heterogeneity**

If data were available, we planned to undertake subgroup analysis according to the type of intervention (for example type of biomedical treatment, type of CHM).

## Sensitivity analysis

If there were sufficient studies, we planned to conduct sensitivity analyses for the primary outcome to determine whether the review conclusions would have differed if eligibility were restricted to studies without high risk of bias.

## RESULTS

### Description of studies

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

### Results of the search

One hundred and ten trials were initially identified in the 2009 review. A further 39 were identified for the updated review in November 2010, and an updated search identified an additional 47 clinical trials in October 2011 using the search strategy described above. All of these trials took place in China and were reported in Chinese. However, no new trials were eligible to be included based on the previous inclusion criteria (see table 'Characteristics of excluded studies').

### Included studies

Only two trials ([Wu SZ 2006a](#); [Wu SZ 2006b](#)) were able to be included in this review. The trials took place in a hospital outpatient department in China and were reported in Chinese. They were presented in four publications: one trial was reported in three publications each describing different outcome measures ([Wu SZ 2006b](#)). The review authors were able to confirm adequate randomisation and they acquired more information about methods and data via telephone discussion.

### Participants

In total, 158 women were included in the two trials. The average age was 30 years (SD 4.5 years) with an age range of 23 to 45 years.

### Diagnostic criteria

Laparoscopic diagnosis and American Fertility Society (AFS) staging  
Vaginal or rectal B-ultrasound  
All participants were diagnosed according to traditional Chinese medicine as having Qi and blood stagnation with an underlying kidney deficiency.

## Herbal intervention

In one trial ([Wu SZ 2006b](#)), women were randomised into three groups: CHM endometriosis pills (Nei Yi Wan) (n = 16), CHM endometriosis pills (Nei Yi Wan) plus CHM enema (n = 24), or danazol (n = 18). In another trial, women were randomised into two groups: Nei Yi Wan plus herbal enema (n = 48) or gestrinone (n = 52) ([Wu SZ 2006a](#)).

## Herb formulation

Details of which herbs were used are included in the table [Characteristics of included studies](#).

## Comparisons and control groups

Chinese herbs were used in the active groups. Danazol or gestrinone were used in the control groups.

## Outcomes measured

The included trials used the same Chinese validated outcomes ([CAITWN 1991](#)) and divided responses to treatment into four categories: 'symptomatic relief' described a complete resolution of all symptoms and signs and included pregnancy, when desired, within three years of stopping treatment; 'significant improvement' described when most symptoms resolved and pelvic masses were reduced in size; 'improvement' described symptomatic improvement and no worsening of symptoms within three months of stopping the treatment but only minor or no change in pelvic masses; and finally 'no effect' was where symptoms either remained unchanged or worsened during the intervention.

Fertility rates were reported in one trial ([Wu SZ 2006a](#)).

The two trials reported the incidence of adverse effects as an outcome.

Data were also presented describing changes in the biochemical markers CA 125, a cancer antigen, and EmAb. Whilst these may reflect the measurable effects of an intervention and contribute to the biological plausibility of CHM, they are not considered in this review. Neither would they be considered as 'objective disease markers' in western gynaecological practice.

## Excluded studies

In the first analysis, 85 trials were excluded from the review for the following reasons: 43 trials did not have equal numbers in the experimental and control groups and did not present a clear account of the randomisation procedures leading to this discrepancy; 13 trials combined CHM with several other non-herbal therapeutic interventions (such as acupuncture) as part of the experimental intervention; 10 trials used non-authorised or experimental treatments such as mifepristone or tamoxifen as the control intervention; six trials did not report results using validated diagnostic criteria or outcomes measures; five trials had insufficient or unclear

data to enable a reasonable assessment of the trial; four trials did not consider the primary or secondary outcomes defined for this review; three trials were not RCTs; and one was a duplicate report. This left 25 randomised trials for consideration. However, insistence on a laparoscopic diagnosis and a new Cochrane requirement to contact all authors of Chinese RCTs to check for adequate randomisation procedures resulted in a second analysis where 12 trials were excluded because they did not have a laparoscopically confirmed diagnosis. Of the remaining 13 trials, 11 were excluded because: for three the authors could not be contacted; two authors refused to respond to questions relating to randomisation; three trials allocated participants according to patient preference; and three trials were quasi-randomised, according to the time of their first visit.

An updated search completed in October 2010 identified another 39 trials for consideration. Only five of these trials reported details of laparoscopic confirmation or randomisation. After phone call confirmations it was apparent that three of these papers did not employ adequate randomisation and for the remaining two trials the authors could not be contacted. As a result there has been no amendment to the previous findings of this review. An further updated search in October 2011 identified 47 trials, and only four trials appeared eligible for inclusion. After checking against inclusion criteria, they were all excluded and the reasons were presented in the table 'Characteristics of excluded studies'.

### Risk of bias in included studies

See [Figure 1](#); [Figure 2](#)

The included trials ([Wu SZ 2006a](#); [Wu SZ 2006b](#)) described adequate ('A') randomisation and allocation concealment methods using a random numbers generated randomisation sequence which was transferred to sealed envelopes. The trials also reported single blinding for participants, and assessor blinding. Both trials were given an overall 'B' status with a moderate risk of bias.

### Allocation

Both studies were rated as at low risk of this bias because they used acceptable methods of randomisation and allocation concealment.

### Blinding

Both studies were rated as at high risk of these biases because of the use of an active herbal enema without any inert control.

### Incomplete outcome data

Both studies were rated as at low risk of this bias because few or no participants were excluded from the analysis.

### Selective reporting

Both studies were rated as at low risk of this bias because they reported the expected outcomes.

### Other potential sources of bias

Both studies were rated as at low risk of other potential sources of bias.

### Effects of interventions

See: [Summary of findings for the main comparison CHM compared to gestrinone and danazol](#)

### Chinese herbal medicine versus gestrinone

Overall, 100% of women in both the CHM and the gestrinone groups showed some improvement in their symptoms. However, in some participants this may have been a relatively minor improvement in symptoms whilst in others it related to more substantial resolution of pelvic masses, disappearance of symptoms, and a successful pregnancy.

There was no significant difference between the CHM Nei Yi Wan (oral plus enema) and gestrinone for the symptomatic relief rate (95.65% versus 93.87%; RR 1.02, 95% CI 0.93 to 1.12) ([Wu SZ 2006a](#)). The intention-to-treat analysis also showed no significant difference between the groups for the symptomatic relief rate (RR 1.04, 95% CI 0.91 to 1.18). The study followed the patients for one to 24 months for pregnancy. The number of participants with confirmed pregnancy was 4 (at 3 months), 17 (at 4 to 6 months), 8 (at 7 to 12 months), 2 (at 13 to 24 months), and 1 (at over 24 months) in the CHM group; while it was 0, 12, 12, 3, and 2 in the gestrinone group, respectively. There was no significant difference between the two groups with regard to the total pregnancy rate (69.6% versus 59.1%; RR 1.18, 95% CI 0.87 to 1.59) ([Wu SZ 2006a](#)).

### Chinese herbal medicine versus danazol

In total, 100% of women in the CHM and danazol groups showed some improvement in their symptoms.

The CHM Nei Yi Wan and Nei Yi Wan plus enema groups reported a greater proportion of women obtaining symptomatic relief than for danazol (56.3% versus 11.1%; RR 5.06, 95% CI 1.28 to 20.05; and 62.5% versus 11.1%; RR 5.63, 95% CI 1.47 to 21.54, respectively) ([Wu SZ 2006b](#)).

Oral plus enema administration of the CHM Nei Yi formulation showed a greater reduction in average dysmenorrhoea pain scores than with danazol (MD -2.90, 95% CI -4.55 to -1.25;  $P < 0.01$ ). There were no significant differences between either CHM Nei Yi pills and danazol (MD -1.01, 95% CI -3.11 to 1.09) or CHM oral plus enema and danazol (MD -1.89, 95% CI -3.89 to 0.11).

Combined administration of CHM Nei Yi, orally and by enema, showed a greater improvement measured as the disappearance or shrinkage of adnexal masses than did treatment with danazol (RR 1.70, 95% CI 1.04 to 2.78). For lumbosacral pain, rectal discomfort, or vaginal nodules tenderness there was no significant difference either between CHM Nei Yi pills and danazol or between CHM oral plus enema and danazol (Comparisons 2.3 to 2.6).

### Adverse effects

No significant adverse effects were observed in the 46 participants who received CHM Nei Yi Wan plus CHM Nei Yi enema (Wu SZ 2006a). Thirteen out of 49 participants who received gestrinone developed acne, 19 developed increased glutamic alanine transaminase (GPT) levels (which returned to normal after termination of the treatment), and 31 had oligomenorrhoea (Wu SZ 2006a). In the second trial (Wu SZ 2006b), four patients had a dry mouth, and one patient had acne of the 16 patients who took CHM Nei Yi Wan; two patients had dry mouth, 11 had rectal tenesmus in the initial two weeks, and one had a weight gain of 3 kg in the 24 patients who received CHM oral plus enema. In contrast, in the danazol group 13/18 developed acne, 3/18 had a weight gain of 3 kg, 2/18 a weight gain of 2 kg, 1/18 a weight gain of 1.5 kg, 2/18 increased GPT levels, and 4/18 oligomenorrhoea.

## DISCUSSION

### Summary of main results

There are only very limited data available from two small trials comparing the same CHM interventions with two conventional treatments for endometriosis, danazol and gestrinone. The comparison of CHM with gestrinone showed no evidence of a difference between the two groups in the rates of symptomatic relief and pregnancy. However, there were fewer side effects in the CHM group than in the gestrinone group. It should be noted that the shrinkage of adnexal masses reported in these trials was determined by ultrasound investigation and not via laparoscopy.

### Overall completeness and applicability of evidence

There was an unexplained discrepancy in the rates of symptomatic relief between the two trials. Wu SZ 2006a reported a symptomatic relief rate for CHM of 95.65% and 93.87% for gestrinone; whilst Wu SZ 2006b reported symptomatic relief rates for oral CHM, oral plus enema CHM, and danazol of 56.3%, 62.5%, and 11.1%, respectively. Both trials used the same standardised assessment measures (CAITWN 1991), however discussion with

the authors revealed that in Wu SZ 2006a laparoscopic investigation and confirmation of endometriosis was combined with active surgical treatment for both groups whilst in Wu SZ 2006b laparoscopy was solely for diagnostic purposes. This explains the substantial difference in rates of symptomatic relief between the two groups but introduces a new variable into the analysis. In effect we have one trial (Wu SZ 2006a) comparing laparoscopic treatment with either gestrinone or CHM as a post-surgical adjuvant treatment and a second trial (Wu SZ 2006b) comparing purely medical interventions. Both trials reflect treatment options that are relevant to the management of endometriosis.

The completeness of the available data is limited by the tendency of Chinese reports to be restricted to two to three pages in length. These reports do not have the same depth of information required by Western journals. With regard to fertility, the papers do describe how many women are married and how many are sexually active but there are no relevant data on fertility (duration, clinical investigations etc). Other symptoms such as dyspareunia may be included in the overall analysis of symptoms but are not described as a separate outcome.

Fundamental to the understanding of endometriosis in Chinese medicine is the notion of stagnation of Qi, or vital energy, as a prerequisite for the subjective experience of pain; and of blood, which tends to localise and intensify the experience of pain and can lead to the formation of distinctive, substantial lesions. Differential diagnosis is further refined into a number of single or complex syndromes on the basis of information derived from traditional methods of clinical assessment such as tongue and pulse diagnosis, investigation of aetiological factors, the subjective presentation of the symptoms of endometriosis (for example a description of the nature and location of the pain), and an evaluation of the general health of the patient as evidenced from sleep patterns, digestive status, and subjective sense of temperature for example. This complex and involved process is considered essential to the successful treatment of the disease.

For a comprehensive introduction to Chinese medicine see Maciocia (Maciocia 1998).

### Quality of the evidence

There are no clear data on participant blinding during the trials. Although Wu SZ 2006a and Wu SZ 2006b claimed to be single blind trials, it is difficult to know how this was maintained in the group receiving the herbal enema. There was no evaluation of the success of blinding during the trials. This increased the risk of bias in the trials.

Many of the trials that were excluded due to poor methodology described the ability of CHM to act as an immunological and hormonal modulator, and to break down the fibrous adhesions that characterize endometriosis. These data are interesting and suggest biologically plausible mechanisms that could underpin the

effectiveness of CHM. However, a detailed analysis of this work is beyond the remit of this review.

### **Agreements and disagreements with other studies or reviews**

Compared with danazol, both the CHM groups produced a greater rate of symptomatic relief. However the confidence intervals for these outcomes were very large, which brings into question the reliability of the findings. The combined oral plus enema approach also led to women in the CHM group having a greater reduction of average dysmenorrhoea scores and more shrinkage of adnexal masses than for those taking danazol. There was no difference between the oral CHM group and the danazol group for any of these outcomes. There was no evidence of a difference between CHM and danazol in the relief of lumbosacral pain or rectal irritation. Women taking danazol exhibited considerably more adverse effects than did women taking CHM.

## **AUTHORS' CONCLUSIONS**

### **Implications for practice**

The included trials suggest that following laparoscopic surgery, combined oral and enema administration of CHM has a comparable beneficial effect to gestrinone but with fewer adverse effects. Oral and enema administration of CHM may be more effective than danazol in providing extended relief of endometriosis symptoms and in shrinking adnexal masses, with fewer adverse effects. However, these are two very small trials and it may not be possible to generalize the results.

Further research, with larger numbers of participants, is required to substantiate these results and to explore the role of CHM as a stand-alone medical option or as a post-surgical adjuvant in the treatment of endometriosis.

### **Implications for research**

Despite the large number of clinical trials exploring the role of CHM in the treatment of endometriosis methodological shortcomings have led to the exclusion of all but two trials. There are a number of reasons for these exclusions including no laparoscopic

confirmation of endometriosis, unequal group sizes, and a lack of validated outcomes. The most worrying shortcoming in the trial reports is a misunderstanding of what is required for a randomised controlled trial. The use of quasi-randomisation or allocation according to patient preference does not constitute adequate randomisation and allows an unacceptably high risk of bias in a trial. There is an urgent need for Chinese researchers to adopt rigorous standards of randomisation and allocation concealment and to present the data in a transparent fashion. The nature of CHM and herbal products make blinding problematic and CHM clinical trials may have to be more pragmatic. In addition, it was not clear from the trial reports that laparoscopy involved active treatment in one case whilst in the other it was used only for diagnostic purposes. This is poor quality reporting that has the potential to confuse and undermine CHM research.

It is important that transparent, pragmatic but rigorous clinical research methodologies are developed that accommodate the complex, individualised, and changing nature of CHM interventions. Future research should provide more detailed accounts of symptomatic changes to include, for example, dyspareunia and daily pelvic pain rather than amalgamating these symptoms into an overall measure of change. In addition, future research should incorporate quality of life outcome measures and qualitative research to provide a more detailed account of the effect of the CHM intervention on the lives of women suffering from this disease. Finally, it is also essential that any research investigating CHM for endometriosis incorporates an extended follow-up period to identify any long-term benefits and to make an accurate record of rates of recurrence after CHM treatment. This will be an important point of comparison between CHM and conventional medicine.

In the period between the original review in 2009 and the revised review in 2012 it appears that the methodological quality of clinical trials of CHM for endometriosis has not improved. This apparent lack of development is unfortunate as it continues to undermine the ability of CHM trials to contribute to rigorous systematic reviews.

## **ACKNOWLEDGEMENTS**

The authors wish to acknowledge the previous authors of this review title, Wang Hongjing, Dave Olive and Sisi Chen, and Yun Xia for helping with data extraction and analyses.

## REFERENCES

### References to studies included in this review

#### Wu SZ 2006a *{published data only}*

Wu SZ, Chen XL, Chen WZ, Li SY. Clinical analysis of the treatment of endometriosis using Nei Yi pills and Nei Yi enema. *Journal of Liaoning University of TCM* 2006;**8**(7): 5–6.

#### Wu SZ 2006b *{published data only}*

Wu SZ, Chen XL, Chen WZ. Clinical observation of Nei Yi pills combined with Nei Yi enema in the treatment of endometriosis. *Chinese Archives of TCM* 2006;**24**(3):431–3.

\* Wu SZ, Chen XL, Deng WH, Chen JF. Clinical observation of Nei Yi pills combined with Nei Yi enema in the treatment of endometriosis. *Journal of Guangzhou University of TCM* 2006;**23**(3):198–202.

Wu SZ, Chen XL, Huang YC, Liu CD. Observation on effect of combined therapy of Neiyi pill and Neiyi enema on endometriosis. *Chinese Journal of Integrated Traditional and Western Medicine* 2006;**26**(6):557–9.

### References to studies excluded from this review

#### Bian 2009 *{published data only}*

Bian WH, Du HL, Chen HJ, et al. Clinical research into the treatment of endometriosis using *bushen wenyang huayu* method [Bu shen wen yang hua yu fa zhi liao zi gong nei mo yi wei zheng de lin chuang yan jiu]. *Chinese General Practice* 2009;**12**(4B):695–7.

