Herbal preparations for uterine fibroids (Review)

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[Intervention Review]

Herbal preparations for uterine fibroids

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ABSTRACT

Background

Uterine fibroids are the most common non-malignant growths in women of childbearing age. They are associated with heavy menstrual bleeding and subfertility. Herbal preparations are commonly used as alternatives to surgical procedures.

Objectives

To assess the benefits and risks of herbal preparations for uterine fibroids.

Search strategy

Authors searched following electronic databases: the Trials Registers of the Cochrane Menstrual Disorders and Subfertility Group and the Cochrane Complementary Medicine Field, the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2008, Issue 3), MEDLINE, EMBASE, the Chinese Biomedical Database, the Traditional Chinese Medical Literature Analysis and Retrieval System (TCMLARS), AMED, and LILACS. The searches ended on 31st December 2008.

Selection criteria

Randomised controlled trials comparing herbal preparations with no intervention, placebo, medical treatment or surgical procedures in women with uterine fibroids. We also included trials of herbal preparations with or without conventional therapy.

Data collection and analysis

Two review authors collected data independently. We assessed trial risk of bias according to our methodological criteria . We presented dichotomous data as risk ratios (RR) and continuous outcomes as mean difference (MD), both with 95% confidence intervals (CI).

Main results

We included two randomised trials (involved 150 women) with clear description of randomisation methods. The methodological risk of bias of the trials varied. There were variations in the tested herbal preparations, and the treatment duration was six months. The outcomes available were not the primary outcomes selected for this review, such as symptom relief or the need for surgical treatment; trials mainly reported outcomes in terms of shrinkage of the fibroids.

Compared with mifepristone, Huoxue Sanjie decoction showed no significant difference in the disappearance of uterine fibroids, number of patients with shrinking of uterine fibroids or average volume of uterine fibroids, but less effective than mifepristone on reducing average size of uterus (mean difference 23.23 cm^3,95% confidence interval 17.85 to 28.61). There was no significant difference between Nona Roguy herbal product and GnRH agonist in average volume of uterine fibroids or size of uterus. No serious adverse effects from herbal preparations was reported.

Authors' conclusions

Current evidence does not support or refute the use of herbal preparations for treatment of uterine fibroids due to insufficient studies of large sample and high quality. Further high quality trials evaluating clinically relevant outcomes are warranted.

PLAIN LANGUAGE SUMMARY

Herbal preparations for the treatment of women with uterine fibroids

Uterine fibroids are benign (non cancerous) growths in the uterus. They are the most common type of growth found in a women's pelvis, being present in about one in four or five women older than 35 years. Although many women with fibroids are not aware of them,the growths may cause symptoms or problems due to their size, number, or location. Common symptoms can include longer or more frequent menstrual periods, heavy bleeding, menstrual pain, pressure in the lower abdomen, infertility, or miscarriages. Women with these symptoms will require treatment. Fibroids can be treated with surgery, such as myomectomy (removal of the fibroids while leaving the uterus in place) or hysterectomy (removal of the uterus). Another approach is uterine artery embolization, by which the blood vessels to the uterus are blocked. Drugs, such as gonadotropin-releasing hormone (GnRH) agonists, may be used to shrink fibroids and to control bleeding.

Herbal preparations are commonly used alternatives for drug treatment, surgery, or both. This systematic review included two randomised clinical trials involving 150 women with uterine fibroids. Compared with medication, two herbal preparations may have similar beneficial effect on the shrinkage of uterine fibroids or uterus. However, these clinical trials are small in terms of the number of participants and the trial quality varied. The effect of herbal preparations for uterine fibroids therefore needs to be studied in further large, good quality trials.

BACKGROUND

Description of the condition

Uterine fibroids are the most common, non-cancerous uterine growths in women of childbearing age. Alternative names are uterine leiomyomata, fibromyoma, myoma, or fibroids. Around 30% of women of childbearing age have clinically symptomatic uterine fibroids (Newbold 2000; Stewart 2001).Common symptoms may include heavy or painful periods; prolonged menstrual periods; bleeding between periods; pelvic pain or low back pain; 'fullness' in the lower abdomen, with or without urinary or rectal symptoms due to compression; and reproductive problems, such as infertility, multiple miscarriages, or early onset of labour during pregnancy. Many women with uterine fibroids do not have any symptoms.It has been estimated that fibroids could affect up to 77% of women of childbearing age in the United States (Cramer 1990). Uterine fibroids constitute the main reason for hysterectomies to be carried out, based on data between 1990 and 1997 in the United States (Farquhar 2002).

Uterine fibroids are growths of muscular and fibrous cells within, or attached to, the wall of the uterus. According to the location of the growth, they can be categorised as submucosal when they grow just underneath the uterine lining, intramural when they are in between the muscles of the uterus, and subserosal when they are on the outside of the uterus. Fibroids may grow as a single tumour or in clusters. A single fibroid can be less than one inch in size or can grow to eight inches or more. A group of fibroids can also vary in size. The cause of uterine fibroids is unknown, however genetic, hormonal, immunological, and environmental factors may play a role in starting the growth of fibroids, or in continuing that growth. Several risk factors for uterine fibroids have been identified. African-American women are at three- to five-times greater risk than white women. Women who are overweight or obese for their height (based on body mass index (BMI)) are also at slightly higher risk than women who are average in weight for their height. Women who have given birth appear to be at lower risk (Marshall

1997).

Description of the intervention

Recommended treatment for uterine fibroids depends on the severity of symptoms, the woman's age, pregnancy status, desire for future pregnancies, general health, and the characteristics of the fibroids (Stewart 2001). If a woman shows no symptoms, or the fibroids are small, she may not need any treatment except regular routine gynaecological examination to monitor whether they have grown. If a woman has mild symptoms, such as pain, the health care provider may suggest non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen or naproxen sodium for symptomatic treatment (Falcone 2002). If a woman has serious symptoms or pain, medical therapy can be used to relieve symptoms. Such treatment may include gonadotropin releasing hormone agonists (GnRHa) (Lethaby 2001); synthetic steroids with antiprogesterone activity, such as mifepristone or RU486 to slow or stop the growth of fibroids; and the use of progesterone and its derivatives (including an intrauterine device releasing levonorgestrel) for short-term treatment of bleeding and for inhibiting the fibroids' growth (Grigorieva 2003; Maruo 2004). GnRHa is often used in conjunction with hormone therapy with the intention of reducing the side effects of GnRHa alone, especially where use is long-term. Several medications are currently under investigation, in use in some countries, or pending FDA approval for use in the management of fibrosis: gestrinone, pirfenidone, tibolone, raloxifene, tamoxifen, and cetrorelix (Newbold 2000).

Surgical therapy is considered to be an effective treatment and includes myomectomy to remove only the fibroids and leave the healthy uterus, or hysterectomy to remove the entire uterus (Griffiths 2006). Another accepted treatment is uterine artery embolization (UAE), which is used to block off the blood supply to the uterus and so make the fibroids shrink (McLucas 2001; Tranquart 2002; Watson 2002; Gupta 2006). Other operative treatments, under development or of limited clinical experience, include cryomyolysis (using liquid nitrogen to 'freeze' the fibroids to make them shrink); myolysis (using electric current to destroy the fibroids and shrink the blood vessels that feed them); and endometrial ablation (removing the lining of the uterus to control the bleeding) (Falcone 2002). However, few women with uterine fibroids prefer surgery and women may seek less invasive options, such as pain medication, medical therapy, or hormone therapy.

How the intervention might work

Among other alternative therapies, herbal treatments for fibroids are used in several medical traditions and countries (Fugh-Berman 2004). For example, in China the use of traditional Chinese herbal medicines for treating uterine fibroids is a common clinical practice. According to the theory of Chinese medicine, practitioners recognise uterine fibroids as a condition of imbalance between yin and yang in the body (in allopathic terms: disturbances of the endocrine system and blood circulation). Therefore, herbal preparations are prescribed by practitioners based on the patients' symptoms and observation of the tongue and pulse. Clinical studies from the Chinese literature show that Chinese herbal preparations might relieve symptoms and shrink the fibroid tumours without significant adverse effects (Huang 2003; Xiong 2002). However, there are huge variations in the herbal preparations used, which will depend on the practitioners themselves and on the individualised treatment of different women.