#### Cai 1999 *{published data only}*

Cai LS, Shu Y, Xie HY. Experimental clinical trial investigating the treatment of endometriosis with Dan E mixture. *Journal of Integrated Chinese and Western Medicine* 1999;**19**(3):159–61.

#### Chai H 1996 *{published data only}*

Chai H, Gu QC, Zhou SY, et al. Clinical investigation of the treatment of endometriosis using Huo Xue Tiao Jing method. *ACTA Chinese Medicine and Pharmacology* 1996;**1**: 19–20.

#### Chai LS 2004 *{published data only}*

Chai LS, Wu K, Yang JP, Pan YX. Observation of the clinical effectiveness of the treatment of endometriosis using Dan E Fu Kang Qian Gao. *Chinese Journal of Practical Obstetrics and Gynaecology* 2004;**20**(8):495–6.

#### Che 2006 *{published data only}*

\* Che CY, Yang XF. The treatment of endometriosis using a combination of Western and Chinese medicine in 30 patients [Zhong Xi Yi jie he zhi liao zi gong nei mo yi wei zheng 30 lie]. *TCM Research* 2006;**19**(8):33–4.

#### Chen 2003 *{published data only}*

Chen S. Clinical observation of TCM treatment of patients with endometriosis and dysmenorrhoea. *Liaoning Journal of TCM* 2003;**8**:17–8.

#### Chen 2006 *{published data only}*

Chen JY. Gui Zhi Fu Ling capsule and provera in the treatment of endometriosis [Gui Zhi Fu Ling jiao nong

he provera zhi liao zi gong nei mo yi wei zheng]. *Modern Journal of Integrated Traditional Chinese and Western Medicine* 2006;**15**(7):878.

#### Chen 2006a *{published data only}*

Chen D, Chen NR, Gou FL. Clinical observation of the effects of “Reduce endometriosis prescription” combined with ultrasound in 42 patients [“Xiao Yi Fang” pei he chao san zhi liao zi gong nei mo yi wei zheng 42 lie]. *Jiang Xi Journal of TCM* 2006;**5**:39–40.

#### Chen 2010 *{published data only}*

Chen J, Zhang X, Chen LS, et al. Clinical observation of the treatment of endometriosis of blood stasis type using laparoscope combined with *zhuyu tang* [Fu qiang jing pei he zi ni zhu yu tang zhi liao xue yu xing zi gong nei mo yi wei zheng de lin chuang guan cha]. *Journal of Chengdu University of Traditional Chinese Medicine* 2010;**33**(2): 29–32.

#### Chui YX *{published data only}*

Chui YX, Zheng XH. Clinical observation of the treatment of endometriosis using a combination of danazol and CHM [Dan Nan Xing yu zhong yao xiang he zi liao zi gong nei mo yi wei zheng de lin chuang guan cha]. *Chinese Journal of Primary Medicine and Pharmacy* 1999;**6**(3):172.

#### Cui 2010 *{published data only}*

Cui YL, Lu YQ. Clinical observation of the treatment of endometriosis related infertility using chinese herbs combined with laparoscope in 34 patients [Zhong yao jie he fu qiang jing zhi liao 34 li zi gong nei mo yi wei zheng xing bu yun de lin chuang guan cha]. *Clinical Research of Traditional Chinese Medicine* 2010;**2**(12):107–8.

#### Fan 2003 *{published data only}*

Fan JB, Qu Q, Zhong L. The treatment of endometriosis in 60 patients using a combination of western and Chinese medicine [Zhong Xi Yi jie he zhi liao zi gong nei mo yi wei zheng 60 lie]. *ShangXi Journal of TCM* 2003;**21**(11): 969–70.

#### Fang 2003 *{published data only}*

Fang DL. Clinical observation of the treatment of endometriosis using Xue Fu Zhu Yu Tang. *Anhui Journal of Clinical TCM* 2003;**15**(4):297–8.

#### Fan HX 2004 *{published data only}*

Fan HX, Wang XJ. Clinical observation of the treatment of endometriosis by replenishing Qi and promoting blood circulation decoction. *Tianjin Journal of TCM* 2004;**21**(4): 287–9.

#### Fei 2004 *{published data only}*

Fei MJ. Clinical observation of the treatment of endometriosis using a combination of Gui Zhi Fu Ling Wan and Shen Qi pills. *Chinese Journal of Integrated Traditional and Western Medicine* 2004;**24**(9):859–60.

#### Fei 2009 *{published data only}*

Fei MJ. Observation of effectiveness of chinese herbs dominated in the treatment of endometriosis [Zhong yao

- wei zhu zhi liao zi gong nei mo yi wei zheng liao xiao guan cha]. *Journal of Liaoning University of Traditional Chinese Medicine* 2009;**11**(1):110–1.
- Fong 2004** *{published data only}*  
Fong GF. Clinical observation of the treatment of endometriosis with a combination of western and Chinese medicine [Zhong Xi Yi jie he zhi liao zi gong nei mo yi wei zheng guan cha]. *Modern Journal of Traditional Chinese and Western Medicine*. 2004;**13**(16):10.
- Fong 2006a** *{published data only}*  
Fong DL, Liu GY. Clinical observation of the treatment of endometriosis related dysmenorrhoea using oral CHM and CHM enema [Zhong Yao nei fu jia guan chang zhi liao zi gong nei mo yi wei zheng tong jing lin chuang guan cha]. *Journal of Liaoning University of TCM* 2006;**8**(7):88.
- Fong DL 2006** *{published data only}*  
Fong DL, Liu GY. Clinical observation of the treatment of endometriosis using oral Chinese herbal medicine and an enema. *Journal of Liaoning University of TCM* 2006;**8**(7):88–9.
- Fu 2005** *{published data only}*  
Fu Y, Xia T. Clinical observation of the treatment of endometriosis using acupuncture and CHM [Zhen yao bing yong zhi liao zi gong nei mo yi wei zheng lin chuang guan cha]. *Shanghai Journal of Acupuncture* 2005;**24**(3):3–5.
- Gao 2003** *{published data only}*  
Gao S, Wang H. Clinical observation of the use of Nei Yi Xiao Zheng pill and Tong Jing Wan in the treatment of endometriosis [Nei Yi Xiao Zheng Wan he Tong Jing Wan zhi liao zi gong nei mo yi wei zheng de lin chuang guan cha]. *Journal of Combined Traditional Chinese and Western Medicine* 2003;**23**(1):31.
- Gu 2005** *{published data only}*  
Gu X. Discussion on the differentiation and treatment of endometriosis according to Chinese medicine [Lun Zhong yi bian zheng zhi liao zi gong nei mo yi wei zheng]. *Journal of Materia Medica Research* 2005;**16**(9):911–2.
- Han 2001** *{published data only}*  
Han HL, Hou XP. The treatment of endometriosis using a combination of western and Chinese medicine in 40 patients [Zhong Xi Yi jie he zhi liao zi gong nei mo yi wei zheng 40 lie]. *Chinese Archives of TCM* 2001;**19**:398.
- Hao 2009** *{published data only}*  
Hao GL, Zhang C. Analysis of the effectiveness of using a combination of chinese and western medicine to treat endometriosis [Zhong xi yi jie he zhi liao zi gong nei mo yi wei zheng liao xiao fen xi]. *Medicine World* 2009;**11**(2):29–30.
- He H 2004** *{published data only}*  
He H. Clinical observation of the treatment of endometriosis using TCM. *Chinese Journal of Guangming TCM* 2004;**19**(3):22–3.
- He JY 2005** *{published data only}*  
He JY, Hang MG, Zhou ZQ. Clinical observation of the treatment of endometriosis using Nei Yi Kang capsules. *West China Medical Journal* 2005;**20**(3):494–5.
- He RZ 2004** *{published data only}*  
He RZ, He X, Wang ZS. Clinical effectiveness of the invigorate the kidney and eliminate endometriosis decoction. *Modern Journal of Integrated Chinese and Western Medicine* 2004;**13**:2157–8.
- Hou 2010** *{published data only}*  
Hou ZX. The treatment of endometriosis using modified *xia yu xue tang* in 49 patients [Xia yu xue tang jia wei zhi liao zi gong nei mo yi wei zheng 49 li]. *Shanxi Journal of Traditional Chinese Medicine* 2010;**26**(1):19–20.
- Hu 2000** *{published data only}*  
Hu SQ, Yu P, Li M. Clinical observation of the treatment of endometriosis using Qu Zhi Ling enema. *Shandong Journal of TCM* 2000;**19**(8):458–9.
- Hu 2005** *{published data only}*  
Hu WJ. The treatment of endometriosis using warm the kidneys and transform stasis method in 60 patients. *Liaoning Journal of TCM* 2005;**32**(7):684–5.
- Hu 2009** *{published data only}*  
Hu B. Observation of clinical effectiveness of Chinese and western medicine in the treatment of endometriosis [Zhong yao he xi yao zhi liao zi gong nei mo yi wei zheng de liao xiao guan cha]. *Chinese Journal of Practical Medicine* 2009;**36**(16):84–5.
- Huang 2000** *{published data only}*  
Huang JL, Si TY, Cheng L, et al. Clinical effect of Pu Tian capsule in the treatment of endometriosis. *Journal of Guangzhou University of Traditional Chinese Medicine* 2000;**17**(1):40–1.
- Huang 2000a** *{published data only}*  
Huang YH, Wang XM. The treatment of endometriosis using a combination of western and Chinese medicine [Zong Xi Yi jie he zhi liao zi gong nei mo yi wei zheng]. *HuBei Journal of TCM* 2000;**22**(7):13–4.
- Huang 2009** *{published data only}*  
Huang YH, Cao LX, Situ Y. Effect of *huoxue huayu xiaozheng* method on expression of MMP-9 and TIMP-3 in patients with endometriosis [Huo xue hua yu xiao zheng fa dui zi gong nei mo yi wei zheng de MMP-9 he TIMP-3 biao da de ying xiang]. *The ninth National Academic Seminar on the Chinese Gynecology* 2009:321–5.
- Huang 2010** *{published data only}*  
Huang BP, Liu W, Chen J, et al. Clinical observation of the treatment of endometriosis using triple therapy with chinese medicine in 52 patients [Zhong yao san lian liao fa zhi liao zi gong nei mo yi wei zheng 52 li lin chuang guan cha]. *Journal of Sichuan Traditional Chinese Medicine* 2010;**28**(10):93–4.
- Jia 2004** *{published data only}*  
Jia WP. Clinical observation of the effectiveness of painful period endometriosis reducing treatment in cases of endometriosis [Tong Jing Nei Yi Xiao he ji zhi liao zi gong nei mo yi wei zheng liao xiao guan cha]. *Liaoning journal of TCM* 2004;**31**(3):234–5.

- Kui JY 2001** *{published data only}*  
Kui JY, Chen M, Jiang SQ. Clinical observation of the treatment of endometriosis using Xiao Zheng Chong prescription. *Traditional Chinese Medicine Journal* 2001;**16**(5):74–7.
- Leng 2009** *{published data only}*  
Leng GQ, Wei YL, Yang LH, et al. Clinical research into the treatment of endometriosis using nei yi qing [Zhong yao nei yi qing zhi liao zi gong nei mo yi wei zheng lin chuang yan jiu]. *Journal of Emergency in Traditional Chinese Medicine* 2009;**18**(7):1063,1074.
- Li 1999** *{published data only}*  
Li J, Zheng J, Wang DZ. Clinical observation of the treatment of endometriosis using tonify the Qi and moving the blood to eliminate stasis method. *Chinese Journal of Integrated TCM and Western Medicine* 1999;**19**(9):533.
- Li 2003** *{published data only}*  
Li XP. Clinical observation of the treatment of endometriosis in 42 participants. *Fujian Journal of TCM* 2003;**34**(6):9.
- Li 2004** *{published data only}*  
Li CY. The treatment of 46 cases of endometriosis using CHM [Zhong yao zhi liao zi gong nei mo yi wei zheng 46 lie]. *Liaoning Journal of CHM* 2004;**31**(4):314–5.
- Li 2006** *{published data only}*  
Li XJ, Zhong H, Liu JM. The treatment of endometriosis using invigorate the kidney and remove endometriosis pill. *Chinese Folk Treatment* 2006;**14**(7):37–8.
- Li 2007** *{published data only}*  
Li XL, Wu XH. Clinical research into the treatment of endometriosis using Kang Zhen Xiao pills. *Gan Su Journal of Chinese Medicine* 2005;**1**:12.
- Li 2007a** *{published data only}*  
Li J, Wang DZ, Zhang SF. Clinical observation of Nei Yi pills in the treatment of endometriosis [Nei Yi Wan zhi liao zi gong nei mo yi wei zheng lin chuang guan cha]. *Shanghai Journal of TCM* 2007;**3**:51–2.
- Li 2009** *{published data only}*  
Li LP. Observation of effectiveness of chinese herbs combined with electrochemical therapy in the treatment of endometriosis [zhong yao lian he dian hua xue liao fa zhi liao zi gong nei mo yi wei zheng de lin chuang liao xiao guan cha]. *Journal of Mathematical Medicine* 2009;**22**(1):43–45.
- Lian 2009** *{published data only}*  
Lian F, Lin X, Sun Z. Effect of Quyu Jiedu Granule on microenvironment of ova in patients with endometriosis. *Chinese Journal of Integrative Medicine* 2009;**15**(1):42–6.
- Liao 2004** *{published data only}*  
Liao W. Observation of the clinical effectiveness of CHM in the treatment of endometriosis [Zhong yao zhi liao zi gong nei mo yi wei zheng liao xiao guan cha]. *Journal of Practical TCM* 2004;**20**(5):231.
- Liao 2010** *{published data only}*  
Liao HH, Li F, Song H. Clinical research into the treatment of mild and moderate endometriosis using laparoscopic surgery and *luoshi neiyi fang* [Fu qiang jing shou shu lian he luo shi nei yi fang zhi liao qing zhong du zi gong nei mo yi wei zheng de lin chuang yan jiu]. *Yunnan Journal of Traditional Chinese Medicine* 2010;**31**(9):16–9.
- Lin 2006** *{published data only}*  
Lin X, Fu LH. Clinical observation of the treatment of endometriosis using Dan E Fu Kang Gao. *Guang Xi Journal of Chinese Medicine* 2006;**29**(3):10–1.
- Lin 2006a** *{published data only}*  
Lin L, Zhao YX. Observation of the clinical effectiveness of using combining western and Chinese medicine in the treatment of endometriosis [Zhong Xi Yi jie he zhi liao zi gong nei mo yi wei zheng liao xiao guan cha]. *Qingdao Medicine & Hygiene* 2006;**38**(3):203.
- Li QX 2009** *{published data only}*  
Li QX, Ma HX, Lai MH. Assessment of effectiveness of using chinese herbs after laparoscopic surgery to treat endometriosis related infertility [Fu qiang jing shu hou zhong yao zhi liao zi gong nei mo yi wei zheng bu yun de liao xiao ping gu]. *Modern Hospital* 2009;**9**(8):65–6.
- Liu 1994** *{published data only}*  
Liu YM. The treatment of endometriosis using a combination of western and Chinese medicine [Zhong Xi jie he zhi liao zi gong nei mo yi wei zheng]. *Tianjin Journal of TCM* 1994;**3**:17–8.
- Liu 1998** *{published data only}*  
Liu J, Li XY, Hu XM. Clinical observation of the treatment of endometriosis by tonifying the kidney and moving blood stasis method [Bu shen qu yu fa zhi liao zi gong nei mo yi wei zheng de lin chuang guan cha]. *Journal of integrated CHM and Western Medicine* 1998;**18**(3):145–7.
- Liu 1998a** *{published data only}*  
Liu J, Li SY, Hu XM. Clinical investigation of the treatment of endometriosis using tonifying the kidney and eliminating stasis method. *Journal of Integrated Chinese and Western Medicine* 1998;**18**(3):145–7.
- Liu 1998b** *{published data only}*  
Liu XL, Zhang XM. Analysis of the effectiveness of combined western and Chinese medical treatment in the treatment of 60 patients with endometriosis [Zhong Xi Yi jie he zhi liao zi gong nei mo yi wei zheng 60 lie liao xiao fen xi]. *Shanghai Medicine* 1998;**21**(1):41–2.
- Liu 2001** *{published data only}*  
Liu JL. Clinical observation of the treatment of endometriosis using Nei Yi pills. *Shandong Journal of TCM* 2001;**20**(6):340–1.
- Liu 2003** *{published data only}*  
Liu YX. Observation of the effectiveness of Wen Tong herbs and acupuncture in the treatment of 76 cases of endometriosis related dysmenorrhoea [Wen Tong Yao jiu zhi liao zi gong nei mo yi wei zheng jiao tong jing 76 lie liao xiao guan cha]. *New Chinese Medicine* 2003;**35**(5):55.
- Liu 2004** *{published data only}*  
Liu HQ. Clinical observation of the treatment of dyspareunia using Yi Tong Ning enema [Yi Tong Ning fang guan chang zhi liao zi gong nei mo yi wei zheng xing jiao

- tong de lin chuang guan cha]. *Chinese Journal of Basic Traditional Chinese Medicine* 2004;**10**(5):78–9.
- Liu 2005** *{published data only}*  
Liu RX, Liu YQ. Experimental study on treating endometriosis related infertility using tonify the kidneys and enliven the blood decoction [Bu Shen Huo Xue Fang dui Zi Gong Nei Mo Yi Wei Zheng Bu Yun zhe Zi Gong Nei Mo Yi Wei de Ying Xiang]. *Chinese Journal of Information on TCM* 2005;**12**(6):14–5.
- Liu 2009** *{published data only}*  
Liu Y, Wang R, Xing HM. Effect of *wenjing heyang fang* on ovulation in patients with endometriosis related infertility [Wen jing he ying fang dui zi gong nei mo yi wei zheng bu yun huan zhe pai luan gong neng de ying xiang]. *Journal of Hebei Traditional Chinese Medicine and Pharmacology* 2009;**24**(3):13–4.
- Liu FY 2003** *{published data only}*  
Liu FY, Zuo GZ, Tang QL. Clinical observation of reinforcing kidney and activating the blood formula combined with laparoscopy for the treatment of endometriosis. *Combined Chinese and Western Emergency Medicine* 2003;**10**:359–61.
- Liu GY 2003** *{published data only}*  
Liu GY, Yang SF, Cong HF. Clinical trial of pelvic cavity administration of Tong Yu injection in the treatment of external endometriosis [Tong Yu zhu she ye pin qiao fa zhi liao wai zai xing zi gong nei mo yi wei zheng de lin chuang yan jiu]. *Journal of Beijing University of TCM* 2003;**26**(3):63–6.
- Li XL 2009** *{published data only}*  
Li XL, Lian F, Sun ZG, et al. Clinical research into the treatment of endometriosis using removing blood stasis and detoxifying herbs combined with IUI [Qu yu jie du zhong yao lian he gong qiang nei ren gong shou jing zhi liao zi gong nei mo yi wei zheng de lin chuang yan jiu]. *World Journal of Integrated Chinese and Western Medicine* 2009;**4**(7):496–8.
- Lu 2003** *{published data only}*  
Lu WP, Wang JY. Research on Yi Wei An granules in the treatment of endometriosis [Yi Wei An ke fen zhi liao zi gong nei mo yi wei zheng de lin chuang yan jiu]. *Modern Journal of Integrated Western and Chinese Medicine* 2003;**12**(18):1930–1.
- Lu 2005** *{published data only}*  
Lu XS, Zhang LF. Observation of the effectiveness of using CHM in the treatment of endometriosis related infertility [Zhong yao zhi liao zi gong nei mo yi wei zheng bu yun30 lie liao xiao guan cha]. *Chinese Journal of Integrated Western and Chinese Medicine* 2005;**25**(9):850–1.
- Lu 2007** *{published data only}*  
Lu CH. Research about the efficacy of Guizhifulin capsule-mifepristone combination therapy for endometriosis. *Modern Medicine Journal of China* 2007;**9**(10):50–1.
- Lu 2007a** *{published data only}*  
Lu X, Xu X, Lin LJ. Clinical observation on treatment of infertile patients with severe endometriosis by Kangyi Zhongyu Decoction combined with gonadotropin releasing hormone-a. *Chinese Journal of Integrated Traditional & Western Medicine* 2007;**27**(11):980–2.
- Luo 2001** *{published data only}*  
Luo JY, Cheng ML, Chen XJ, Shi L. Clinical observation of Gui Zhi Fu Ling capsule combined with a herbal retention enema in the treatment of endometriosis. *Journal of Yunnan Chinese Medicine Research* 2001;**22**(6):33–4.
- Luo 2006** *{published data only}*  
Luo JY. Research on variations on Yi Kun Tang in the treatment of endometriosis [Jia jian zhi liao zi gong nei mo yi wei zheng de lin chuang yan jiu]. *Modern Journal of integrated Traditional Chinese and Western Medicine* 2006;**15**(12):1626.
- Lu XP 1999** *{published data only}*  
Lu XP, Wang HL, Mao L. Clinical observation of 50 patients with endometriosis treated with Nei Yi Fang. *Journal of Chinese Traditional Medical Technology* 1999;**6**(2):120–1.
- Ma 2009** *{published data only}*  
Ma SX. Clinical observation of the treatment of endometriosis using modified *guizhi fuling wan* [Gui zhi fu ling wan hua cai zhi liao zi gong nei mo yi wei zheng lin chuang guan cha]. *Journal of Xinjiang Traditional Chinese Medicine* 2009;**27**(5):9–11.
- Mo 2010** *{published data only}*  
Mo BF. Observation of clinical effectiveness of *sanjie zhentong* capsule combined with chinese herbs enema in the treatment of endometriosis [San jie zhen tong jiao nang pei he zhong yao bao liu guan chang zhi liao zi gong nei mo yi wei zheng liao xiao guan cha]. *Journal of Medical Information* 2010;**23**(5):1344–1345.
- Ou 2007** *{published data only}*  
Ou BJ. Observation of the effects of Da Ling Wang in the treatment of 20 cases of endometriosis [Zhong yao Da Ling Wang zhi liao zi gong nei mo yi wei zheng 20 lie liao xiao guan cha]. *Journal of Youjiang Medical College for Nationalities* 2001;**23**(2):315.
- Pan XR 2003** *{published data only}*  
Pan XR. The treatment of endometriosis in 41 patients using a combination of TCM and western medicine. *New TCM* 2003;**35**(11):54–5.
- Qi 2006** *{published data only}*  
Qi YH, Liu RF, Shi W. Clinical observation of the use of the “Nei Yi” method in the treatment of endometriosis [Nei Yi fang zhi liao zi gong nei mo yi wei zheng lin chuang guan cha]. *Journal of Shandong University of TCM* 2006;**30**(1):53–4.
- Qian 2000a** *{published data only}*  
Qian Q. Clinical investigation of the treatment of endometriosis using modifications of Gui Zhi Fu Ling Wan [Gui Zhi Fu Ling Wan jia wei zhi liao zi gong nei mo yi wei zheng de lin chuang yan jiu]. *Liaoning journal of TCM* 2000;**27**(4):170.

- Qian J 2000** *{published data only}*  
Qian J, Zhen LX. Treatment of endometriosis by warming the kidneys and removing blood stasis. *Journal of Nanjing University of TCM (Natural Science)* 2000;**16**(5):277–9.
- Qiu L 2005** *{published data only}*  
Qiu L, Xu ZP, Peng XP. The treatment of endometriosis using a combination of Tong Yu Jian and western medicine. *Jiang Xi Journal of TCM* 2005;**6**:40.
- Qiu YJ 2004** *{published data only}*  
Qiu YJ, Liu ZH, Wang ZX. Clinical observation of the treatment of endometriosis using replenish the Qi and transform stasis method. *Ji Ling TCM* 2004;**24**(3):23–5.
- Qi YH 2011** *{published data only}*  
Qi YH, Lian F. Clinical study on treatment of endometriosis-related infertility patients by laparoscopic surgery in combination of Quyu Jiedu recipe. *Chinese Journal of Integrated Traditional and Western Medicine* 2011;**31**(7):892–5.
- Quan 2010** *{published data only}*  
Quan YH. Clinical observation of the treatment of endometriosis using *liqi quyu* method [Li qi qu yu fa zhi liao zi gong nei mo yi wei zheng lin chuang guan cha]. *Chinese Practical Medicine* 2010;**5**(1):124–5.
- Ren YL2005** *{published data only}*  
Ren YL, Hu SH, Zhang HJ. Clinical observation of the treatment of endometriosis using Qu Zhi. *Jiang Xi Journal of TCM* 2005;**36**(1):31–2.
- Ren YL 2005** *{published data only}*  
Ren YL, Hu SH, Zhang HJ. The effectiveness of San Jie Zheng Tong capsules in the treatment of 112 patients with endometriosis. *Practical Treatment and Diagnosis* 2005;**19**(4):279–80.
- Shen XJ 2011** *{published data only}*  
Shen XJ. Clinical study on treatment of endometriosis-related infertility patients using blood activating and stasis resolving method combined with intrauterine insemination. *China Journal of Chinese Medicine* 2011;**26**(8):1013–4.
- Shong 2005** *{published data only}*  
Shong QX. Observation of the clinical effectiveness of the tonify kidney and regulate the cycle method in the treatment of endometriosis [Zhong yao bu shen tiao zhou fa zhi liao zi gong nei mo yi wei zheng liao xiao guan cha]. *Journal of Mudan Jiang Medical College* 2005;**26**(4):25–6.
- Si 2006** *{published data only}*  
Si TY, Xu L. Effectiveness of the tonify the kidney and promote blood circulation method on TNF and SOD in endometriosis related infertility. *Shanghai Journal of TCM* 2006;**40**(3):25–6.
- Su CZ 2002** *{published data only}*  
Su CZ, Hou JF, Zhou Q. Observation of the treatment of endometriosis using Dang Gui Zhu Yu decoction. *Journal of Practical Traditional Chinese Medicine* 2002;**18**(6):3–4.
- Sun YZ 2003** *{published data only}*  
Sun YZ. Clinical observation of the treatment of endometriosis using Xiao Zheng Shu Tong Tang. *Hebei Journal of TCM* 2003;**25**(2):89–90.
- Tang 2009** *{published data only}*  
Tang LH. Investigation of the treatment of endometriosis using a combination of Chinese and western medicine [Zhong xi yi jie he zhi liao zi gong nei mo yi wei zheng tan xi]. *Asia-Pacific Traditional Medicine* 2009;**5**(12):77–8.
- Tang 2010** *{published data only}*  
Tang YQ, Chen YG. Clinical research into the treatment of endometriosis using *yiwei yihao fang* in 31 patients [Yi wei yi hao fang zhi liao zi gong nei mo yi wei zheng 31 li lin chuang yan jiu]. *Jiangsu Journal of Traditional Chinese Medicine* 2010;**42**(10):21–2.
- Wang 1996** *{published data only}*  
Wang JL, Luo YK, O YHQ, Liu YQ, Luo SP. A clinical trial of Dr Luo's Nei Yi method for the treatment of endometriosis. *Guangzhou TCM University Report* 1996;**13**(1):9–12.
- Wang 1999** *{published data only}*  
Wang YY, Shi SL. The treatment of endometriosis using a combination of western medicine and TCM [Zhong Xi Yi jie he zhi liao zi gong nei mo yi wei zheng]. *Inner Mongolia* 1999;**4**:22–3.
- Wang 2001** *{published data only}*  
Wang S. The treatment of endometriosis using Hong Teng prescription [Hong Teng fang zhi liao zi gong nei mo yi wei zheng]. *Henan Journal of TCM* 2001;**3**(15):63.
- Wang 2002** *{published data only}*  
Wang JY, Lu WP, Yu P, Wang W. Evaluation of the clinical effectiveness of Tong Jing Ling granules in the treatment of endometriosis [Tong Jing Ling Fen zhi liao zi gong nei mo yi wei zheng de lin chuang yan jiu]. *Chinese Traditional Patent Medicine* 2002;**24**(4):274–6.
- Wang 2002a** *{published data only}*  
Wang BJ, Huang HH. Clinical observation of the treatment of 126 of endometriosis related infertility using Hei Lao Hu enema [Hei Lao Hu tang bao liu guan chang zhi liao zi gong nei mo yi wei zheng bing bu yun 126 lie lin chuang guan cha]. *China Community Doctor* 2002;**18**(14):38.
- Wang 2002b** *{published data only}*  
Wang NG. Comparison of the effectiveness of treating endometriosis using either gestrinone or a combination of TCM and western medicine [Zhong Xi Yi jie he yu gestrinone zhi liao zi gong nei mo yi wei zheng lin chuang liao xiao de bi jiao]. *Journal of Xianning Medical College* 2002;**16**(4):293–4.
- Wang 2004** *{published data only}*  
Wang RY, Zhou L. Clinical observation of the treatment of endometriosis using Huo Xue Zhi Yu method. *Journal of Integrated Chinese and Western Medicine* 2004;**24**(3):258–9.
- Wang 2004a** *{published data only}*  
Wang Y. The treatment of endometriosis using scatter accumulation and settle pain (San Jie Zhen Tong) capsules

- [San Jii Zhen Tong jiao nong zhi liao zi gong nei mo yi wei zheng]. *Journal of Medical Forum* 2004;**25**(16):39.
- Wang 2005** *{published data only}*  
Wang LF, Wu XL. The treatment of endometriosis in 36 patients using a combination of TCM and western medicine. *Chinese Archives of TCM* 2005;**23**(2):380–1.
- Wang 2006a** *{published data only}*  
Wang LR. The treatment of endometriosis in 42 patients using a combination of western and Chinese medicine [Zhong Xi Yi jie he zhi liao zi gong nei mo yi wei zheng 42 lie]. *Chinese TCM Technology* 2006;**13**(3):195.
- Wang 2006b** *{published data only}*  
Wang DM. Clinical observation of 78 cases of endometriosis treated with Xue Jie (Resina Draconis) [Zhong yao xue jie zhi liao zi gong nei mo yi wei zheng 78 lie lin chuang guan cha]. *TCM Research* 2006;**47**(3):197–8.
- Wang 2009** *{published data only}*  
Wang XB, Liu X, Wei JY. The treatment of endometriosis related infertility using laparoscopic surgery combined with Chinese herbs in 41 patients [Fu qiang jing shou shu lian he zhong yao zhi liao zi gong nei mo yi wei zheng ban bu yun 41 li]. *Journal of Traditional Chinese Medicine* 2009;**50**(10):911–2.
- Wang 2010** *{published data only}*  
Wang R. The treatment of endometriosis related infertility using *wenjing heyang fang* in 30 patients [Wen jing he ying fang zhi liao zi gong nei mo yi wei zheng xiang guan bu yun zheng 30 li]. *Journal of Traditional Chinese Medicine* 2010;**51** Suppl 2:155–6.
- Wang LX 2006** *{published data only}*  
Wang LX. Clinical observation of the treatment of endometriosis using Xiao Zheng Guang Chang and gestrinone. *Journal of Liaoning College of TCM* 2006;**8**(3):69–70.
- Wang W 2009** *{published data only}*  
Wang W, Wang CX, Yang QY. Clinical observation of the treatment of endometriosis using sanjie analgesic capsule [San jie zhen tong jiao nang zhi liao zi gong nei mo yi wei zheng lin chuang guan cha]. *Medicine World* 2009;**11**(4):23.
- Wang XR 2009** *{published data only}*  
Wang XR. Clinical observation of the treatment of endometriosis using mifepristone combined with Chinese herbs in 62 patients [Mi fei si tong lian he zhong yao zhi liao zi gong nei mo yi wei zheng 62 li lin chuang guan cha]. *China Foreign Medical Treatment* 2009;**24**:84–5.
- Wu 1999** *{published data only}*  
Wu Y. The differentiation and treatment of 33 patients with endometriosis. *Journal of Nanjing University of TCM* 1999;**15**(4):248–9.
- Wu 2000a** *{published data only}*  
Wu YN, Hua L, Jin Y, et al. Clinical study of the treatment of ovarian endometrioma by combined laparoscopy and CHM [Fu Qiang Jing yu Zhong Yao jie he zhi liao zi luan chao zi gong nei mo yi wei nong zhong de Lin Zhuang Yan Za]. *Chinese journal of Integrated Chinese and Western Medicine* 2000;**20**(3):183–6.
- Wu 2003** *{published data only}*  
Wu F, Zhang HF, Chen SL. Observation of the clinical effectiveness of the treatment of endometriosis using Yi Wei San [Yi Wei San zhi liao zi gong nei mo yi wei zheng lin chuang guan cha]. *New TCM* 2003;**35**(10):15–6.
- Wu 2004** *{published data only}*  
Wu LL, Wang JL, Tang F. The treatment of endometriosis using Dan E Fu Kang Jian Gao. *Guangdong Medical Journal* 2004;**25**(6):728–9.
- Wu 2006c** *{published data only}*  
Wu SZ, Chen XL, Huang YC. Observation of the effect of combined therapy - Nei Yi pill with Nei Yi enema on endometriosis [Nei Yi Wan he Nei Yi Guang Chang Ye fu he zhi liao zi gong nei mo yi wei zheng zi liao guan cha]. *Chinese Journal of Integrated Traditional and Western Medicine* 2006;**26**(6):557–9.
- Wu 2009** *{published data only}*  
Wu T. Effect of *luoshi neiyi fang* combined with laparoscopic surgery on the serum MMP-9 and TIMP-3 in patients with mild endometriosis related infertility [Luo shi nei yi fang lian he fu qiang jing shou shu dui qing xing zi gong nei mo yi wei zheng bu yun huan zhe xue qing MMP-9 he TIMP-3 de ying xiang]. Guangzhou University of Traditional Chinese Medicine 2009.
- Wu HY 2009** *{published data only}*  
Wu HY. Clinical observation of the treatment of endometriosis related infertility using a Chinese herb enema in 33 patients [Zhong yao guan chang zhi liao zi gong nei mo yi wei zheng xing bu yun 33 li guan cha]. *China Modern Doctor* 2009;**47**(13):77, 107.
- Wu SS 2000** *{published data only}*  
Wu SS. Clinical observation of the treatment of endometriosis using Nei Yi pills and Nei Yi enema [Nei Yi wan he Nei Yi guan chang ye nei wai he zhi liao zi gong nei mo yi wei zheng lin chuang guan cha]. *Chinese Herbal Medicine* 2000;**23**(8):509–10.
- Wu XJ 2009** *{published data only}*  
Wu XJ. Observation of effectiveness of oral and enema herbs in the treatment of endometriosis [Zhong yao nei fu ji bao liu guan chang zhi liao zi gong nei mo yi wei zheng de liao xiao guan cha]. *China Traditional Chinese Medicine advisory* 2009;**1**(6):70.
- Xia 2010** *{published data only}*  
Xia WH, Liu YL, Liu FJ. Clinical observation of the treatment of endometriosis using *fuzheng kang neiyi tang* in 30 patients [Fu zheng kang nei yi tang zhi liao zi gong nei mo yi wei zheng 30 li lin chuang guan cha]. *New Traditional Chinese Medicine* 2010;**42**(6):45–7.
- Xiang 2001** *{published data only}*  
Xiang CF. Research into the use of retained ear acupuncture in the treatment of 37 cases of endometriosis related dysmenorrhoea [Er mai zhen fa zhi liao zi gong nei mo yi wei zheng tong ting 37 lie li chunag guan cha]. *Journal of Traditional Chinese Medicine* 2001;**42**(10):596–7.