Why it is important to do this review

Is the practice of using herbs for fibroids supported by well-designed clinical evidence? We aim to review the clinical research studies systemically and inform practice by presenting comprehensive, critically appraised evidence.

OBJECTIVES

The primary objective is to assess or evaluate the benefits and risks of herbal preparations for treating uterine fibroids. The secondary objective is to assess participant compliance in the use of herbal preparations for treating uterine fibroids.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials regardless of blinding, publication status, or language were included. We planned to include cross-over randomised trials, but to use only data from the pre cross over period. We excluded quasi-randomised trials or randomised trials with false or unclear methods for random allocation of participants.

Types of participants

Women with uterine fibroids diagnosed by clinical symptoms and physical signs,and confirmed by ultrasound scanning, CT, MRI, or a combination of more than one of the procedures. We planned to include women with fibroid related symptoms and palpable uterine fibroids, without confirmation by imaging technology, and to compare these in sensitivity analyses. We also planned to include

women without any symptoms who were found to have uterine fibroids during routine gynaecological examination and which were confirmed by imaging techniques.

Types of interventions

Experimental interventions included Chinese patent herbal medicine, other patent herbal products pertaining to different traditional medicines, extracts of a single herb or compound of herbs, or other individualised herbal remedies. The control interventions included no treatment, placebo, medical therapy, or surgical procedures.

Types of outcome measures

Primary outcomes

- Uterine fibroid related symptoms such as heavy, irregular, or prolonged menstrual periods; bleeding between the periods; pelvic or low back pain; and low abdominal pressure symptoms such as frequent or urgent urination, or constipation. Symptoms could be measured by either patient reporting or instrument, regardless of blinding.
- Number and size of the fibroids.
- Need for surgical treatment (myomectomy, hysterectomy, embolization) due to failure of medical prevention/management of the above symptoms.

Secondary outcomes

- Complications such as anaemia, infertility, miscarriage, premature labour and delivery, abnormal fetal position.
- Quality of life (measured by validated scale or instrument).
- Uterine-volume reduction.
- Amount of bleeding.
- Adverse events.

Search methods for identification of studies

Electronic searches

The following electronic databases were searched, irrespective of language and publication status.

1. The Trials Registers of the Cochrane Menstrual Disorders and Subfertility Group and the Cochrane Complementary Medicine Field.
2. The Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2008, Issue 3).
3. The databases MEDLINE (1966 to Dec 2008), EMBASE (1998 to Dec 2008), Chinese Biomedical Database (1979 to Dec 2008), Traditional Chinese Medical Literature Analysis and Retrieval System (TCMLARS), AMED, and LILACS (www.bireme.br/bvs/I/ibd.htm) from their date of inception onwards.

We used the search terms: uterine fibroids, hysteromyoma, uterine leiomyomata, fibromyoma, myoma; and combined with traditional medicine, alternative medicine, plant extracts, medicinal plants, non-prescription drugs, herbs, complementary medicine, Chinese medicine, phytodrug or phytopharmaceutical. The detailed search strategy is listed Table 1.

Table 1. Detailed search strategy

Database	Time Range	Search Strategy
AMED	1985 to Dec 2008	1 traditional medicine$.tw. (5881) 2 exp plant extracts/ or exp drugs, chinese herbal/ (15672) 3 chinese herb$.tw. (1492) 4 plant extract$.tw. (9931) 5 chinese medicine$.tw. (1026) 6 exp Plants, Medicinal/ (14154) 7 (Plant$ adj2 Medicin$).tw. (13318) 8 herb$.tw. (9770) 9 exp Phytotherapy/ (1049) 10 Phytotherap$.tw. (1346) 11 alternative medicine$.tw. (1201)

Table 1. Detailed search strategy (*Continued*)

		12 exp ethnopharmacology/ or exp remedies/ or exp traditional medicine chinese/ (4761) 13 exp herbal drugs/ (6344) 14 or/1-13 (26465) 15 exp uterine neoplasms/ (20) 16 (uterine adj5 neoplasm$).tw. (28) 17 fibroid$.tw. (23) 18 (fibroma$ or leiomyom$).tw. (48) 19 (myoma$ or hysteromyom$).tw. (15) 20 fibroid$.tw. (23) 21 or/15-20 (87) 22 14 and 21 (17) 23 from 22 keep 1-17 (17)
CENTRAL	Issue 3, 2008	1 exp Fibroma/ (1) 2 fibroma$.tw. (16) 3 leiomyom$.tw. (148) 4 exp Myoma/ (7) 5 myoma$.tw. (150) 6 hysteromyom$.tw. (7) 7 fibroma$.tw. (16) 8 fibroid$.tw. (153) 9 exp Leiomyoma/ (247) 10 or/1-9 (442) 11 exp medicine, traditional/ or exp medicine, oriental traditional/ (351) 12 traditional medicine$.tw. (69) 13 exp plant extracts/ or exp drugs, chinese herbal/ (2840) 14 chinese herb$.tw. (331) 15 plant extract$.tw. (72) 16 chinese medicine$.tw. (428) 17 exp Plants, Medicinal/ (742) 18 (Plant$ adj2 Medicin$).tw. (35) 19 herb$.tw. (1117) 20 exp Phytotherapy/ (1566) 21 Phytotherap$.tw. (48) 22 alternative medicine$.tw. (69) 23 or/11-22 (4822) 24 10 and 23 (7) 25 from 24 keep 1-7 (7)
CINAHL	1982 to March week 1, 2008	1 exp Fibroma/ (0) 2 fibroma$.tw. (184) 3 leiomyom$.tw. (177) 4 exp Myoma/ (36) 5 myoma$.tw. (72)

Table 1. Detailed search strategy (*Continued*)

		6 hysteromyom$.tw. (0) 7 fibroma$.tw. (184) 8 fibroid$.tw. (297) 9 exp Leiomyoma/ (569) 10 or/1-9 (879) 11 exp medicine, traditional/ or exp medicine, oriental traditional/ (10482) 12 traditional medicine$.tw. (294) 13 exp plant extracts/ or exp drugs, chinese herbal/ (2691) 14 chinese herb$.tw. (313) 15 plant extract$.tw. (123) 16 chinese medicine$.tw. (678) 17 exp Plants, Medicinal/ (13658) 18 (Plant$ adj2 Medicin$).tw. (236) 19 herb$.tw. (4109) 20 exp Phytotherapy/ (3397) 21 Phytotherap$.tw. (93) 22 alternative medicine$.tw. (2179) 23 or/11-22 (26022) 24 10 and 23 (14) 25 exp clinical trials/ (57427) 26 Clinical trial.pt. (29998) 27 (clinic$ adj trial$1).tw. (13150) 28 ((singl$ or doubl$ or trebl$ or tripl$) adj (blind$3 or mask$3)).tw. (7801) 29 Randomi?ed control$ trial$.tw. (11197) 30 Random assignment/ (17445) 31 Random$ allocat$.tw. (1211) 32 Placebo$.tw. (10846) 33 Placebos/ (4145) 34 Quantitative studies/ (3735) 35 Allocat$ random$.tw. (73) 36 or/25-35 (79254) 37 24 and 36 (2) 38 from 37 keep 1-2 (2)
EMBASE	2008 Week 11	1 exp traditional medicine/ or exp chinese medicine/ or exp herbal medicine/ or exp oriental medicine/ (21306) 2 exp Plant Extract/ (57548) 3 exp Medicinal Plant/ (40872) 4 (traditional adj2 medicin$).tw. (6936) 5 chinese herb$.tw. (2504) 6 plant extract$.tw. (2889) 7 chinese medicine.tw. (3872) 8 (herbal adj2 medicin$).tw. (3621) 9 (oriental adj2 medicine).tw. (354) 10 (Medicin$ adj2 Plant$).tw. (4699)