**Xiong 2004** {published data only}

Xiong L. Report of the treatment of endometriosis in 41 patients using a combination of western and Chinese medicine [Zhong Xi Yi jie he zhi laiao zi gong nei mo yi wei zheng 41 lie zong he]. *Hunan Journal of TCM* 2004;**20**(1):20–1.

**Xu 2004** {published data only}

Xu XJ. Clinical observation of the treatment of endometriosis using Hua Yu Zhi Tong pills. *Journal of Cheng Du University of TCM* 2004;**2**:1–3.

**Xu 2004a** {published data only}

Xu L, Xie B, Zhang YR. Clinical investigation of the treatment of endometriosis using nourish the kidneys and enliven the blood method. *Fujian Journal of TCM* 2004;**35**(2):13–4.

**Xu 2004b** {published data only}

Xu YJ, Ji ZS. The treatment of endometriosis using Shao Fu Zhu Yu Tang. *Journal of Zhejiang TCM College* 2004;**28**(5):36.

**Xu 2005** {published data only}

Xu HJ, Wang HJ. Clinical observation of the treatment of endometriosis using Wu Mei Hei Ji. *Journal of Chinese Women and Children's Healthcare* 2005;**20**:2189–90.

**Xuan JS 2005** {published data only}

Xuan JS. Comparative observation of the effectiveness of treating endometriosis using CHM and gestrinone. *Journal of Jinzhou Medical College* 2005;**26**(4):88.

**Xue 2009** {published data only}

Xue L. Observation of the treatment of endometriosis in 40 patients using modified *danggui sini tang* [Dang gui si ni tang jia jian zhi laiao zi gong nei mo yi wei zheng 40 li guan cha]. *Journal of Practical Traditional Chinese Medicine* 2009;**25**(9):592.

**Xu HX 2011** {published data only}

Xu HX. Clinical observation of treatment of endometriosis-related infertility using herbal enema. *Journal of Practical Traditional Chinese Medicine* 2011;**27**(3):153–4.

**Yan 2004** {published data only}

Yan YJ. Clinical observation of the treatment of ovarian endometriomas using transform 'abdominal mass' decoction [Zi ni Hua Zheng Fang zhi laiao luan chao che ke li nong zhong zhong de lin zhuang yan jiu]. *Modern Journal of Integrated TCM and Western Medicine* 2004;**13**(12):62.

**Yang 2006** {published data only}

Yang JB, Chui XP, Mong JR, et al. Clinical observation of the treatment of endometriosis using Zhi Yi Kang. *Journal of Emergency TCM* 2006;**15**(1):35–6.

**Yang 2006a** {published data only}

Yang B, Zhang J, Li HL. Observation of the post-operative treatment of endometriosis using a combination of western and Chinese medicine [Zhong Xi Yi jie he zhi laiao shu hou zi gong nei mo yi wei zheng zhi laiao guan cha]. *Hebei Journal of TCM* 2006;**28**(9):678–9.

**Yang 2006b** {published data only}

Yang WL, Pu JF, Yu LQ. Clinical observation of the treatment of endometriosis using Dan E Fu Kang Jian Gao [Dan E fu kang gao zhi laiao zi gong nei mo yi wei zheng lin chuang guan cha]. *Health Occupation Education* 2006;**13**:18–9.

**Yang HY 2001** {published data only}

Yang HY, Li CH, Shi ZH, et al. Analysis of the clinical effectiveness of using a Chinese herbal enema to treat endometriosis. *Acta Universitatis Medicinalis Secundae Shanghai* 2001;**21**(5):478.

**Yang Y** {published data only}

Yang Y. The treatment of endometriosis in 40 patients using 'triple therapy'. *Henan Traditional Chinese Medicine* 2006;**26**(7):35–6.

**Ye LQ 2004** {published data only}

Ye LQ. Clinical observation of the treatment of endometriosis in 66 patients using Nei Yi Fang. *Zhe Jiang Clinical Medicine* 2004;**6**(1):32.

**Yu 1996** {published data only}

Yu SL. The treatment of endometriosis using a combination of western medicine and TCM in 90 patients [Zhong Xi Yi jie he fen qi zhi laiao zi gong nei mo yi wei zheng 90 lie]. *Chinese Journal of Integrated Western Medicine and TCM* 1996;**16**(2):109–10.

**Yu 2003** {published data only}

Yu X. Diagnosis and treatment of endometriosis using combined Chinese and western medicine [Zi gong nei mo yi wei zheng de zhong xi yi jie he zhen zhi]. *Chinese Journal of Integrated Chinese and Western Medicine*. 2003;**23**(3):168–9.

**Yu 2010** {published data only}

Yu JW, Zhao L, Li RL, et al. Clinical observation of the treatment of endometriosis using activating blood circulation and resolving stasis herbs [Huo xue hua yu zhong yao zhi laiao zi gong nei mo yi wei zheng de lin chuang guan cha]. *Chinese Journal of Traditional Medical Science and Technology* 2010;**17**(4):344–5.

**Yuan 2003** {published data only}

Yuan FQ. Treatment of endometriosis related infertility using a combination of western and Chinese medicine [Zhong Xi Yi jie he zhi laiao zi gong nei mo yi wei zheng shou bu yun 122 lie]. *Medical Sciences Communication* 2003;**17**(6):694–5.

**Zhang 2004** {published data only}

Zhang YC. The treatment of endometriosis using San Jie Zhen Tong capsules in 100 patients. *Medical Pharmacology Report* 2004;**23**(5):42.

**Zhang 2009** {published data only}

Zhang SB, Du XL, Liu HY, et al. Clinical observation of the treatment of endometriosis using *dangui quyuan* combined with gestrinone [Dan gui qu yu wan lian he yun san xi tong zhi laiao zi gong nei mo yi wei zheng de lin chuang guan cha]. *Maternal and Child Health Care of China* 2009;**24**(24):3453–4.

**Zhang 2010** {published data only}

Zhang B, Zhao JH, Shang TY. Observation of effectiveness of *dane fukang* jiangao in the treatment of endometriosis related pelvic cavity pain [Dan e fu kang jian gao zhi liao zi gong nei mo yi wei zheng pen qiang teng tong de liao xiao guan cha]. *Proceeding of Clinical Medicine* 2010;**19**(3B): 360–2.

**Zhang HQ2009** {published data only}

Zhang HQ, Zhao SP, Liu YJ, et al. Clinical research into the treatment of endometriosis using *yi wei kang* [Yi wei kang chong ji zhi liao zi gong nei mo yi wei zheng de lin chuang yan jiu]. *Modern Medicine Journal of China* 2009;**11**(7): 13–8.

**Zhao 2002** {published data only}

Zhao JL, Mu CL. Treatment of 75 cases of endometriosis related dysmenorrhoea using a combination of western and Chinese medicine [Zhong Xi Yi jie he zhi liao zi gong nei mo yi wei zheng tong jing 75 lie]. *Fujian Journal of TCM* 2002;**33**(3):11–2.

**Zhao 2010** {published data only}

Zhao HY, Ni YC, Zhou Y. Clinical research into the treatment of endometriosis combined with infertility using laparoscopic surgery and *huayu xiaozheng tang* [Fu qiang jing shu fu yi hua yu xiao zheng tang zhi liao zi gong nei mo yi wei zheng he bing bu yun lin chuang yan jiu]. *Journal of Practical Traditional Chinese Medicine* 2010;**26**(7):450–1.

**Zhong 2009** {published data only}

Zhong XL, Wang XL, Zhang Z. Clinical research into the treatment of endometriosis using a combination of Chinese and western medicine [Zhong xi yi jie he zhi liao zi gong nei mo yi wei zheng de lin chuang yan jiu]. *Chinese Medical Herald* 2009;**6**(24):65–6.

**Zhou 2010** {published data only}

Zhou DX. Observation of clinical effectiveness of laparoscope combined with mifepristone and Chinese herbs in the treatment of endometriosis [Fu qiang jing lian he mi fei si tong he zhong yao zhi liao zi gong nei mo yi wei zheng de liao xiao guan cha]. *Cotemporary Medicine* 2010;**16**(16): 105–6.

**Zhu 2000a** {published data only}

Zhu JH. Treatment of 20 cases of endometriosis using CHM enema combined with mifepristone [Zhong Yao guan chang pei he mifepristone zhi liao zi gong nei mo yi wei zheng 20 lie]. *Shanxi Journal of TCM* 2000;**16**(5):33.

**Zhu 2001** {published data only}

Zhu QG. Clinical observation of the treatment of endometriosis using regulate the Qi and eliminate stasis method. *Unclear* 2001;**4**:29–31.

**Zhu FH 2011** {published data only}

Zhu FH, Jiang L. Clinical observation on treatment of 42 patients with endometriosis after surgery by using kidney tonifying and blood activating therapy. *Fujian Journal of Traditional Chinese Medicine* 2011;**42**(1):32–3.

**Zhu HY 2002** {published data only}

Zhu HY, Qin XM. Clinical observation of the treatment of endometriosis using Xue Fu Zhu Yu Tang and a Chinese herbal enema. *Guang Xi Journal of TCM* 2002;**25**(3):17–8.

**Zhu L 2000** {published data only}

Zhu L. Research into Liang Fang Wen Yao Tang [Liang Fang Wen Yao Tang zhi liao zi gong nei mo yi wei zheng lin chuang yan jiu]. *Journal of combined Chinese and Western Medicine (Zhong Guo Zhong Xi Yi Jie He Ya Zhi)* 2000;**20**(9):30–1.

**Zou 2010** {published data only}

Zou AX, Wang LH. The treatment of moderate and severe endometriosis combined with infertility using *quyu tiaojing tang* in 80 patients [Qu yu tiao jing tang zhi liao zhong zhong xing xi gong nei mo yi wei zheng ji he bing bu yun zheng 80 li]. *Shanxi Journal of Traditional Chinese Medicine* 2010;**31**(3):267–8.

## Additional references

**Abbott 2003**

Abbott JA, Hawe J, Clayton RD, Garry R. The effects and effectiveness of laparoscopic excision of endometriosis: a prospective study with a 2-5 year follow up. *Human Reproduction* 2003;**18**(9):1922–7.

**Abbott 2004**

Abbott J, Hawe D, Hunter M, Holmes P, Garry F, Garry R. Laparoscopic excision of endometriosis: a randomized, placebo-controlled trial. *Fertility and Sterility* 2004;**82**: 878–84.

**Anderson 2004**

Anderson GL, Limacher M, Assaf AR, et al. Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial. *JAMA* 2004;**291**(14):1769–71.

**Ballweg 2004**

Ballweg ML. Impact of endometriosis on women's health: comparative historical data show that the earlier the onset, the more severe the disease. *Best Practice & Research Clinical Obstetrics and Gynaecology* 2004;**18**:201–18.

**Biberoglu 1981**

Biberoglu KO, Behrman SJ. Dosage aspects of danazol therapy in endometriosis short and long term effectiveness. *American Journal of Obstetrics and Gynecology* 1981;**139**: 645–54.

**Bischoff 2004**

Bischoff F, Simpson JL. Genetics of endometriosis: heritability and candidate genes. *Best Practice & Research. Clinical Obstetrics and Gynaecology* 2004;**18**:219–32.

**CAITWN 1991**

Chinese Association of Integrated Traditional and Western Medicine. Criteria for diagnosis and treatment of integrated Chinese and western medicine for endometriosis, pregnant hypertension, and female infertility. *Chinese Journal of Integrated Traditional and Western Medicine* 1991;**11**(6): 376–9.

**Cottreau 2003**

Cottreau CM, Ness RB, Modugno F, Allen GO, Goodman MT. Endometriosis and its treatment with danazol or pupron in relation to ovarian cancer. *Clinical Cancer Research* 2003;**9**:5142–4.

**Dmowski 1998**

Dmowski WP, Cohen M. Antigonadotrophin (danazol) in the treatment of endometriosis - evaluation of post treatment fertility and three year follow up data. *American Journal of Obstetrics and Gynecology* 1998;**131**:1978.

**Eskenazi 1997**

Eskenazi B, Warner ML. Epidemiology of Endometriosis. *Obstetrics and Gynecology Clinics of North America* 1997;**24**: 235–58.

**Fedele 2004**

Fedele L, Bianchi S, Zanconato G, Bettoni G, Gotsch F. Long term follow up after conservative surgery for rectovaginal endometriosis. *American Journal of Obstetrics and Gynecology* 2004;**190**:1020–4.

**Feste 1999**

Feste JR, Winkel CA. Is the standard of care what we think it is?. *Journal of the Society of Laparoendoscopic Surgery* 1999; **3**:331–4.

**GISG 1996**

The Gestrinone Italian Study Group (GISG). Gestrinone versus a gonadotrophin-releasing hormone agonist for the treatment of pelvic pain associated with endometriosis: a multicenter, randomized, double blind study. *Fertility and Sterility* 1996;**66**:911–9.

**Higgins 2003**

Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;**327**: 557–60.

**Huang 2006**

Huang YH, Si TY. Advance of research on mechanism of Chinese medicine for the treatment of endometriosis. *Hubei Journal of Traditional Chinese Medicine* 2006;**28**(3):56–7.

**Hughes 2004**

Hughes E, Fedorkow D, Collins J, Vandekerchove P. Ovulation suppression for endometriosis. Cochrane Database of Systematic Reviews. Chichester: John Wiley & Sons, Ltd, 2004, issue 2 DOI: 10.1002/14651858.CD000155.pub2.

**Koninckx 1996**

Koninckx PR, Timmermans B, Meuleman C, Penninckx F. Complications of CO<sub>2</sub>-laser endoscopic excision of deep endometriosis. *Human Reproduction* 1996;**11**(10):2263–8.

**Lapp 2000**

Lapp T. ACOG issues recommendations for the management of endometriosis. *American Family Physician* 2000;**11**(10):2263–8.

**Lebovic 2001**

Lebovic DI, Mueller MD, Taylor RN. Immunobiology of endometriosis. *Fertility and Sterility* 2001;**75**:1–10.

**Ling 1999**

Ling 1999. Randomised controlled trial of depot leuprolide in patients with chronic pelvic pain and clinically suspected endometriosis. *Obstetrics and Gynecology* 1999;**93**:51–8.

**Low 1993**

Low WY, Edelmann RJ, Sutton C. A psychological profile of endometriosis patients in comparison to patients with pelvic pain of other origin. *Journal of Psychosomatic Research* 1993;**37**:111–6.

**Maciocia 1998**

Maciocia G. Obstetrics and Gynaecology in Chinese medicine. *Obstetrics & Gynecology in Chinese Medicine*. First Edition. Vol. 1, Singapore: Churchill Livingstone, 1998.

**Malinak 1980**

Malinak LR, Buttram Jr VC, Elias S, Simpson JL. Heritage aspects of endometriosis. II. Clinical characteristics of familial endometriosis. *American Journal of Obstetrics and Gynecology* 1980;**137**:332–7.

**Moore 2004**

Moore J, Kennedy S, Prentice A. Modern combined oral contraceptives for pain associated with endometriosis. Cochrane Database of Systematic Reviews. Chichester: John Wiley & Sons, 2004, issue 2 DOI: 10.1002/14651858.CD001019.pub2.

**Noble 1997**

Noble LS, Takayama K, Makagawa M, Putman JM, Johns DA, Hinshelwood MM, et al. Prostaglandin E2 stimulates aromatase expression in endometriosis-derived stromal cells. *Journal of Clinical Endocrinology and Metabolism* 1997;**82**: 600–6.

**Ohtake 2003**

Ohtake F, Takayama K, Matsumoto T, Kitagawa H, Yamamoto Y, Nohara K, et al. Modulation of oestrogen receptor signalling by association with the activated dioxin receptor. *Nature* 2003;**423**:487–8.

**Parazzini 2000**

Parazzini F, Di Cintio E, Chatenoud L, Moroni S, Ardocono I, Struzziero E, et al. Estroprogestin vs. gonadotrophin agonists plus estroprogestin in the treatment of endometriosis-related pelvic pain: a randomized trial. *European Journal of Obstetrics, Gynecology, and Reproductive Biology* 2000;**88**:4–11.

**Prentice 2004**

Prentice A, Deary AJ, Goldbeck-Wood S, Farquhar C, Smith SK. Gonadotrophin-releasing hormone analogues for pain associated with endometriosis. *Cochrane Database of Systematic Reviews* 2004, Issue 2. [DOI: 10.1002/14651858]

**Selak 2007**

Selak V, Farquhar C, Prentice A, Singhla A. Danazol for pelvic pain associated with endometriosis. *Cochrane Database of Systematic Reviews* 2007, Issue 4. [DOI: 0100110010014210]

**Sheng 1998**

Sheng H, Shao JD, Morrow JD, Beauchamp RD, DuBois RN. Moderation of apoptosis and Bcl-2 expression by prostaglandin E2 in human colon cancer cells. *Cancer Research* 1998;**58**:362–6.

**Stenchever 2001**

Stenchever M, Droegemueller W, Herbst A, Mishell D. *Comprehensive Gynecology*. Mosby, 2001.

**Strauss 1992**

Strauss B, Didzus A, Speidel H. A study of the psychosomatic aspects of endometriosis. *Psychotherapie, Psychosomatik, Medizinische Psychologie* 1992;**42**:242–52.

**Sutton 1994**

Sutton C, Ewen S, Whitelaw N, Haines P. Prospective, randomized, double-blind, controlled trial of laser laparoscopy in the treatment of pelvic pain associated with minimal, mild, and moderate endometriosis. *Fertility and Sterility* 1994;**62**(4):696–700.

**Vasilakis 1999**

Vasilakis C, Jick H, del Mar Melero-Montes M. Risk of idiopathic venous thromboembolism in users of progestagens alone. *Lancet* 1999;**354**:1610–1.

**Vercellini 1993**

Vercellini P, Bocciolone L, Vendola N, Colombo A, Marchini M, Crosignani PG. A gonadotrophin releasing

hormone agonist versus a low-dose oral contraceptive for pelvic pain associated with endometriosis. *Fertility and Sterility* 1993;**60**(1):75–9.

**Wheeler 1983**

Wheeler JM, Malinak LR. Recurrent endometriosis: incidence, management and prognosis. *American Journal of Obstetric and Gynecology* 1983;**146**(3):247–53.

**Winkel 2003**

Winkel CA. Evaluation and management of women with endometriosis. *Obstetrics and Gynecology* 2003;**102**:397–408.

**Wu 1997**

Wu Y, Fischer W. *Practical Therapeutics of Traditional Chinese Medicine*. Paradigm, 1997.

**Xu et al 2004**

Xu M, Si TY, Lao YR, Guo XF, Wen ZH, Lai SL. A literature review of clinical trials on Chinese medicine for endometriosis. *Journal of Guangzhou University of Traditional Chinese Medicine* 2004;**21**(5):399–402.

**Zondervan 2001**

Zondervan KT, Yudkin PL, Vessey MP, Jenkinson CP, Dawes MG, Barlow DH, et al. Chronic pelvic pain in the community - symptoms, investigations, and diagnoses. *American Journal of Obstetrics and Gynecology* 2001;**184**:1149–55.

\* Indicates the major publication for the study

## CHARACTERISTICS OF STUDIES

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

Wu SZ 2006a

Methods	<p>Trial design: parallel randomised controlled trial          Blinding: single blinding          Study duration: December 1999 to May 2005          Statistics: adequate (Chi<sup>2</sup> test used for 'overall improvement')          Funding source declared</p>	
Participants	<p>100 cases of endometriosis complicated by infertility          Experimental group: 48          Control group: 52          Drop-out rate: 5% (2 from experimental group, 3 from control group)          Laparoscopic diagnosis: yes          Other diagnostic criteria: Chinese validated criteria          Baseline comparison: adequate</p>	
Interventions	<p>Nei Yi pills (10g twice daily) plus Nei Yi enema (70ml daily) versus gestrinone (0.25 mg twice a week) for 3 months          Nei Yi pills consisted of:          Dan Shen (<i>Salviae multiorrhizae Radix</i>), Xue Jie (<i>Draconis Sanguis</i>), San Leng (<i>Sparganii Rhizoma</i>), E Zhu (<i>Curcumae Rhizoma</i>), Tao Ren (<i>Persicae Semen</i>), San Qi (<i>Notoginseng Radix</i>), Dang Gui (<i>Angelica sinensis</i>), Gui Zhi (<i>Cinnamomi Ramulus</i>), Xiang Fu (<i>Cyperii Rhizoma</i>), Niu Xi (<i>Achyranthis bidentate Radix</i>)          Nei Yi enema consisted of:          Dan Shen (<i>Salviae multiorrhizae Radix</i>), Xue Jie (<i>Draconis Sanguis</i>), Chi Shao (<i>Paeonia rubra Radix</i>), Hu Zhang (<i>Radix et Rhizoma Polygoni Cuspidati</i>), San Leng (<i>Sparganii Rhizoma</i>), E Zhu (<i>Curcumae Rhizoma</i>), Tao Ren (<i>Persicae Semen</i>)          Treatment duration: 3 months</p>	
Outcomes	<p>A) Clinical outcomes:          1. symptomatic relief (defined as disappearance of symptoms, pelvic mass; pregnancy or birth within 3 years for those with infertility)          2. significant improvement (almost complete disappearance of symptoms or shrinkage of pelvic mass by ultrasound; or pregnancy)          3. improvement (relief of symptoms but not disappearance, no change or moderate shrinkage of pelvic mass)          4. no effect (no change of symptoms or become worse)          5. overall improvement (1+2+3)          B) Adverse effects</p>	
Notes	<p>Follow up from 1-24 months</p>	
<b><i>Risk of bias</i></b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>

**Wu SZ 2006a** (Continued)

Adequate sequence generation	Low risk	Randomisation achieved using random number sequence from table in statistical textbook
Allocation concealment	Low risk	Allocation concealment achieved by sorting numbers into envelopes
Blinding All outcomes	High risk	Although described as patient and assessor blinded (and confirmed with author) there is no description of an attempt to match the herbal enema with an inert control, so it is very unlikely patients were not aware of which group they were allocated to
Incomplete outcome data addressed All outcomes	Low risk	Two cases in treatment group and three cases in control group were lost during follow up. Adequate outcomes data presented
Free of selective reporting	Low risk	Identified outcomes adequately reported as compared with the description in methods
Free of other bias	Low risk	No source of other bias noted

**Wu SZ 2006b**

Methods	Trial design: parallel randomised controlled trial Blinding: described as single blinding Study duration: December 1999 to October 2003 Statistics: adequate (Mann-Whitney test and Annova test used for data analyses) Funding source declared
Participants	58 cases of endometriosis with clear inclusion and exclusion criteria Experimental group 1: 16 Experimental group 2: 24 Control group: 18 Drop-out rate: 0 Laparoscopic diagnosis: yes Other diagnostic criteria: Chinese validated criteria Baseline comparison: adequate
Interventions	Experimental group 1: Nei Yi pills (10g twice daily) Experimental group 2: Nei Yi pills (10g twice daily) plus Nei Yi enema (70ml daily) Control group: danazol (400mg/day) Nei Yi pills consisted of: Dan Shen ( <i>Salviae multiorrhizae Radix</i> ), Xue Jie ( <i>Draconis Sanguis</i> ), San Leng ( <i>Sparganii Rhizoma</i> ), E Zhu ( <i>Curcumae Rhizoma</i> ), Tao Ren ( <i>Persicae Semen</i> ), San Qi ( <i>Notoginseng Radix</i> ), Dang Gui ( <i>Angelica sinensis</i> ), Gui Zhi ( <i>Cinnamomi Ramulus</i> ), Xiang Fu ( <i>Cyperii Rhizoma</i> ), Niu Xi ( <i>Achyranthis bidentate Radix</i> )

	<p>Nei Yi enema consisted of:                  Dan Shen (<i>Salviae multiorrhizae Radix</i>), Xue Jie (<i>Draconis Sanguis</i>), Chi Shao (<i>Paeonia rubra Radix</i>), Hu Zhang (<i>Radix et Rhizoma Polygoni Cuspidati</i>), San Leng (<i>Sparganii Rhizoma</i>), E Zhu (<i>Curcumae Rhizoma</i>), Tao Ren (<i>Persicae Semen</i>)                  Treatment duration: 3 months</p>	
Outcomes	<p>A) Clinical outcomes:                  1. symptomatic relief (defined as disappearance of symptoms, pelvic mass; pregnancy or birth within 3 years for those with infertility)                  2. significant improvement (almost complete disappearance of symptoms, shrinkage of pelvic mass by ultrasound; or pregnancy)                  3. improvement (relief of symptoms but not disappearance, no change or moderate shrinkage of pelvic mass)                  4. no effect (no change of symptoms or become worse)                  5. overall improvement (1+2+3)                  B) Adverse effects</p>	
Notes		
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Adequate sequence generation	Low risk	Randomisation for allocation of three groups was generated through random number table
Allocation concealment	Low risk	Allocation sequence was concealed through numbered, sealed, opaque envelopes
Blinding All outcomes	High risk	Although described as patient and assessor blinded (and confirmed with author) there is no description of an attempt to match the herbal enema with an inert control, so it is very unlikely patients were not aware of which group they were allocated to
Incomplete outcome data addressed All outcomes	Low risk	No patient was lost during treatment or follow up
Free of selective reporting	Low risk	Identified outcomes adequately reported compared with the descriptions in the methods
Free of other bias	Low risk	No source of other bias noted

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

Study	Reason for exclusion
Bian 2009	No laparoscopic confirmation
Cai 1999	Unequal group size with no account of randomisation process.
Chai H 1996	Unequal group size with no account of randomisation process.
Chai LS 2004	Unequal group size with no account of randomisation process.
Che 2006	Unequal group size with no account of randomisation process. Also non validated outcomes measures
Chen 2003	Unequal group size with no account of randomisation process.
Chen 2006	Uses an experimental treatment (oral provera) as part of the active and control intervention
Chen 2006a	Combines CHM with therapeutic ultrasound.
Chen 2010	Didn't consider pain as a primary outcome
Chui YX	No clear data on diagnostic or outcomes criteria.
Cui 2010	No clear data on diagnostic criteria. Didn't consider pain as a primary outcome
Fan 2003	Combined TCM with experimental WM treatment (mifepristone).
Fan HX 2004	Group allocation according to patient preference
Fang 2003	Unequal group size with no account of randomisation process.
Fei 2004	Unequal group size with no account of randomisation process.
Fei 2009	No laparoscopic confirmation. Didn't consider pain as a primary outcome
Fong 2004	Insufficient and unclear data to enable a reasonable assessment of the trial
Fong 2006a	Control group used experimental WM treatment (tamoxifen)
Fong DL 2006	Group allocation according to patient preference
Fu 2005	Acupuncture used together with CHM in active group.
Gao 2003	Unequal group size with no account of randomisation process.
Gu 2005	Not an randomised controlled trial.

(Continued)

Han 2001	Used experimental treatment (tamoxifen) as the control group
Hao 2009	Combined TCM with experimental WM treatment(mifepristone)
He H 2004	Unequal group size with no account of randomisation process.
He JY 2005	Randomised according to patient preference
He RZ 2004	No laparoscopic confirmation
Hou 2010	No laparoscopic confirmation.Didn't consider pain as a primary outcome
Hu 2000	Unequal group size with no account of randomisation process.
Hu 2005	Unequal group size with no account of randomisation process.
Hu 2009	Control group used experimental WM treatment(mifepristone)
Huang 2000	Unequal group size with no account of randomisation process.
Huang 2000a	No validated outcomes criteria.
Huang 2009	Didn't consider pain as a primary outcome
Huang 2010	Group allocation according to the time of the patients' first visit
Jia 2004	Insufficient data to enable a reasonable assessment of the trial
Kui JY 2001	Did not respond to questions relating to randomisation
Leng 2009	No laparoscopic confirmation. Didn't consider pain as a primary outcome
Li 1999	Unequal group size with no account of randomisation process.
Li 2003	Unequal group size with no account of randomisation process.
Li 2004	The trial did not use validated outcomes.
Li 2006	Unequal group size with no account of randomisation process.
Li 2007	Unequal group size with no account of randomisation process.
Li 2007a	Insufficient data on the primary outcome to enable a reasonable assessment
Li 2009	Control group used electrochemical therapy

(Continued)

Li QX 2009	Didn't consider pain as a primary outcome
Li XL 2009	No laparoscopic confirmation
Lian 2009	Adequate and reliable details lacking regarding randomisation
Liao 2004	Unequal group size with no account of randomisation process.
Liao 2010	No laparoscopic confirmation
Lin 2006	Unequal group size with no account of randomisation process.
Lin 2006a	Too many treatment variables-including experimental treatment mifepristone
Liu 1994	Too many treatment variables-combined TCM plus hormonal treatment compared to a variety of hormonal control interventions
Liu 1998	Unequal group size with no account of randomisation process.
Liu 1998a	Unequal group size with no account of randomisation process.
Liu 1998b	Too many treatment variables (CHM combined with Gossypol acetic acid and acupuncture)
Liu 2001	Unequal group size with no account of randomisation process.
Liu 2003	Use of acupuncture in the active treatment group.
Liu 2004	Unequal group size with no account of randomisation process. No validated outcomes measures
Liu 2005	Did not consider pain as a primary outcome.
Liu 2009	No laparoscopic confirmation
Liu FY 2003	Did not respond to questions relating to randomisation
Liu GY 2003	Quasi-randomised according to time of initial presentation
Lu 2003	Unequal group size with no account of randomisation process. Experimental treatment (tamoxifen) used as a control
Lu 2005	Unequal group size with no account of the randomisation process and the use of an experimental treatment (mifepristone) as a control
Lu 2007	Randomised trial in participants with endometriosis, but the diagnosis was not confirmed by laparoscopic procedure
Lu 2007a	Adequate and reliable details lacking regarding randomisation

(Continued)

Lu XP 1999	Unequal group size with no account of randomisation process.
Luo 2001	Used mifepristone-experimental treatment for endometriosis as the control group
Luo 2006	Unequal group size with no account of randomisation process.
Ma 2009	No clear data on diagnostic or outcomes criteria
Mo 2010	Control group used experimental WM treatment(mifepristone)
Ou 2007	The trial did not use validated outcomes measures.
Pan XR 2003	No laparoscopic confirmation
Qi 2006	Unequal group size with no account of randomisation process.
Qi YH 2011	130 confirmed endometriosis patients were randomised into herbal treatment group (n=75) or no intervention control group (n=55) after laparoscopic surgery. After our telephone interview, we were told they used random number table to allocate patients. However, some patients (about 10) assigned to control group asked for herbal treatment and they were analysed in the herbal treatment group
Qian 2000a	No validated outcomes criteria.
Qian J 2000	No laparoscopic confirmation
Qiu L 2005	Authors could not be contacted to confirm randomisation details
Qiu YJ 2004	No laparoscopic confirmation
Quan 2010	Group allocation according to the time of the patients' first visit
Ren YL 2005	Unequal group size with no account of randomisation process.
Ren YL2005	No laparoscopic confirmation
Shen XJ 2011	A clinical case series study without control group.
Shong 2005	Unequal group size with no account of randomisation process.
Si 2006	No validated outcomes criteria.
Su CZ 2002	No laparoscopic confirmation
Sun YZ 2003	No laparoscopic confirmation
Tang 2009	No laparoscopic confirmation

(Continued)

Tang 2010	Group allocation according to the time of the patients' first visit
Wang 1996	Unequal group size with no account of randomisation process.
Wang 1999	Too many treatment variables. CHM combined with penicillin, metronidazole + oral contraceptive compared with gestrinone
Wang 2001	No validated outcomes measures. Control group used experimental treatment (tamoxifen)
Wang 2002	Used tamoxifen as a control for CHM. This is not a standard Western medical treatment for endometriosis
Wang 2002a	No information on pain as a primary outcome.
Wang 2002b	Identical paper to Wang 1999.
Wang 2004	Unequal group size with no account of randomisation process.
Wang 2004a	Unequal group size with no account of randomisation process.
Wang 2005	Used experimental treatment (tamoxifen) as the control group
Wang 2006a	Too many treatment variables. Also use Tamoxifen with CHM as active treatment with unequal group size and no account of randomisation
Wang 2006b	Pain was not the primary outcome and the trial only provided data for pain reduction on 7/78 participants in the trial group and 12/78 in the control group
Wang 2009	Didn't consider pain as a primary outcome
Wang 2010	Didn't consider pain as a primary outcome
Wang LX 2006	Authors could not be contacted to confirm details of randomisation
Wang W 2009	Didn't consider pain as a primary outcome
Wang XR 2009	Didn't consider pain as a primary outcome
Wu 1999	Unequal group size with no account of randomisation process.
Wu 2000a	Confounding Comparison of Laparoscopy + CHM with CHM and with Danazol. Too many treatment variables
Wu 2003	No control group-not a randomised controlled trial.
Wu 2004	Unequal group size with no account of randomisation process.
Wu 2006c	Part of a series of reports on the same trial. However this report considered the endometriosis markers EmAb and CA125 and did not provide any new clinical data relevant to this review