Table 1. Detailed search strategy (*Continued*)

		11 herb$.tw. (27378) 12 exp Phytotherapy/ (3672) 13 Phytotherap$.tw. (1297) 14 alternative medicine$.tw. (2950) 15 or/1-14 (109922) 16 exp benign uterus tumor/ or exp leiomyoma/ or exp uterus myoma/ (8988) 17 exp Fibroma/ (2830) 18 (Fibroma$ or leiomyom$).tw. (9914) 19 (myoma$ or hysteromyom$).tw. (2258) 20 fibroid$.tw. (2241) 21 or/16-20 (17218) 22 15 and 21 (35) 23 Clinical trial/ (495185) 24 Randomized controlled trials/ (155511) 25 Random Allocation/ (25203) 26 Single-Blind Method/ (7410) 27 Double-Blind Method/ (68576) 28 Cross-Over Studies/ (20046) 29 Placebos/ (111054) 30 Randomi?ed controlled trial$.tw. (28060) 31 RCT.tw. (2194) 32 Random allocation.tw. (605) 33 Randomly allocated.tw. (9592) 34 Allocated randomly.tw. (1314) 35 (allocated adj2 random).tw. (552) 36 Single blind$.tw. (7066) 37 Double blind$.tw. (81296) 38 ((treble or triple) adj blind$).tw. (127) 39 Placebo$.tw. (104327) 40 Prospective Studies/ (73142) 41 or/23-40 (651841) 42 Case study/ (5369) 43 Case report.tw. (110903) 44 Abstract report/ or letter/ (461484) 45 or/42-44 (575754) 46 41 not 45 (629234) 47 animal/ (18235) 48 human/ (6058876) 49 47 not 48 (14465) 50 46 not 49 (629138) 51 or/23-50 (6253078) 52 22 and 51 (33) 53 from 52 keep 1-33 (33)

Table 1. Detailed search strategy (*Continued*)

MDSG	17th March 2008	Keywords CONTAINS "fibroid" or "Leiomyoma" or "myoma" or "myomas" or "myomata" or "uterine fibroids" or "uterine leiomyomas" or "uterine myoma" or "uterine myomas" or "Uterine Neoplasms" or "fibroids" or Title CONTAINS "fibroid" or "Leiomyoma" or "myoma" or "myomas" or "myomata" or "uterine fibroids" or "uterine leiomyomas" or "uterine myoma" or "uterine myomas" or "Uterine Neoplasms" or "fibroids" AND Keywords CONTAINS "Chinese herbal medicine" or "chinese herbal preparations" or "Chinese herbal remedy" or "Chinese traditional medicine" or "plant extracts" or "herbal preparations" or "herbal remedy", "herbal supplement" or "herbal supplements" or Title CONTAINS "Chinese herbal medicine" or "chinese herbal preparations" or "Chinese herbal remedy" or "Chinese traditional medicine" or "plant extracts" or "herbal preparations" or "herbal remedy", "herbal supplement" or "herbal supplements"
MEDLINE	1950 to Dec 2008	1 exp Fibroma/ (9610) 2 fibroma$.tw. (7047) 3 leiomyom$.tw. (7602) 4 exp Myoma/ (1626) 5 myoma$.tw. (3317) 6 hysteromyom$.tw. (26) 7 fibroma$.tw. (7047) 8 fibroid$.tw. (2244) 9 exp Leiomyoma/ (13308) 10 or/1-9 (29717) 11 exp medicine, traditional/ or exp medicine, oriental traditional/ (17249) 12 traditional medicine$.tw. (2357) 13 exp plant extracts/ or exp drugs, chinese herbal/ (59586) 14 chinese herb$.tw. (2614) 15 plant extract$.tw. (2601) 16 chinese medicine$.tw. (3950) 17 exp Plants, Medicinal/ (44249) 18 (Plant$ adj2 Medicin$).tw. (4189) 19 herb$.tw. (29907) 20 exp Phytotherapy/ (17380) 21 Phytotherap$.tw. (781) 22 alternative medicine$.tw. (3563) 23 or/11-22 (132460) 24 10 and 23 (43) 25 randomised controlled trial.pt. (251334) 26 controlled clinical trial.pt. (77422) 27 randomised controlled trials as topic/ (53023) 28 random allocation/ (60395) 29 double blind method/ (96065) 30 single blind method/ (11789) 31 or/25-30 (424467)

Table 1. Detailed search strategy (*Continued*)

		32 animals/ not (animals/ and humans/) (3189559) 33 31 not 32 (397756) 34 clinical trial.pt. (446433) 35 exp clinical trials as topic/ (201557) 36 (clinic$ adj25 trial$).ti,ab. (142061) 37 cross-over studies/ (21493) 38 (crossover or cross-over or cross over).tw. (40169) 39 ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab. (95360) 40 placebos/ (26962) 41 placebo$.ti,ab. (108242) 42 random$.ti,ab. (401463) 43 research design/ (51618) 44 or/34-43 (910204) 45 44 not 32 (843399) 46 33 or 45 (865071) 47 24 and 46 (8) 48 from 47 keep 1-8 (8)
PSYCHINFO	1806 to March Week 2 2008	1 exp Fibroma/ (0) 2 fibroma$.tw. (15) 3 leiomyom$.tw. (2) 4 exp Myoma/ (0) 5 myoma$.tw. (12) 6 hysteromyom$.tw. (1) 7 fibroma$.tw. (15) 8 fibroid$.tw. (15) 9 exp Leiomyoma/ (0) 10 or/1-9 (44) 11 exp medicine, traditional/ or exp medicine, oriental traditional/ (0) 12 traditional medicine$.tw. (205) 13 exp plant extracts/ or exp drugs, chinese herbal/ (0) 14 chinese herb$.tw. (65) 15 plant extract$.tw. (41) 16 chinese medicine$.tw. (212) 17 exp Plants, Medicinal/ (0) 18 (Plant$ adj2 Medicin$).tw. (68) 19 herb$.tw. (3468) 20 exp Phytotherapy/ (0) 21 Phytotherap$.tw. (14) 22 alternative medicine$.tw. (790) 23 or/11-22 (4537) 24 10 and 23 (1) 25 from 24 keep 1 (1)

Searching other resources

1. We checked the reference lists of identified randomised controlled trials and review articles in order to find further trials not identified by the electronic searches.
2. We searched for ongoing trials through the National Research Register and the web site www.controlled-trials.com.
3. We also checked 'grey' literature including unpub-

lished conference proceedings or abstract books,and contacted pharmaceutical companies which produce herbal medicines for uterine fibroids, to identify unpublished trials.

Data collection and analysis

Selection of studies

Two authors (Jianping Liu and Hong Yang) independently selected the trials to be included in the review according to the prespecified selection criteria. Any disagreements were resolved by discussion. Yun Xia confirmed the randomisation through phone call to Chinese trialist's.

Data extraction and management

Two authors (JP Liu and H Yang) independently extracted data using a self-developed data extraction form. Papers not in Chinese, English, Japanese, or Italian were translated with the help of the Cochrane Menstrual Disorder and Subfertility Group. We extracted the following characteristics and data from each included trial: primary author, study setting, methodology, age, gender, and ethnicity of participants, number of participants randomised and analysed, participant inclusion and exclusion criteria, symptoms and methods for measurement, the diagnostic criteria, type of herb or herbs, quality of the products, route of delivery, dosage and duration of intervention, details of the comparison regime, duration of follow up, reasons for and number dropped out or lost during follow up, outcome measures (end of treatment and at follow up), and number and type of adverse events.

We sought data on the number of participants with each outcome, by allocated treatment group, irrespective of compliance or follow up to allow an intention-to-treat analysis.

Assessment of risk of bias in included studies

Two authors (JP Liu and H Yang) independently assessed methodological risk of bias based on quality components, i.e. adequacy of the generation of the allocation sequence, allocation concealment, double blinding, and follow up (Jadad 1996; Kjaergard 2001; Moher 1998; Schulz 1995). Any disagreement was discussed and consensus reached through a third party (F Cardini). See also Figure 1; Figure 2.

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

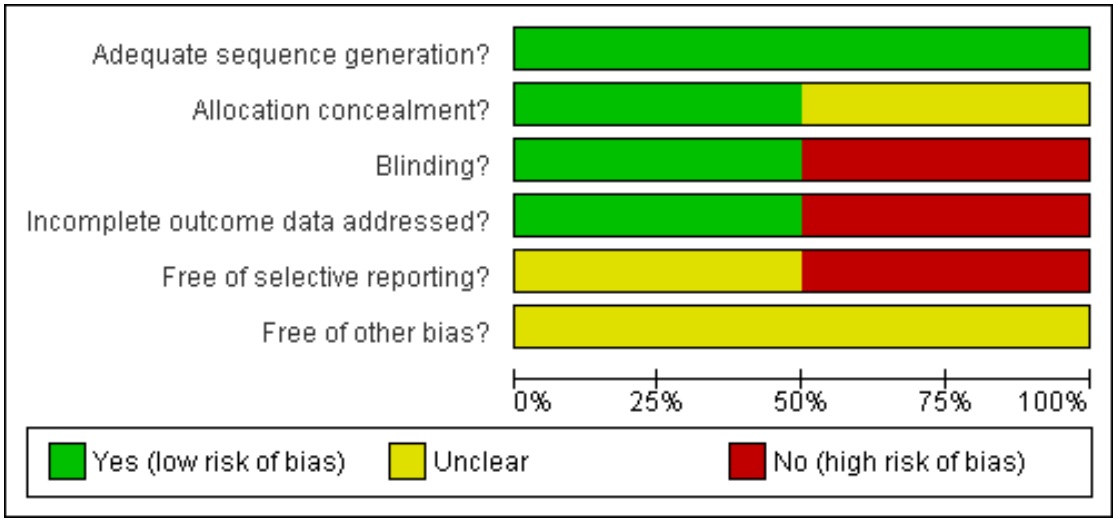
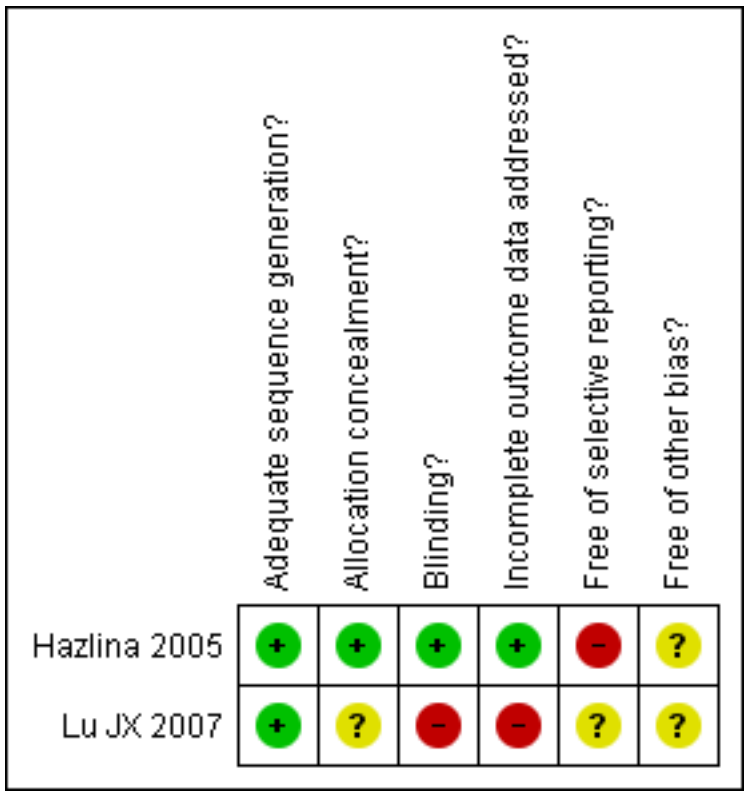


Figure 2. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.



Generation of the allocation sequence

A. Adequate if the allocation sequence was generated by a computer or random number table. Drawing of lots, tossing of a coin, shuffling of cards, or throwing dice may also be considered as adequate if a person who was not otherwise involved in the recruitment of participants performed the procedure;
B. Unclear if the trial was described as randomised but the method used for the allocation sequence generation was not described;
C. Inadequate if a system involving dates, names, or admittance numbers was used for the allocation of participants (i.e. quasi-randomisation).

Allocation concealment

A. Adequate if the allocation of participants involved a central independent unit, on-site locked computer, identically appearing numbered drug bottles or containers prepared by an independent pharmacist or investigator, or sealed envelopes. Envelopes should be serially numbered, sealed, and opaque. However, this information is rarely provided, indicating an increased risk of bias. In that case, sealed envelopes may constitute an intermediate category between adequate and unclear;
B. Unclear if the trial was described as randomised but the method used to conceal the allocation was not described;
C. Inadequate if the allocation sequence was known to the investigators who assigned participants, or if the study was quasi-randomised.

Blinding (or masks)

A. Double blinding if the trial was described as double blind and both the participant and physician were blinded, or participant and outcome assessor;
B. Single blinding if the participants, or physicians, or outcome assessors were blinded;
C. Open-label if blinding was not applied.

Follow up

A. Adequate if the numbers and reasons for withdrawals or losses to follow up from the trial in all intervention groups were described or if it was specified that there were no withdrawals or losses to follow up;
B. Unclear if the report gave the impression that there had been no withdrawals or losses to follow up but this was not specifically stated;
C. Inadequate if the number of, or reasons for, withdrawals or losses to follow up were not described.

Measures of treatment effect

We presented dichotomous data as risk ratio (RR) and continuous outcomes as mean difference (MD), both with 95% confidence intervals (CI). We performed analyses by intention-to-treat where possible. For dichotomous outcomes, participants with incomplete or missing data were to be included in a sensitivity analysis by counting them as treatment failures to explore the possible effect of loss to follow up on the findings ('worst-case' scenario).

Unit of analysis issues

For continuous data, we took 'carry forward' to use last observed patient data in analysis.

Dealing with missing data

For missing data or inadequately reported data, we contacted the trial investigators for clarification.

Assessment of heterogeneity

Due to limited number of trials included, we were not able to do the test for heterogeneity.

Assessment of reporting biases

Due to limited number of trials included, we were not able to assess reporting bias.

Data synthesis

We compared every type of herbal medicine individually with each control (e.g. medical therapy) regardless of route of administration, dose, or preparation. We planned to combine data from individual trials for meta-analysis when the interventions were sufficiently similar (i.e. individual trials compared the same herb versus the same control), and when participants were similar, such as symptomatic or not, or seeking fertility treatment or not.
For three-arm trials, the data from the control group would be split in half, so that half of the participants and half of the events would be used in each comparison.
We tabulated the following comparisons where data were available: herbal medicine versus no treatment, herbal medicine versus placebo, herbal medicine versus pharmacological treatment, and herbal medicines versus surgical procedure. We presented trials of herbal medicines plus conventional therapy versus conventional therapy alone as a separate comparison.
If a sufficient number of randomised trials were identified, and data were available, we would have performed subgroup analyses according to symptom (presence or absence), and location of uterine fibroids (submucosal, intramural, or subserosal fibroids).
Furthermore, if a sufficient number of randomised trials were identified for the same interventions, we planned to perform sensitivity analyses to explore the influence of trial quality or diagnosis, with or without imaging confirmation, on effect estimates. The quality components would include adequacy of generation of allocation sequence, concealment of allocation, blinding, and the use of intention-to-treat (yes or no). Potential biases (Vickers 1998) would be investigated using the funnel plot or other corrective analytical methods (Egger 1997).
We intend to complete an update the review every 24 months.