(Continued)

Wu 2009	Authors could not be contacted to confirm randomisation details
Wu HY 2009	Didn't consider pain as a primary outcome
Wu SS 2000	No laparoscopic confirmation
Wu XJ 2009	Too many treatment variables
Xia 2010	No laparoscopic confirmation
Xiang 2001	Uses acupuncture as part of the active intervention.
Xiong 2004	Too many treatment variables (CHM combined with indomethacin or norethisterone or danazol)
Xu 2004	Unequal group size with no account of randomisation process.
Xu 2004a	Unequal group size with no account of randomisation process.
Xu 2004b	Unequal group size with no account of randomisation process.
Xu 2005	Unequal group size with no account of randomisation process.
Xu HX 2011	Trial was claimed to be randomised, but after we contacted with authors, we were confirmed that they did not implement real randomisation process to allocate patients
Xuan JS 2005	Quasi randomised according to the time of patient presentation
Xue 2009	Didn't consider pain as a primary outcome
Yan 2004	Insufficient data about outcomes criteria and unequal group size with no account of randomisation process
Yang 2006	Quasi randomised according to the time of patient presentation
Yang 2006a	Uses experimental treatment (tamoxifen) as a control. Also unclear outcomes measures and no report on pain reduction
Yang 2006b	Unequal group size with no account of randomisation process and insufficient data for evaluation
Yang HY 2001	No laparoscopic confirmation
Yang Y	Included acupuncture in the active treatment group.
Ye LQ 2004	No laparoscopic confirmation
Yu 1996	Too many treatment variables-combined TCM plus hormonal treatment compared to a variety of hormonal control interventions. Also unequal group size with no account of randomisation process

(Continued)

Yu 2003	Not a randomised controlled trial.
Yu 2010	Control group used experimental WM treatment(mifepristone)
Yuan 2003	Unequal group size with no account of randomisation process. Also too many treatment variables including CHM, surgery, danazol and tamoxifen
Zhang 2004	Unequal group size with no account of randomisation process.
Zhang 2009	No validated outcomes criteria
Zhang 2010	Didn't respond to questions relating to randomisation
Zhang HQ2009	No laparoscopic confirmation
Zhao 2002	The trial did not use validated outcomes measures.
Zhao 2010	Randomised according to patient preference
Zhong 2009	Authors could not be contacted to confirm randomisation details
Zhou 2010	No clear data on diagnostic critetia
Zhu 2000a	Combined TCM with experimental WM treatment (mifepristone). Also unequal group size with no account of randomisation process
Zhu 2001	Unequal group size with no account of randomisation process.
Zhu FH 2011	Trial was claimed to be randomised, but no information on randomisation methods. Our telephone contacts failed after trying several times
Zhu HY 2002	No laparoscopic confirmation
Zhu L 2000	No laparoscopic confirmation
Zou 2010	No laparoscopic confirmation

## DATA AND ANALYSES

### Comparison 1. CHM versus gestrinone

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Symptomatic relief	1	95	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.93, 1.12]
2 Symptomatic relief rate (intention-to-treat)	1	100	Risk Ratio (M-H, Fixed, 95% CI)	1.04 [0.91, 1.18]
3 Pregnant rate (accumulated from 3-24 months of follow-up)	1	95	Risk Ratio (M-H, Fixed, 95% CI)	1.18 [0.87, 1.59]

### Comparison 2. CHM versus danazol

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Symptomatic relief	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 CHM Nei Yi pills vs Danazol	1	34	Risk Ratio (M-H, Fixed, 95% CI)	5.06 [1.28, 20.05]
1.2 CHM Nei Yi pills + CHM Nei Yi enema vs Danazol	1	42	Risk Ratio (M-H, Fixed, 95% CI)	5.63 [1.47, 21.54]
2 Dysmenorrhea score	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.1 CHM Nei Yi pills vs Danazol	1	34	Mean Difference (IV, Fixed, 95% CI)	-1.01 [-3.11, 1.09]
2.2 CHM Nei Yi pills + CHM Nei Yi enema vs Danazol	1	42	Mean Difference (IV, Fixed, 95% CI)	-2.9 [-4.55, -1.25]
3 Lumbosacral pain relief	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 CHM Nei Yi pills versus Danazol	1	34	Risk Ratio (M-H, Fixed, 95% CI)	1.21 [0.86, 1.70]
3.2 CHM Nei Yi pills + CHM Nei Yi enema vs Danazol	1	42	Risk Ratio (M-H, Fixed, 95% CI)	1.15 [0.82, 1.62]
4 Rectal Irritation relief	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 CHM Nei Yi pills vs Danazol	1	24	Risk Ratio (M-H, Fixed, 95% CI)	1.67 [0.90, 3.10]
4.2 CHM Nei Yi pills + CHM Nei Yi enema vs Danazol	1	30	Risk Ratio (M-H, Fixed, 95% CI)	1.78 [0.99, 3.20]
5 Tenderness of vaginal nodules in posterior fornix	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 CHM Nei Yi pills vs Danazol	1	24	Risk Ratio (M-H, Fixed, 95% CI)	1.31 [0.87, 1.97]
5.2 CHM Nei Yi pills + CHM Nei Yi enema vs Danazol	1	29	Risk Ratio (M-H, Fixed, 95% CI)	1.26 [0.84, 1.90]
6 Adnexal masses disappearance or shrinkage	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

6.1 CHM Nei Yi pills vs Danazol	1	27	Risk Ratio (M-H, Fixed, 95% CI)	1.41 [0.79, 2.50]
6.2 CHM Nei Yi pills + CHM Nei Yi enema vs Danazol	1	36	Risk Ratio (M-H, Fixed, 95% CI)	1.70 [1.04, 2.78]

### Comparison 3. CHM versus CHM

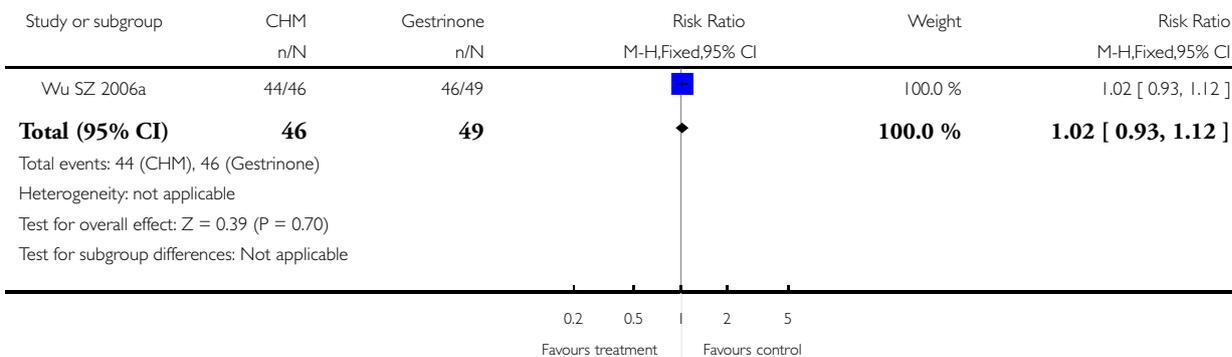
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Symptomatic relief	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 CHM Nei Yi pills + CHM Nei Yi enema vs Nei Yi pills	1	40	Risk Ratio (M-H, Fixed, 95% CI)	1.11 [0.65, 1.89]
2 Dysmenorrhea score	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.1 CHM Nei Yi pills + CHM Nei Yi enema vs Nei Yi pills	1	40	Mean Difference (IV, Fixed, 95% CI)	-1.89 [-3.89, 0.11]
3 Lumbosacral pain relief	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 CHM Nei Yi pills + CHM Nei Yi enema vs Nei Yi pills	1	40	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.74, 1.23]
4 Rectal Irritation relief	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 CHM Nei Yi pills + CHM Nei Yi enema vs Nei Yi pills	1	30	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.79, 1.44]
5 Tenderness of vaginal nodules in posterior fornix	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 CHM Nei Yi pills + CHM Nei Yi enema vs Nei Yi pills	1	27	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.74, 1.25]
6 Adnexal masses disappearance or shrinkage	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
6.1 CHM Nei Yi pills + CHM Nei Yi enema vs Nei Yi pills	1	33	Risk Ratio (M-H, Fixed, 95% CI)	1.21 [0.85, 1.72]

### Analysis 1.1. Comparison 1 CHM versus gestrinone, Outcome 1 Symptomatic relief.

Review: Chinese herbal medicine for endometriosis

Comparison: 1 CHM versus gestrinone

Outcome: 1 Symptomatic relief

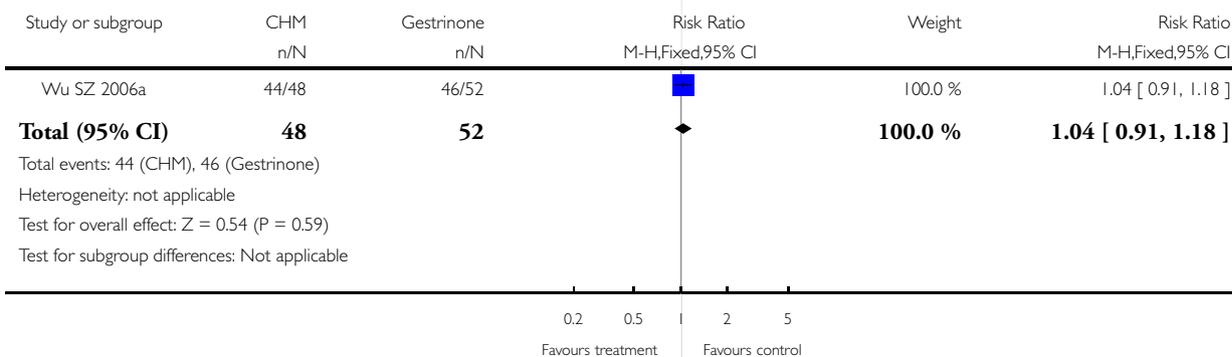


### Analysis 1.2. Comparison 1 CHM versus gestrinone, Outcome 2 Symptomatic relief rate (intention-to-treat).

Review: Chinese herbal medicine for endometriosis

Comparison: 1 CHM versus gestrinone

Outcome: 2 Symptomatic relief rate (intention-to-treat)

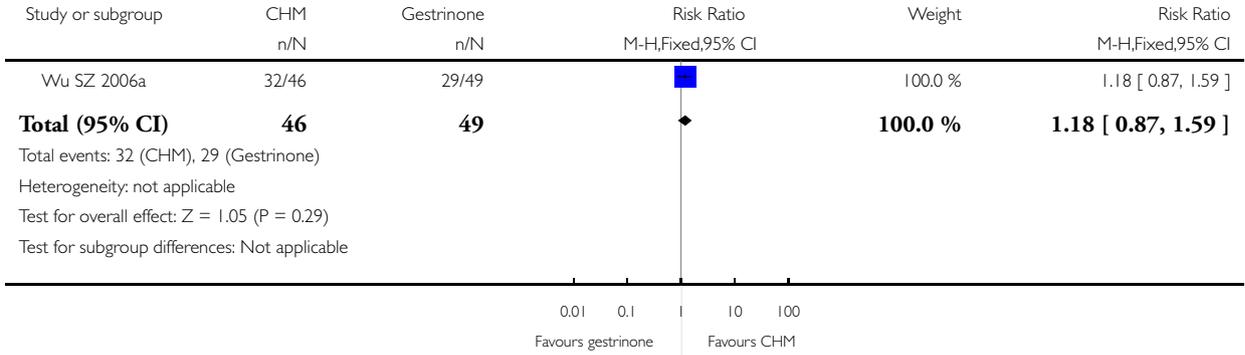


**Analysis 1.3. Comparison 1 CHM versus gestrinone, Outcome 3 Pregnant rate (accumulated from 3-24 months of follow-up).**

Review: Chinese herbal medicine for endometriosis

Comparison: 1 CHM versus gestrinone

Outcome: 3 Pregnant rate (accumulated from 3-24 months of follow-up)