Subgroup analysis and investigation of heterogeneity

Heterogeneity was tested by using the Chi^2 test, with significance being set at a P value of less than 0.10 and the I^2 greater than 50% being considered as substantial heterogeneity. Whenever there was significant heterogeneity we used a random-effects model and investigated heterogeneity in both clinical characteris-

tics and methodological differences between studies. We carried out the analyses in Review Manager 5.0 (RevMan 2008).

Sensitivity analysis

The number of trials did not allow us to perform meaningful sensitivity analysis.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

Our initial electronic searches identified 852 citations, with a further 35 from additional handsearches.After reading titles and abstracts we excluded 768 of these because they were either :duplicates, non-clinical studies, review articles, case reports, case series, or had study objectives different from this review. A total of 119 references published in Chinese or in English were retrieved for further assessment. We excluded 94 of these studies because they did not meet our inclusion criteria. We contacted with the trial authors to confirm the randomisation methods and missing data, and this procedure allowed us to excluded 21 claimed 'randomised' trials by phone calls.

Results of the search

Our initial electronic searches identified 852 citations, with a further 35 from additional handsearches.

Included studies

We were able to include 2 randomised controlled trials in this review (Hazlina 2005;Lu JX 2007). These RCTs reported random allocation of participants with uterine fibroids to herbal medicines or mifepristone, or GnRH agonist. The 2 randomised trials are listed in the table of 'Characteristics of included studies'. One trial was published in Chinese, and the other in English.

Participants

A total of 150 women with uterine fibroids were randomised. One trial was conducted in China and one trial in Malaysia. The two trials included childbearing-age women with uterine fibroids, diagnosed through routine gynaecological examination and confirmed by type B ultrasound. The two trials reported baseline comparability between groups. As the number of trials included was limited, we could not perform prespecified subgroup analyses, such as symptom type or location of fibroids.

Interventions

Two herbal preparations were tested in the two trials (see Table 2). The controls were pharmaceutical medicines including mifepristone and GnRH agonist. The treatment duration was six months.

Table 2. Compositions of herbal preparations in 23 randomised trials

Name of herbal drugs	Composition	Formulation	Study ID
Herbal product Nona Roguy	Cassia angustifolia, Parkia roxburghii, Zingiber officinale, Trachyspermum ammi, Glycyrrhiza glabra, Usnea barbata, Curcuma domestica, Gastrochilus pandurata, Eryngium foetidum, Citrus Hystrix	Semi-liquid	Hazlina 2005
Huoxue Sanjie Tang	Herbal formula composed of 11 herbs: Radix Angelicae Sinensis 20 g, Herba Leonuri 20 g, Raidix Paeoniae Alba 15 g, Spina Gleditsiae 15 g, Radix Salviae Miltiorrhiae 15 g, Rhizoma Cyperi 12 g, Rhizoma Sparganii 12 g, Rhizoma Curcumae 12 g, Squama Manitis 12 g, Portulaca grandiflora 12 g, Concha Ostreae 10 g	Decoction	Lu JX 2007

Outcomes

Neither trial reported need for surgical treatment, quality of life, fertility, participant compliance, or cost-effectiveness. Outcomes were reported as disappearance of uterine fibroids, volume of fi-

broids or size of uterus, and adverse effect. The two trials reported follow up after the completion of treatment, ranging from 3 to 6 months. Neither trial assessed acceptability and satisfaction of using herbal preparations.

Excluded studies

The reasons for exclusion are listed in the table of 'Characteristics of excluded studies'.

Risk of bias in included studies

The two included trials were reported as parallel group, randomised trials. Neither was a multicentre trial (see Characteristics of included studies). One trial, published in English, reported the randomisation method and adequate allocation concealment (Hazlina 2005),and was considered to have a low risk of bias. Another trial published in Chinese reported the method for generation of allocation randomisation, but provided no information on allocation concealment or blinding.

Our contact with trial authors by phone resulted in our exclusion of 21 randomised trials that originally planned to include (see Characteristics of excluded studies). We were not able to perform meaningful sensitivity or study publication analysis bias due to the limited number of trials.

Effects of interventions

Herbal medicine versus medical treatment

Two trials compared herbal medicines versus conventional drug treatment. Since there was no trial testing the same herbal medicine and control for the same outcome twice, a meta-analysis was not possible for the reported outcomes.

Disappearance of uterine fibroids

Compared with mifepristone, herbal preparation Huoxue Sanjie decoction showed no significant difference in the effect on the disappearance of the fibroids (Lu JX 2007).

Shrinkage of uterine fibroids or uterus

There was no significant difference between Huoxue Sanjie decoction and mifepristone in either the number of patients with shrank uterine fibroids or average volume of uterine fibroids (mean difference 4.98 cm^3, 95% CI -6.08 to 16.04) (Lu JX 2007) see Table 3. However, Huoxue Sanjie decoction was less effective than mifepristone for the average size of uterine fibroids. The comparisons and effect estimates are presented in Table 4.

Table 3. Volume change of uterine fibroids (cm^3)

Study ID	Interventions	Treatment mean SD (n)	Control mean SD (n)	Mean difference	95% CI
Lu JX 2007	Huoxue Sanjie decoction versus mifepristone	56.36 28.74 (59)	51.38 31.62 (56)	4.98	-6.08 to 16.04
Hazlina 2005	Nona Roguy versus GnRH agonist	42.88 63.69 (18)	36.14 36.57 (17)	6.74	-27.43 to 40.91

GnRH = gonadotropin-releasing hormone

Table 4. Outcome of fibroid shrinkage for individual studies

Study ID	No. patients	Comparisons	Outcome measure	RR (95%CI)
Lu JX 2007	115	Huoxue Sanjie decoction vs mifepristone	Disappearance of uterine fibroids	1.33 (0.45 to 3.94)

Table 4. Outcome of fibroid shrinkage for individual studies (*Continued*)

Lu JX 2007	115	Huoxue Sanjie decoction vs mifepristone	Fibroids shrinking over 1/2	0.99 (0.64 to 1.54)
Lu JX 2007	115	Huoxue Sanjie decoction vs mifepristone	Fibroids shrinking over 1/3	1.16 (0.70 to 1.92)

There was no significant difference between the herbal preparation Nona Roguy and gonadotropin releasing hormone (GnRH) agonist regarding uterus size (MD -23.61 cm^3, 95% CI -223.63 to 176.41) (Hazlina 2005).

Adverse effects

Two trials reported outcome of adverse effects (see Table 5) and one trial reported one case of discomfort stomach (Lu JX 2007). No serious adverse effects from taking herbal preparations were reported.

Table 5. Adverse effects of herbal medicines reported in the included trials

Herbs	Formulation	No. of cases	Study ID
Huoxue Sanjie Tang	Decoction	One case (1.7%) had stomach discomfort	Lu JX 2007

DISCUSSION

Summary of main results

This systematic review included only two randomised trials on herbal preparations for the treatment of uterine fibroids. One trial with good quality was published in English (Hazlina 2005) and one trial published in Chinese was of low quality (Lu JX 2007). The trials in this review showed a similar effect of herbal preparations with medication in terms of shrinkage or disappearance of uterine fibroids. However, due to the small sample of the trials and methodological flaws in one trial, any indicated benefit is not conclusive. Further large and rigorous trials are needed.

Overall completeness and applicability of evidence

The included studies tested two different herbal medicines with conventional therapy including mifepristone or GnRHa. There was no significant difference between herbs and medical treatment. However, lack of statistical significant difference does not mean equal effect as none of the trials were designed as equivalence and the sample size was no more than 100 in each arm.

With regard to the conventional medical treatments used in the included studies, the efficacy of mifepristone for uterine fibroids has not been firmly established. A systematic review only identified six before and after clinical trials without placebo or double blinding (Fiscella 2006; Steinauer 2004).

The evidence from this review is not sufficiently convincing to support a clinical recommendation due to the following aspects of the trials.

1. There is a lack of evidence comparing the efficacy of individual herbal preparation with placebo for uterine fibroids. Comparisons with placebo are needed, as there is no clear evidence of efficacy of the comparators used in the trials.
2. Although Chinese herb Huoxue Sanjie decoction showed promising effect compared with mifepristone, the findings are not confirmed as we still lack established efficacy of mifepristone for treatment of uterine fibroids.
3. The trials reported outcomes by end of treatment or short-term follow up. For those women with asymptomatic or mild symptom fibroids, the use of herbal therapies is intended to prevent fibroid growth, or to manage of mild symptoms. For this (wide) subgroup of patients the main outcome is the avoidance of surgical treatment, measured through long-term follow up. Future trialist's are encouraged to adopt this outcome, as women may simply reach their menopause without needing surgery. In addition, reproductive outcomes re-

lated to uterine fibroids, such as the relationship between submucosal, intramural, or subserosal fibroids and pregnancy rates, miscarriage, and malpresentation should be addressed in future trials (Klatsky 2008)

Quality of the evidence

This systematic review has several methodological limitations. Firstly, there are lack of high quality trials and we have to exclude some of the trials that claimed to be randomised because of an unexplainable skew in the distribution of participants among the compared groups or unclear randomisation, which means they are highly prone to selection bias.

Secondly, trials did not reporting use of double blinding, which may be related to performance and detection bias (Schulz 1995; Moher 1998).

Thirdly, the trials had a small sample size. Although some data analyses did not demonstrate a statistically significant difference between herbal medicines and conventional medicine, the results are likely to have been underpowered. Therefore, the size of the trials may mean that the analyses may not establish with confidence that the two interventions have equivalent effects.

The above limitations mean that potential bias may have been present in the selection of participants, administration of treatment, and assessment of outcomes in the primary studies. Methodologically less rigorous trials show significantly larger intervention effects than more robust trials (Egger 2003; Kjaergard 2001; Moher 1998; Schulz 1995). An empirical study has shown that Chinese trials are significantly affected by publication bias (Vickers 1998). When interpreting the present findings, publication bias should be taken into consideration accordingly.

In summary, the findings of this review should be interpreted with caution due to the small sample sizes, low methodological quality in one of the two trials, and the limited number of trials included.

Potential biases in the review process

The use of herbal medicines for uterine fibroids may not be warranted unless we have firm evidence of their efficacy and safety. In future clinical trials both the beneficial and harmful effects should be paid equal attention, and the recording and reporting of adverse effects should be improved.

In this systematic review, quality of herbal medicines was not reported in details, and for future trials, it is important to investigate herbal medicines according to a set of criteria which include preparation consistent with the description in the pharmacopoeia, chemical standardisation, biological assays, animal models, and clinical testing (Yuan 2000). It will be necessary to improve the description of the herbal medicines being tested, for example, plant species, geographical origin, harvest season, preparation procedures, and the quality of the products.

AUTHORS' CONCLUSIONS

Implications for practice

Current evidence does not support the use of herbal preparations for treatment of uterine fibroids. There is no conclusive evidence of benefit due to limited number of trials conducted, the methodological quality of the primary studies and their insufficient power to meet robust conclusions.

Implications for research

Further well-designed, randomised, double blind, placebo-controlled trials are needed to evaluate herbal preparations in uterine fibroids. To improve quality, trials needs to use appropriate allocation concealment, blinding of participants, researchers and outcome assessors, and clarify the number of participants randomised and the number analysed. Clinically relevant outcomes, such as symptoms, infertility, and anaemia, should be addressed and measured using validated patient-reported instruments. Potentially promising herbal preparations require further trials with large samples. Trial reports should follow international standards, such as the CONSORT Statement (http:/ / www.consort- statement.org/).

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REFERENCES

References to studies included in this review

Hazlina 2005 *{published data only}*

Hazlina NNH, Pazudin MI, Nor Aliza AG, Mohsin Sahil SJ. Clinical study to compare the efficacy and adverse effects of Nona Roguy herbal formulation and gonadotrophin releasing hormone agonist (GnRH) in the treatment of uterine fibroids. *International Medical Journal* 2005;**12**(4):295–302.

Lu JX 2007 *{published data only}*

Lu JX. [Comparison of Huoxue Sanjie Decoction with mifepristone in the treatment of uterine fibroids]. *Shandong Journal of Medicine and Pharmacology* 2007;**47**(19):109–10.

References to studies excluded from this review

Akase 2003 *{published data only}*

Akase T, Onodera S, Jobo T, Matsushita R, Kaneko M, Tashiro S-I. [A comparative study of the usefulness of Toki-shakuyaku-san and an oral iron preparation in the treatment of hypochromic anaemia in cases of uterine myoma]. *Yakugaku Zasshi* 2003;**123**(9):817–24.

An ZR 2005 *{published data only}*

An ZR. [43 cases of uterine fibroids treated by Gong Liu Tang]. *Modern Traditional Chinese Medicine* 2005;**25**(6):30.

Chen QM 2007 *{published data only}*

Chen QM, Li FS, Wang JP. [Observation of therapeutic effects of Rupi Anxiao capsules plus small dosage of methyltestosterone in treatment of hysteromyoma]. *Maternal and Child Health Care of China* 2007;**22**(11):1459–61.

Cuan CL 2002 *{published data only}*

Cuan CL, Shang HQ, Fu YP. [30 cases of uterine fibroids treated by Ding Jing Tang]. *Shaanxi Journal of Traditional Chinese Medicine* 2002;**23**(11):975–6.

Du WH 1993 *{published data only}*

Du WH. [Retentive enema and oral taking of Guizhi Fuling Wan for treatment of 40 cases of uterine fibroids]. *Shandong Journal of Traditional Chinese Medicine* 1993;**12**(2):28–9.

Fang RD 2001 *{published data only}*

Fang RD, Zhang XH, Wang QY, Lin YZ, Yang SP, Rao WN, et al.[Clinical study on the treatment of uterine leiomyoma with Xiao Liu Yin iontophoresis]. *Chinese Journal of Information on Traditional Chinese Medicine* 2001;**12**(8):47–9.

Feng FQ 2003 *{published data only}*

Feng FQ. [Therapeutic effect of treating uterine fibroids with Guizhi Fuling capsules]. *Modern Practical Medicine* 2003;**15**(6):389.

Feng X 2004 *{published data only}*

Feng X. [Clinical observation of 39 cases of uterine fibroids treated by self-prescribed Ping Liu Tang]. *Journal of Hebei Traditional Chinese Medicine and Pharmacology* 2004;**19**(2):17.

Fu 2003 *{published data only}*

Fu J. Treatment of 48 cases of uterine fibroids by Yiqi Guchong and Huayu Sanjie therapy. *Journal of Traditional Chinese Medicine* 2003; **44**(9):706.

Fu P 2004 *{published data only}*

Fu P, He JL, Cui L, Chen XC. [Clinical observation on effect of Xuejie Hualiu Granule in treating hysteromyoma]. *Chinese Archives of Traditional Chinese Medicine* 2004;**22**(10):1082–4.

Fu WJ 2005 *{published data only}*

Fu WJ, Ni J, Zheng LJ, Wang XF. [Observation on therapeutic effects of small dosage of Tripterygium Wilfordii Hook for treatment of uterine leiomyoma]. *Journal of Hebei North University (Medical Edition)* 2005;**22**(1):46–8.

Gao SM 2006 *{published data only}*

Gao SM, Liu HY. [Clinical observation of 40 cases of hysteromyoma treated with therapy of nourishing Qi and activating blood circulation]. *Journal of Practical Traditional Chinese Internal Medicine* 2006; **20**(2):190–91.

Gao XL 2001 *{published data only}*

Gao XL, Zhang XR. [Clinical observation of 104 cases of hysteromyoma treated by Xiao Zheng No. 1]. *Shanxi Journal of Traditional Chinese Medicine* 2001;**17**(1):17–8.