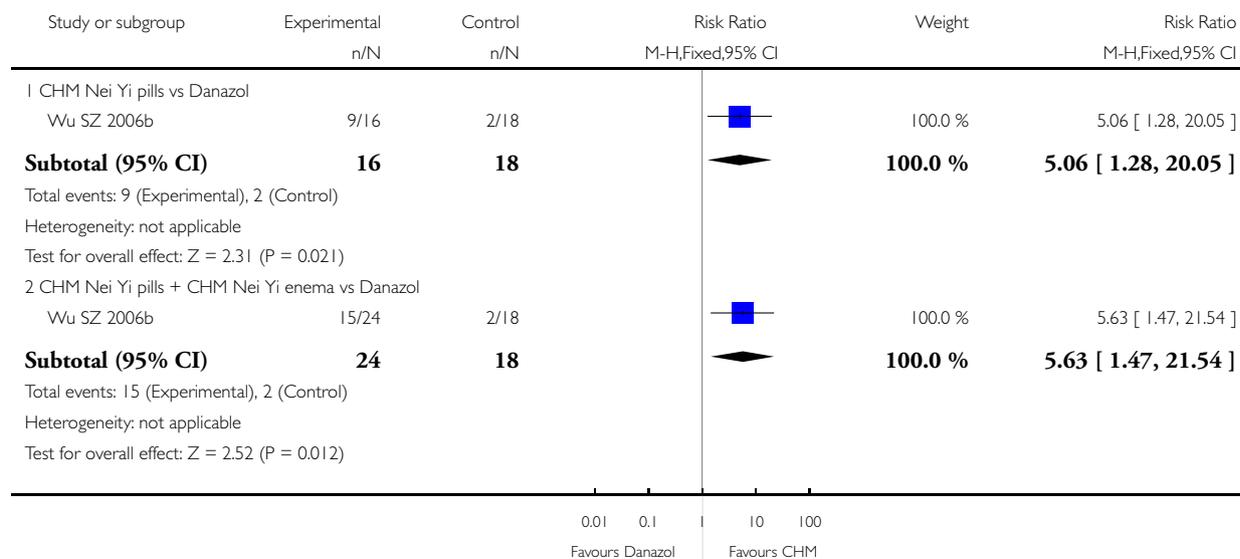


## Analysis 2.1. Comparison 2 CHM versus danazol, Outcome 1 Symptomatic relief.

Review: Chinese herbal medicine for endometriosis

Comparison: 2 CHM versus danazol

Outcome: 1 Symptomatic relief

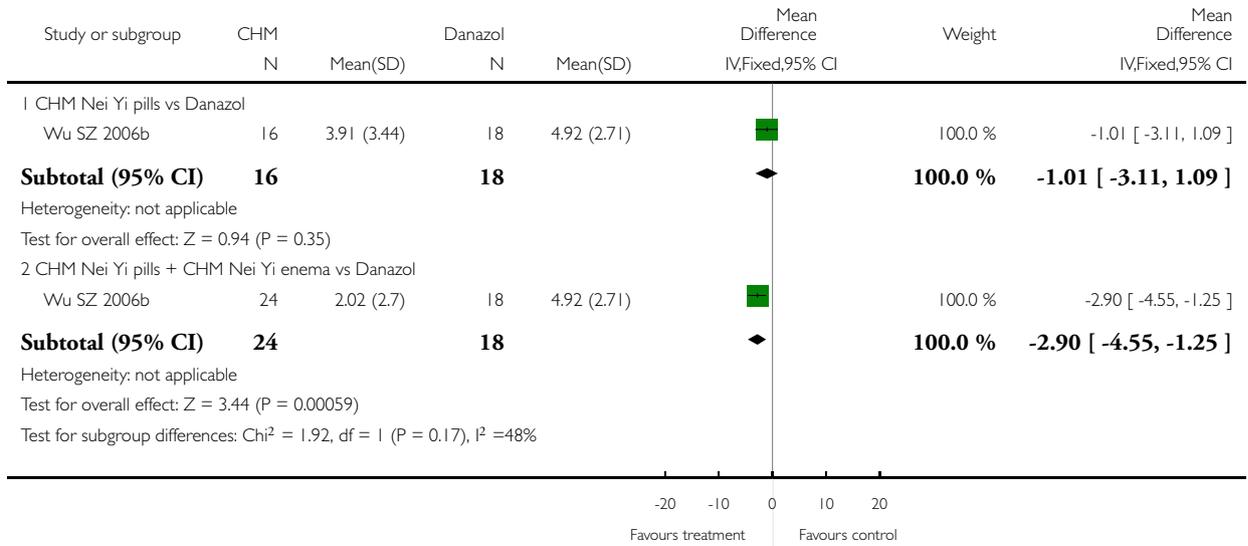


## Analysis 2.2. Comparison 2 CHM versus danazol, Outcome 2 Dysmenorrhea score.

Review: Chinese herbal medicine for endometriosis

Comparison: 2 CHM versus danazol

Outcome: 2 Dysmenorrhea score

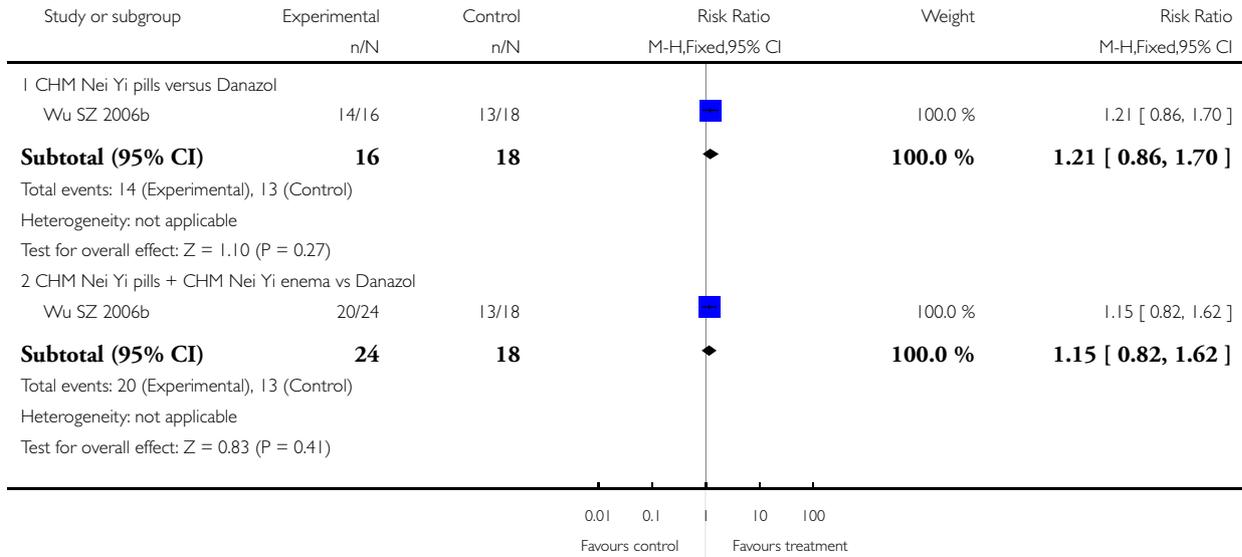


### Analysis 2.3. Comparison 2 CHM versus danazol, Outcome 3 Lumbosacral pain relief.

Review: Chinese herbal medicine for endometriosis

Comparison: 2 CHM versus danazol

Outcome: 3 Lumbosacral pain relief

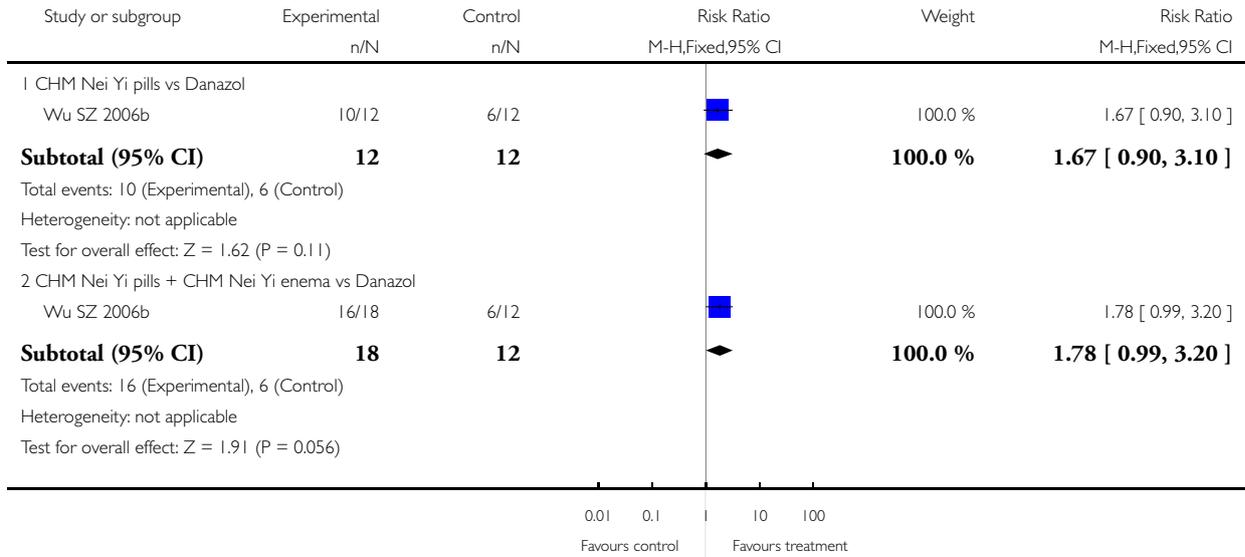


### Analysis 2.4. Comparison 2 CHM versus danazol, Outcome 4 Rectal Irritation relief.

Review: Chinese herbal medicine for endometriosis

Comparison: 2 CHM versus danazol

Outcome: 4 Rectal Irritation relief

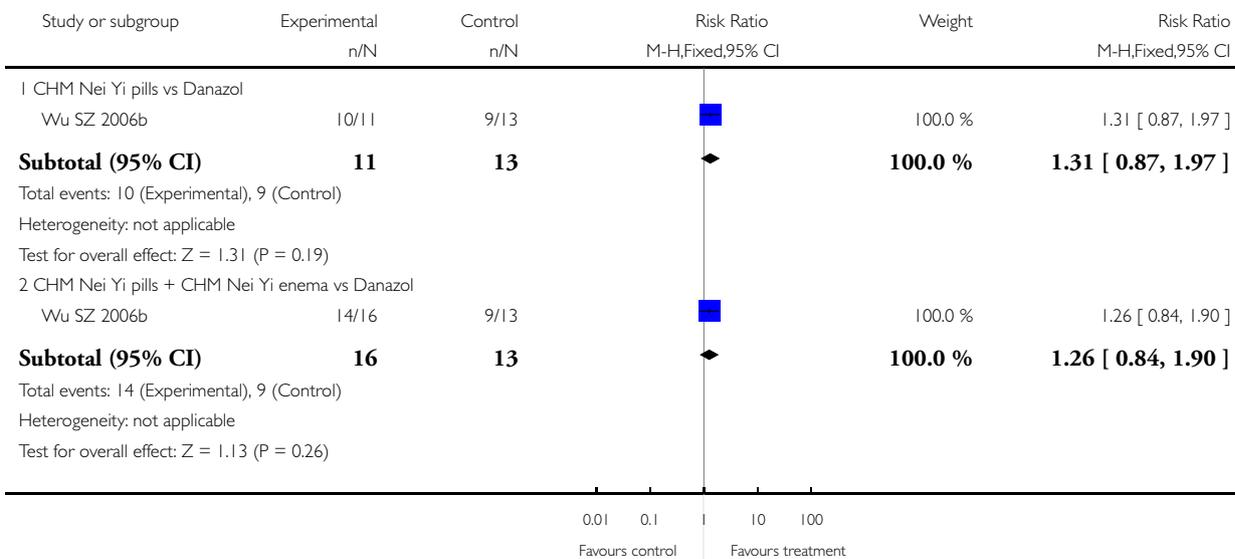


### Analysis 2.5. Comparison 2 CHM versus danazol, Outcome 5 Tenderness of vaginal nodules in posterior fornix.

Review: Chinese herbal medicine for endometriosis

Comparison: 2 CHM versus danazol

Outcome: 5 Tenderness of vaginal nodules in posterior fornix

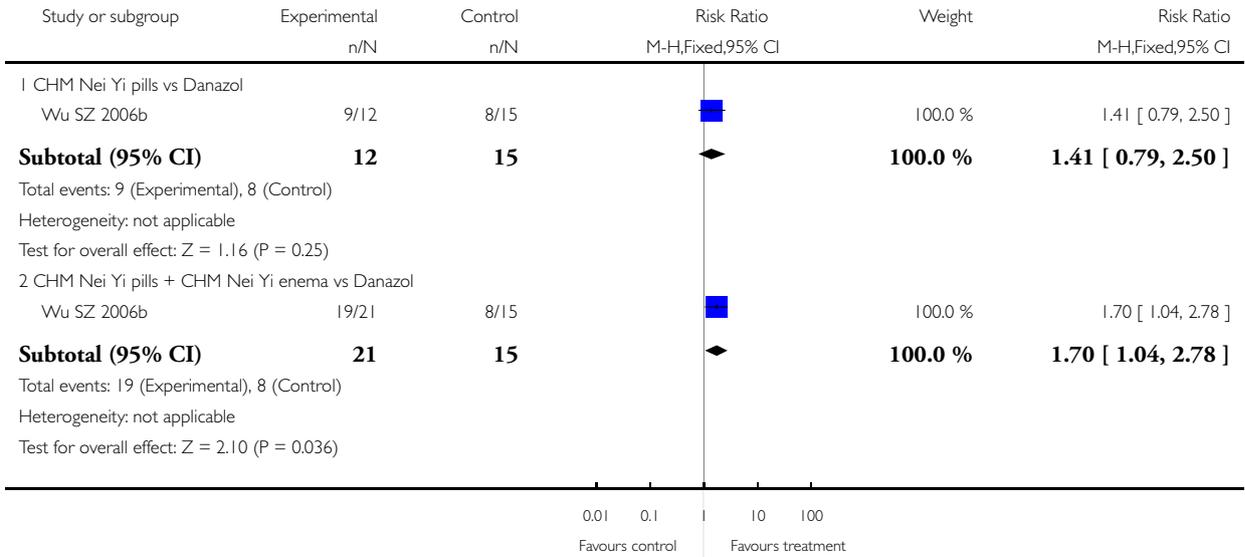


**Analysis 2.6. Comparison 2 CHM versus danazol, Outcome 6 Adnexal masses disappearance or shrinkage.**

Review: Chinese herbal medicine for endometriosis

Comparison: 2 CHM versus danazol

Outcome: 6 Adnexal masses disappearance or shrinkage

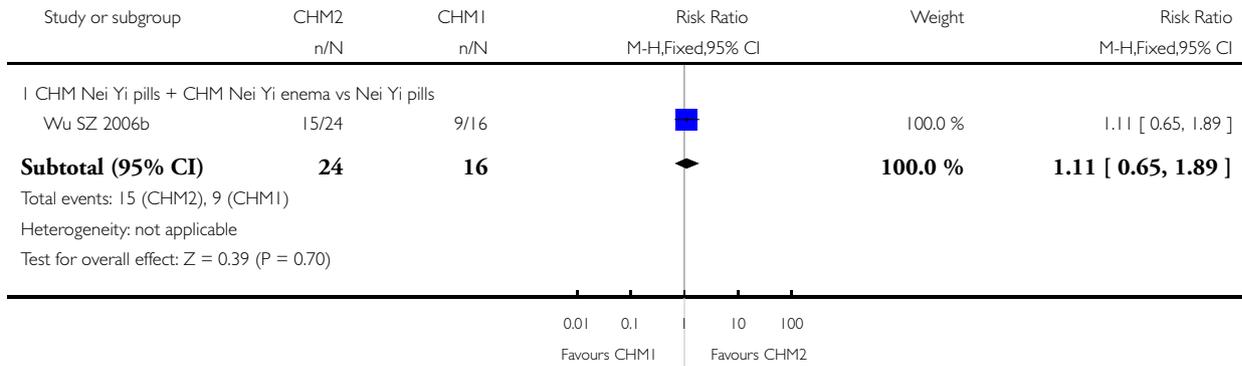


### Analysis 3.1. Comparison 3 CHM versus CHM, Outcome 1 Symptomatic relief.

Review: Chinese herbal medicine for endometriosis

Comparison: 3 CHM versus CHM

Outcome: 1 Symptomatic relief

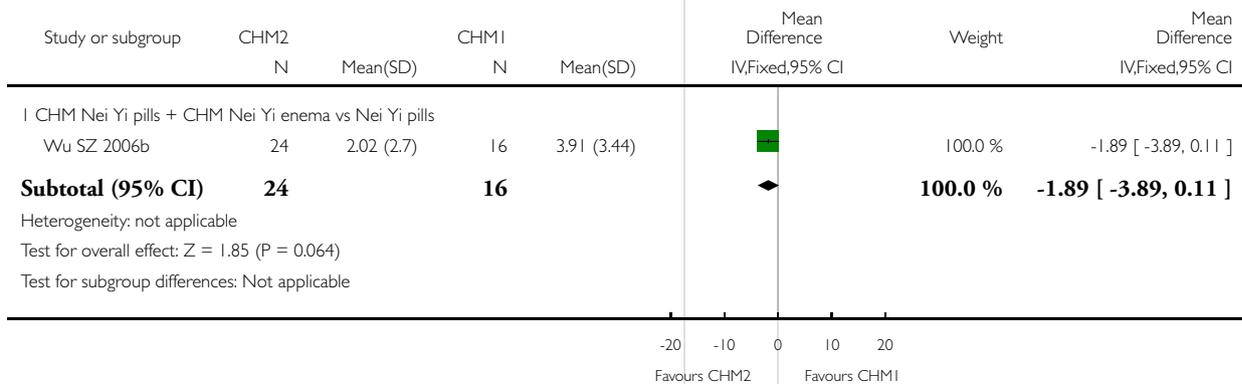


### Analysis 3.2. Comparison 3 CHM versus CHM, Outcome 2 Dysmenorrhea score.

Review: Chinese herbal medicine for endometriosis

Comparison: 3 CHM versus CHM

Outcome: 2 Dysmenorrhea score

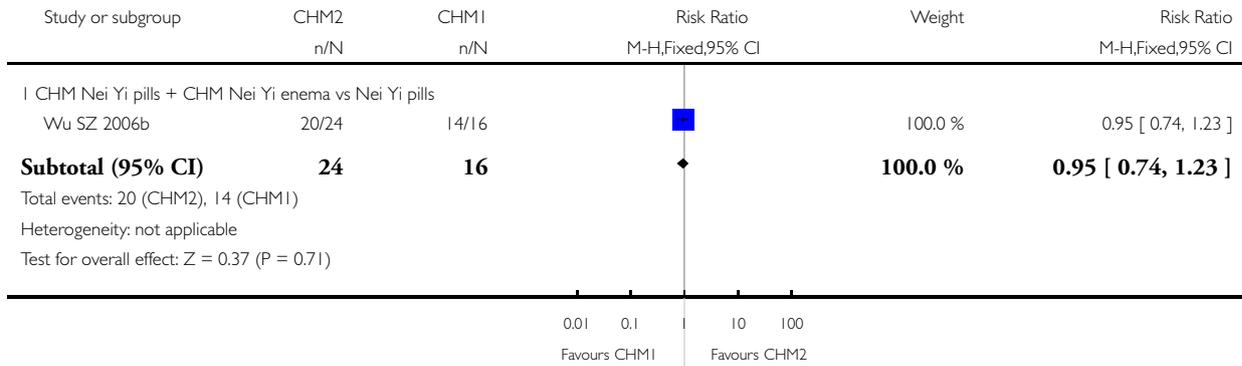


### Analysis 3.3. Comparison 3 CHM versus CHM, Outcome 3 Lumbosacral pain relief.

Review: Chinese herbal medicine for endometriosis

Comparison: 3 CHM versus CHM

Outcome: 3 Lumbosacral pain relief

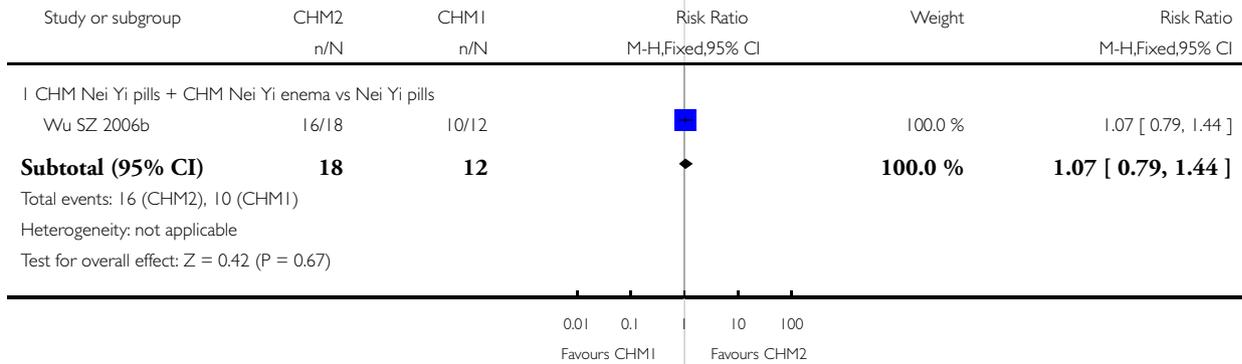


### Analysis 3.4. Comparison 3 CHM versus CHM, Outcome 4 Rectal Irritation relief.

Review: Chinese herbal medicine for endometriosis

Comparison: 3 CHM versus CHM

Outcome: 4 Rectal Irritation relief

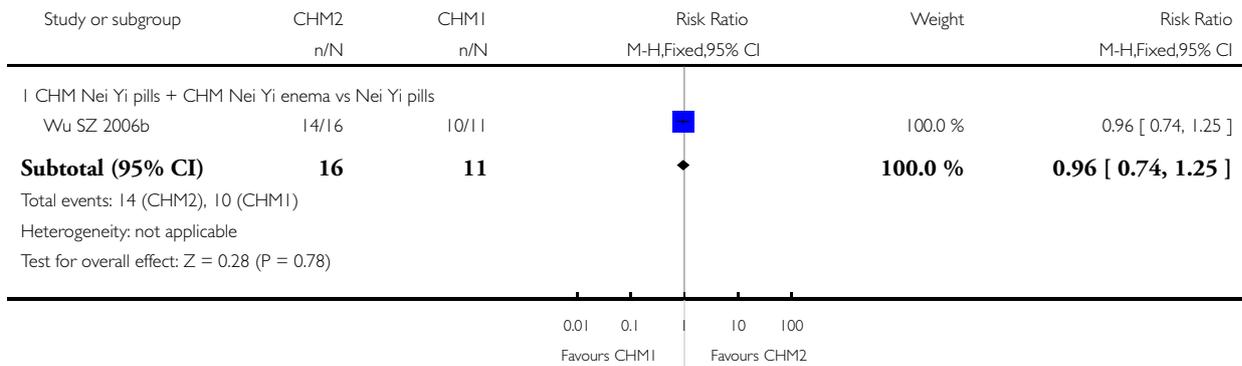


### Analysis 3.5. Comparison 3 CHM versus CHM, Outcome 5 Tenderness of vaginal nodules in posterior fornix.

Review: Chinese herbal medicine for endometriosis

Comparison: 3 CHM versus CHM

Outcome: 5 Tenderness of vaginal nodules in posterior fornix

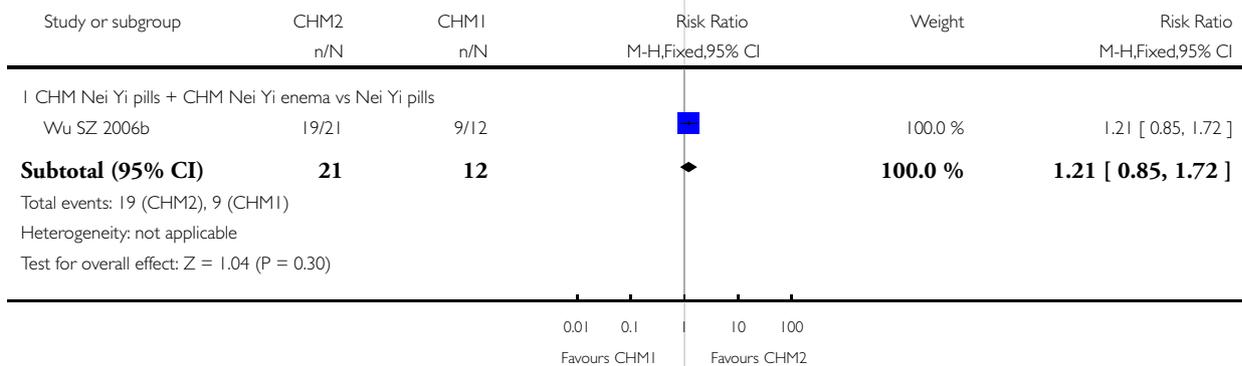


### Analysis 3.6. Comparison 3 CHM versus CHM, Outcome 6 Adnexal masses disappearance or shrinkage.

Review: Chinese herbal medicine for endometriosis

Comparison: 3 CHM versus CHM

Outcome: 6 Adnexal masses disappearance or shrinkage



## APPENDICES

### Appendix I. Search strategies

#### AMED (Allied and Complementary Medicine)

- 1 Controlled study/ or Randomized Controlled Trial/
- 2 Placebo/
- 3 Random\$.tw.
- 4 latin square.tw.
- 5 crossover.tw.
- 6 cross-over.tw.
- 7 placebo\$.tw.
- 8 ((doubl\$ or singl\$ or tripl\$ or trebl\$) adj5 (blind\$ or mask\$)).tw.
- 9 (comparativ\$ adj5 trial\$).tw.
- 10 (clinical adj5 trial\$).tw.
- 11 animal/ not (human/ and animal/)
- 12 alternative medicine/ or traditional medicine/ or chinese medicine/
- 13 Complementary Therapie\$.ti,ab,hw,tn,mf.
- 14 Plant Extract/
- 15 phytodrug\$.ti,ab,hw,tn,mf.
- 16 phytopharmaceutic\$.ti,ab,hw,tn,mf.
- 17 (traditional adj medicine).ti,ab,hw,tn,mf.
- 18 alternative medicine.ti,ab,hw,tn,mf.
- 19 Complementary Therap\$.ti,ab,hw,tn,mf.
- 20 plant extract\$.ti,ab,hw,tn,mf.
- 21 herb\$.ti,ab,sh.
- 22 or/1-10
- 23 22 not 11
- 24 or/12-21
- 25 Endometriosis/ or endometriosis.mp.
- 26 24 and 25
- 27 23 and 26
- 28 from 27 keep 1-2

#### EBM Reviews - Cochrane Central Register of Controlled Trials

- 1 randomized controlled trial.pt.
- 2 controlled clinical trial.pt.
- 3 Randomized Controlled Trials/
- 4 Random allocation/
- 5 double-blind method/
- 6 single-blind method/
- 7 Random\$.tw.
- 8 clinical trial.pt.
- 9 exp clinical trials/
- 10 (clin\$ adj25 trial\$).ti,ab,sh.
- 11 ((singl\$ or doubl\$ or tripl\$ or trebl\$) adj25 (blind\$ or mask\$)).ti,ab,sh.
- 12 Placebos/
- 13 placebo\$.ti,ab,sh.
- 14 random\$.ti,ab,sh.
- 15 Research design/
- 16 or/8-15
- 17 animal/ not (human/ and animal/)
- 18 7 or 16

- 19 18 not 17
- 20 medicine, traditional/ or medicine, chinese traditional/
- 21 Complementary Therapies/
- 22 plant extracts/ or drugs, chinese herbal/
- 23 Plants, Medicinal/
- 24 Drugs, Non-Prescription/
- 25 herb\$.ti,ab,sh.
- 26 Chinese medicine.ti,ab,sh.
- 27 Phytotherapy/
- 28 phytopharmaceutic\$.ti,ab,sh.
- 29 (herb\$ adj5 therap\$).ti,ab,sh.
- 30 (traditional adj medicine).ti,ab,sh.
- 31 alternative medicine.ti,ab,sh.
- 32 Complementary Therap\$.ti,ab,sh.
- 33 plant extract\$.ti,ab,sh.
- 34 or/20-33
- 35 endometriosis.mp. or Endometriosis/
- 36 34 and 35
- 37 19 and 36
- 38 from 37 keep 1-4
- CINAHL - Cumulative Index to Nursing & Allied Health Literature**
- 1 Controlled study/ or Randomized Controlled Trial/
- 2 Double blind procedure/
- 3 Single Blind Procedure/
- 4 Crossover procedure/
- 5 Drug comparison/
- 6 Placebo/
- 7 Random\$.tw.
- 8 latin square.tw.
- 9 crossover.tw.
- 10 cross-over.tw.
- 11 placebo\$.tw.
- 12 ((doubl\$ or singl\$ or tripl\$ or trebl\$) adj5 (blind\$ or mask\$)).tw.
- 13 (comparativ\$ adj5 trial\$).tw.
- 14 (clinical adj5 trial\$).tw.
- 15 or/7-14
- 16 animal/ not (human/ and animal/)
- 17 15 not 16
- 18 alternative medicine/ or traditional medicine/ or chinese medicine/
- 19 Complementary Therapie\$.ti,ab,hw,tn,mf.
- 20 Plant Extract/
- 21 Chinese Drug/
- 22 Chinese Herb/
- 23 Medicinal Plant/
- 24 Non Prescription Drug/
- 25 Herb/
- 26 phytodrug\$.ti,ab,hw,tn,mf.
- 27 phytopharmaceutic\$.ti,ab,hw,tn,mf.
- 28 (traditional adj medicine).ti,ab,hw,tn,mf.
- 29 alternative medicine.ti,ab,hw,tn,mf.
- 30 Complementary Therap\$.ti,ab,hw,tn,mf.
- 31 plant extract\$.ti,ab,hw,tn,mf.
- 32 or/18-31

33 endometriosis.mp. or ENDOMETRIOSIS/

34 32 and 33

35 17 and 34