Gao YP 2000 *{published data only}*

Gao YP, Chen DF. [Clinical study on effect of Tripterygium Wilfordii Hook on uterine leiomyoma]. *Chinese Journal of Obstetrics and Gynaecology* 2000;**35**(7):430–2.

Gu H 1992 *{published data only}*

Gu H. [Clinical summary of 35 cases of uterine fibroids treated with traditional Chinese medicine]. *Jiangsu Journal of Traditional Chinese Medicine* 1992;**13**(12):7–8.

Guo AQ 2000 *{published data only}*

Guo AQ, Guo YL, Wang XQ. [Clinical observation on treatment of 38 cases of climacteric myoma of uterus by combined traditional Chinese and western medicine]. *Journal of Heze Medical College* 2000;**12**(1):50–2.

Han HL 1992 *{published data only}*

Han HL, Wang GF, Yang RX. [118 cases of uterine fibroids treated by Xiao Liu Wan]. *Chinese Archives of Traditional Chinese Medicine* 1992;**10**(1):36.

Han MX 2002 *{published data only}*

Han MX, Zhu ZS, Liu F. [32 cases of uterine fibroids treated by Qizhi Xiangfu Wan]. *Shanxi Journal of Traditional Chinese Medicine* 2002;**18**(1):21.

He H 2003 *{published data only}*

He H. [Treatment of 38 cases of hysteromyoma by Huangqi Danshen decoction]. *Journal of Guangming Traditional Chinese Medicine* 2003; **18**(109):36.

Hu WD 2007 *{published data only}*

Hu WD. [Analysis on clinical efficacy of Shugan Xiaozheng decoction on hysteromyoma]. *Modern Diagnosis andTreatment* 2007;**18** (5):283,320.

Ji CW 2004 *{published data only}*

Ji CW, Li QS, Pei ZY. [Clinical observation on treating hysteromyoma by Kunyaosan capsule]. *Chinese Journal of Practical Integrated Chinese and Western Medicine* 2004;**4**(1):117.

Jiang JF 2002 *{published data only}*

Jiang JF. [Observation of therapeutic effects in 60 cases of hysteromyoma treated by Eleng Xiaoliu Tang]. *Shandong Journal of Traditional Chinese Medicine* 2002;**21**(4):215.

Jiang LG 2006 *{published data only}*

Jiang LG. [Clinical observation of 36 cases of hysteromyoma treated with Chinese herbal medicine compound]. *Chinese Journal for Clinicians* 2006;**34**(9):40–1.

Jiang P 2003 *{published data only}*

Jiang P, Zhao Y, Ruan YL, Han Y. [Clinical observation of 70 cases of hysteromyoma treated with integrated traditional Chinese and western medicine]. *Modern Journal of Integrated Traditional Chinese and Western Medicine* 2003;**12**(7):707–8.

Jiang XJ 2007 *{published data only}*

Jiang XJ, He FH. [Clinical analysis of mifepristone sequential treatment with Guizhi Fuling capsule on uterine myoma]. *Zhejiang Journal of Clinical Medicine* 2007;**9**(10):1338.

Jiang Y 2003 *{published data only}*

Jiang Y, Xie PS. [186 cases of uterine fibroids treated by traditional Chinese medicine]. *Chinese Journal of Information on Traditional Chinese Medicine* 2003;**10**(1):44.

Jiao ML 2005 *{published data only}*

Jiao ML, Jiao XW. [Clinical observation of 53 cases of hysteromyoma treated by Gong Ji Ning pills]. *Modern Traditional Chinese Medicine* 2005;**3**(3):49.

Kang YP 2005 *{published data only}*

Kang YP, Zheng SG. [46 cases of hysteromyoma at early stage treated with integrated traditional Chinese and western medicine]. *Shaanxi Journal of Traditional Chinese Medicine* 2005;**26**(5):402–3.

Lai HH 2004 *{published data only}*

Lai HH, Gao SF, Deng YM, Zhu ZH, Feng LP, Lai XF. [Clinical observation on Pugui Pill for treatment of 30 cases of hysteromyoma of stagnant heat type]. *Journal of Traditional Chinese Medicine* 2004; **45**(3):201–3.

Li CY 2004 *{published data only}*

Li CY. [Clinical observation of Chinese herbal medicine plus ear acupoints pressing for the treatment of uterine fibroids with blood stasis]. *Liaoning Journal of Traditional Chinese Medicine* 2004;**31** (12):1015.

Li DM 1998 *{published data only}*

Li DM, Gao M, Li HM. [Observation of therapeutic effect of self-prescribed Xiao Zheng Yin for the treatment of hysteromyoma]. *Chinese Journal of Traditional Medical Science and Technology* 1998;**5**(2): 85.

Li FY 1993 *{published data only}*

Li FY. [40 cases of uterine fibroids at early stage treated by Chinese herbal medicine]. *New Journal of Traditional Chinese Medicine* 1993; **25**(10):39–40.

Li JX 2005 *{published data only}*

Li JX. [Clinical observation of 125 cases of hysteromyoma with Qi-stagnancy and blood stasis treated with Zigong Xiaoliu tablets]. *Practice on Chinese Clinical Medicines* 2005;**3**(29):47–8.

Li JX 2006 *{published data only}*

Li JX, Zhang HZ. [Observation on therapeutic effects in hysteromyoma treated with integrated traditional Chinese and western medicine]. *Journal of Changzhi Medical College* 2006;**20**(4):300–1.

Li KY 2005 *{published data only}*

Li KY, Luo SP, Kuang ZS, Deng GP, Tao LL, Xie YH. [Effect of Lizhi Sanjie pill on levels of oestrogen and progestin of hysteromyoma patients]. *Journal of Nanjing TCM University* 2005;**21**(4):228–30.

Li LZ 2003 *{published data only}*

Li LZ, Li GH, Chen P. [Clinical observation of Sanjie Xiaoliu Decoction for treatment of hysteromyoma]. *Tianjin Journal of Traditional Chinese Medicine* 2003;**20**(5):22–3.

Li WY 1999 *{published data only}*

Li WY, Yang GH, Jiang YH. [Clinical observation of Xiao Zheng Pill for treatment of hysteromyoma]. *Hebei Journal of Traditional Chinese Medicine* 1999;**21**(6):331–2.

Li WY 2002 *{published data only}*

Li WY. [Clinical study of treating hysteromyoma by Xiao Zheng Wan]. *Chinese Journal of the Practical Chinese with Modern Medicine* 2002;**2**(15):839–40.

Li Y 2003 *{published data only}*

Li Y, Qin SF, Wang LN. [Clinical observation of Danqi Huazheng capsule in the treatment of hysteromyoma]. *Journal of Henan University of Chinese Medicine* 2003;**18**(3):39–40.

Li YY 2002 *{published data only}*

Li YY. [Oral taking and external application of Chinese herbal medicine for treatment of 98 cases of uterine fibroids]. *Hubei Journal of Traditional Chinese Medicine* 2002;**24**(8):38–9.

Liang YY 2006 *{published data only}*

Liang YY, Huang YH. [Ruanjian Sanjie granule for treatment of 42 cases of uterine fibroids]. *Shaanxi Journal of Traditional Chinese Medicine* 2006;**27**(6):677–8.

Liu DX 2005 *{published data only}*

Liu DX, Luo X. [Clinical observation on the results in treatment of hyperplasia of mammary glands, hysteromyoma and oviduct blocking cases with Xiaoliu pills]. *China Tropical Medicine* 2005;**5**(8): 1684–5.

Liu GY 2005 *{published data only}*

Liu GY. [Clinical observation on the treatment of 45 cases of uterine myoma with Zhechong Siwu decoction]. *Guiding Journal of TCM* 2005;**11**(2):33–4.

Liu JY 2002 *{published data only}*

Liu JY, Meng FL, Zhu L, Yu B, Liu YH, Nie FH. [Treatment of 64 cases of hysteromyoma in perimenopause women with integrated traditional Chinese and western medicine]. *Chinese Journal of Integrated Traditional and Western Medicine* 2002;**22**(4):248.