36 from 35 keep 1

**EMBASE**

1 Controlled study/ or Randomized Controlled Trial/

2 Double blind procedure/

3 Single Blind Procedure/

4 Crossover procedure/

5 Drug comparison/

6 Placebo/

7 Random\$.tw.

8 latin square.tw.

9 crossover.tw.

10 cross-over.tw.

11 placebo\$.tw.

12 ((doubl\$ or singl\$ or tripl\$ or trebl\$) adj5 (blind\$ or mask\$)).tw.

13 (comparativ\$ adj5 trial\$).tw.

14 (clinical adj5 trial\$).tw.

15 or/7-14

16 animal/ not (human/ and animal/)

17 15 not 16

18 alternative medicine/ or traditional medicine/ or chinese medicine/

19 Complementary Therapie\$.ti,ab,hw,tn,mf.

20 Plant Extract/

21 Chinese Drug/

22 Chinese Herb/

23 Medicinal Plant/

24 Non Prescription Drug/

25 Herb/

26 phytodrug\$.ti,ab,hw,tn,mf.

27 phytopharmaceutic\$.ti,ab,hw,tn,mf.

28 (traditional adj medicine).ti,ab,hw,tn,mf.

29 alternative medicine.ti,ab,hw,tn,mf.

30 Complementary Therap\$.ti,ab,hw,tn,mf.

31 plant extract\$.ti,ab,hw,tn,mf.

32 or/18-31

33 endometriosis.mp. or ENDOMETRIOSIS/

34 32 and 33

35 17 and 34

36 from 35 keep 1-8

**MEDLINE**

1 randomized controlled trial.pt.

2 controlled clinical trial.pt.

3 Randomized Controlled Trials/

4 Random allocation/

5 double-blind method/

6 single-blind method/

7 or/1-6

8 clinical trial.pt.

9 exp clinical trials/

10 (clin\$ adj25 trial\$).ti,ab,sh.

11 ((singl\$ or doubl\$ or tripl\$ or trebl\$) adj25 (blind\$ or mask\$)).ti,ab,sh.

12 Placebos/  
 13 placebo\$.ti,ab,sh.  
 14 random\$.ti,ab,sh.  
 15 Research design/  
 16 or/8-15  
 17 animal/ not (human/ and animal/)  
 18 7 or 16  
 19 18 not 17  
 20 medicine, traditional/ or medicine, chinese traditional/  
 21 Complementary Therapies/  
 22 plant extracts/ or drugs, chinese herbal/  
 23 Plants, Medicinal/  
 24 Drugs, Non-Prescription/  
 25 herb\$.ti,ab,sh.  
 26 Chinese medicine.ti,ab,sh.  
 27 Phytotherapy/  
 28 phytopharmaceutic\$.ti,ab,sh.  
 29 (herb\$ adj\$ therap\$).ti,ab,sh.  
 30 (traditional adj medicine).ti,ab,sh.  
 31 alternative medicine.ti,ab,sh.  
 32 Complementary Therap\$.ti,ab,sh.  
 33 plant extract\$.ti,ab,sh.  
 34 or/20-33  
 35 endometriosis.mp. or Endometriosis/  
 36 34 and 35  
 37 19 and 36  
 38 from 37 keep 1-11

## Appendix 2. Commonly used Chinese herbs in the treatment of endometriosis.

### Commonly used herbs in the treatment of endometriosis

#### Herbs to move Blood

- E Zhu (Curcuma Rhizoma)
- San Leng (Sparganii Rhizoma)
- Dang Gui (Wei) (Angelica sinensis)
- Chi Shao (Paeoniae Radix rubra)
- Tao Ren (Persicae Semen)
- Dan Shen (Salviae miltiorrhizae Radix)
- Yan Hu Suo (Corydalis Rhizoma)
- Chuan Xiong (Chuanxiong Rhizoma)
- Wu Ling Zhi (Troglodytes Faeces)
- Hong Hua (Carthami Flos)
- Da Huang (Rhei Radix et Rhizoma)
- Mu Dan Pi (Moutan Cortex)
- Pu Huang (Pollen Typhae)
- Shui Zhi (Hirudo seu Whitmaniae)
- Yi Mu Cao (Leonuri Herba)
- Tu Bie Chong (Eupolyphaga/Steleophaga)
- Mo Yao (Myrrha)
- Ru Xiang (Olibanum)
- Xue Jie (Draconis Sanguis)
- San Qi (Notoginseng Radix)

- Chuan Niu Xi (Cyathulae Radix)

#### **Herbs to move Qi**

- Xiang Fu (Cyperi Rhizoma)
- Wu Yao (Linderae Radix)
- Chai Hu (Bupleuri Radix)
- Chuan Lian Zi (Semen Nelumbinis Nuciferae)
- Zhi Ke (Aurantii Fructus)

#### **Herbs to nourish Blood**

- Dang Gui (Angelica Radix sinensis)
- Bai Shao (Paeoniae Radix alba)
- Gou Qi Zi (Lycii Fructus)

#### **Herbs to nourish Qi**

- Huang Qi (Astragali Radix)
- Dang Shen (Codonopsis Radix)
- Bai Zhu (Atractylodes radix)

#### **Herbs to invigorate Yang**

- Du Zhong (Eucommiae Cortex)
- Ba Ji Tian (Morindae officinalis Radix)
- Xu Duan (Dipsaci Radix)
- Yin Yang Huo (Herba Epimedii)
- Tu Si Zi (Cuscutae Semen)

#### **Herbs to dispel Cold**

- Gan Jiang (Zingiberis Rhizoma)
- Wu Zhu Yu (Evodiae Fructus)
- Rou Gui (Cinnamomi Cortex)
- Hui Xiang (Foeniculu Fructus)

#### **Herbs to resolve Phlegm and soften hardness**

- Zao Jiao Ci (Spina Gleditsiae Sinensis)
- Mu Li (Ostreae Concha)
- Xia Ku Cao (Prunellae Spica)
- Hai Zao (Herba Sargassii)
- Kun Bu (Eckloniae Thallus)

#### **Herbs to clear Fire Poison**

- Hong Teng (Sargentodoxae Caulis)
- Bai Jiang Cao (Patriniae Herba)

## **WHAT'S NEW**

Last assessed as up-to-date: 31 October 2011.

Date	Event	Description
19 March 2012	New citation required but conclusions have not changed	No new studies could be added to the review.
19 March 2012	New search has been performed	An updated search of the same electronic databases has been conducted. No additional studies were able to be included in the review

## HISTORY

Protocol first published: Issue 2, 2007

Review first published: Issue 3, 2009

Date	Event	Description
7 April 2008	Amended	Converted to new review format.
9 February 2007	New citation required and major changes	Substantive amendment

## CONTRIBUTIONS OF AUTHORS

AF adapted the original title, developed the protocol, co-authored the final review, and co-ordinated the project.

AF and JPL co-drafted the first versions of the protocol, and the final review.

AF and JPL conducted provisional Chinese and English language searches, and QL updated the searches and contacted authors to confirm trial eligibility for inclusion.

GL and PL reviewed and commented upon the initial drafts of the review.

SC and AF conducted the initial processes of trial selection and data extraction, reviewed and commented on by JPL. For the revised review LQ searched for and identified relevant studies. Any studies that may have been eligible for inclusion were discussed between LQ, JPL and AF.

## DECLARATIONS OF INTEREST

None known

## SOURCES OF SUPPORT

### Internal sources

- JP Liu and Q Li were supported by Beijing University of Chinese Medicine, China.

### External sources

- Complementary Medicine Research Unit, UK.

## DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In the protocol it was stated that quasi-randomised trials would be included in the review. However these trials were excluded from the main review.

## INDEX TERMS

### Medical Subject Headings (MeSH)

Danazol [therapeutic use]; Drugs, Chinese Herbal [administration & dosage; \*therapeutic use]; Dysmenorrhea [drug therapy]; Endometriosis [complications; \*drug therapy]; Enema [methods]; Estrogen Antagonists [therapeutic use]; Gestrinone [therapeutic use]; Pelvic Pain [\*drug therapy; etiology]; Progestins [therapeutic use]; Randomized Controlled Trials as Topic

### MeSH check words

Female; Humans