Liu QP 2001 *{published data only}*

Liu QP, He YN, Guo H. [Clinical observation of Guizhi Fuling Wan Jiawei for treatment of 37 cases of uterine fibroids]. *Yunan Journal of Traditional Chinese Medicine and Materia Medica* 2001;**22**(3):35–6.

Lu M 2007 *{published data only}*

Lu M. [Clinical observation of Yiqi Huayu Xiaozheng Tang for treatment of 60 cases of uterine fibroids]. *Shandong Journal of Traditional Chinese Medicine* 2007;**26**(9):604–6.

Lu SQ 2000 *{published data only}*

Lu SQ, Lin YC, Peng ZY. [Clinical observation of Xiaozheng Sanjie tablet in treating 120 cases of hysteromyoma]. *Correspondence Journal of Traditional Chinese Medicine* 2000;**19**(5):48–9.

Lu Y 2005 *{published data only}*

Lu Y, Deng ZH. [Clinical observation on the treatment of hysteromyoma with Qi-stagnancy and blood-stasis syndrome with Huazheng Decoction]. *Journal of Anhui Traditional Chinese Medical College* 2005;**24**(6):16–7.

Luo L 2003 *{published data only}*

Luo L, Zhu YP. [Effect of treating 110 cases of uterine fibroids with the use of Qing Gong Liu capsules]. *Chinese Journal of Traditional Medical Science and Technology* 2003;**10**(6):382–3.

Lv 2007 *{published data only}*

Lv M. [Clinical observation of 60 cases of hysteromyoma treated by Yiqi Huayu Xiaozheng Decoction]. *Shandong Journal of Traditional Chinese Medicine* 2007;**26**(9):604–6.

Ma WX 2003 *{published data only}*

Ma WX, Li CP. [Xiao Liu Tang for treatment of 42 cases of uterine fibroids]. *Traditional Chinese Medicine Research* 2003;**16**(4):43–4.

Miao XL 2002 *{published data only}*

Miao XL. [Clinical curative observation of Xiao Liu granule for treatment of 130 cases of uterine fibroids]. *Yunan Journal of Traditional Chinese Medicine and Materia Medica* 2002;**23**(5):9–10.

Min XL 2007 *{published data only}*

Min XL. [Treatment of 42 cases of hysteromyoma by Xiao Liu formula]. *Shaanxi Journal of Traditional Chinese Medicine* 2007;**28**(3): 298–9.

Miu XY 2003 *{published data only}*

Miu XY. [Treatment of 280 cases of hysteromyoma by Ji Liu San]. *Fujian Journal of Traditional Chinese Medicine* 2003;**34**(6):7–8.

Miu XY 2007 *{published data only}*

Miu XY. [Observation on therapeutic effect on Ji Liu San and Guizhi Fuling Tang for treatment of uterine fibroids]. *Guangming Journal of Chinese Medicine* 2007;**22**(2):31–3.

Peng XJ 2007 *{published data only}*

Peng XJ, Gao Y, Wang K. [Clinical Study on Huaji-Ye for treatment of uterine leiomyoma]. *Shandong Journal of Traditional Chinese Medicine* 2007;**26**(7):459–60.

Qi C 2003 *{published data only}*

Qi C, Qian B, Zhang QH, Huang ZH. [Clinical observation of 63 cases of hysteromyoma treated with herbal formula of nourishing kidney and activating blood circulation]. *Journal of Sichuan of Traditional Chinese Medicine* 2003;**21**(5):45–6.

Qian L 2007 *{published data only}*

Qian L, Qi C, Zhang QH. [Clinical observation of Bushen Xiaoliu recipe for 80 patients with myoma of uterus]. *Journal of Practical Diagnosis and Therapy* 2007;**21**(8):574–6.

Qiu HN 2006 *{published data only}*

Qiu HN, Li FS. [Clinical observation of mifepristone combined with Guizhi Fuling capsules in perimenopause women with hysteromyoma]. *Journal of Clinical Medicine in Practice* 2006;**10**(3):103–4.

Sakamoto 1992 *{published data only}*

Sakamoto S, Yoshino H, Shirahata Y, Shimodairo K, Okamoto R. Pharmacotherapeutic effects of kuei-chih-fu-ling-wan (keishibukuryo-gan) on human uterine myomas. *American Journal of Chinese Medicine* 1992;**20**(3-4):313–7.

Sakamoto 1998 *{published data only}*

Sakamoto S, Mitamura T, Iwasawa M, Kitsunai H, Shindou K, Yagishita Y, et al.Conservative management for perimenopausal women with uterine leiomyomas using Chinese herbal medicines and synthetic analogs of gonadotropin-releasing hormone. *In Vivo* 1998;**12** (3):333–7.

Sang H 2004 *{published data only}*

Sang H, Wu B. [Clinical and experimental research into treatment of hysteromyoma with promoting Qi flow and blood circulation, softening and resolving hard lump]. *Journal of Traditional Chinese medicine* 2004;**24**(4):274–9.

Sang HL 2002 *{published data only}*

Sang HL, Zhang QW, Jia SH. [Treatment of 150 cases of hysteromyoma with Kangfu Xiaozheng tablets]. *Shandong Journal of Traditional Chinese Medicine* 2002;**21**(3):143–4.

Sang HL 2003 *{published data only}*

Sang HL, Wu BQ. [Clinical and experimental study on Xingqi Huoxue and Ruanjian Sanjie therapy for treatment of uterine fibroids]. *Journal of Traditional Chinese Medicine* 2003;**44**(1):41–3.

Shen D 2006 *{published data only}*

Shen D, Shen XP. [Clinical observation on hysteromyoma treated by testosterone with or without Guizhi Fuling capsules]. *Chinese Modern Medicine and Clinics* 2006;**1**(5):12–3.

Shu S 2001 *{published data only}*

Shu S, Shu C. [Clinical observation of 30 cases of hysteromyoma treated with integrated traditional Chinese and western medicine]. *Journal of Luoyang Medical College* 2001;**19**(4):308–9.

Song SM 2006 *{published data only}*

Song SM, Hou YZ, Wang AF, Qian JY. [Clinical observation of 504 cases of hysteromyoma treated with Guizhi Fuling capsules]. *Applied Journal of General Practice* 2006;**4**(3):319.

Su GH 2005 *{published data only}*

Su GH. [Observation on therapeutic effect of Chinese medicine for treatment of uterine fibroids]. *Shanxi Journal of Traditional Chinese Medicine* 2005;**21**(6):60.

Su XC 2005 *{published data only}*

Su XC, Wang YL, Zheng YS, Liu CL, Yan BC, Kong JX, et al.[Summary of 50 cases of uterine fibroids treated selectively by period with Zi Bao Kang capsule]. *Hunan Journal of Traditional Chineses Medicine* 2005;**21**(1):19–20.

Sun DJ 2007 *{published data only}*

Sun DJ. [Observation on therapeutic effect of integrated Chinese and western medicine for treatment of 68 cases of uterine fibroids]. *Asia-Pacific Traditional Medicine* 2007;**3**(8):55.

Sun L 1995 *{published data only}*

Sun L. [38 cases of hysteromyoma treated with tumour-resolving decoction]. *Journal of Traditional Chinese Medicine* 1995;**15**(4):273–6.

Tan SY 2003 *{published data only}*

Tan SY. [Therapeutic observation of hysteromyoma treated with integrated traditional Chinese and western medicine]. *Practical Clinical Journal of Integrated Traditional Chinese and Western Medicine* 2003;**3**(3):11–2.

Tian LJ 2005 *{published data only}*

Tian LJ. [Clinical observation of Fu Liu Qing No. 1 for treatment of hysteromyoma in perimenopausal women]. *Journal of Sichuan of Traditional Chinese Medicine* 2005;**23**(6):69–70.

Wang D 2000 *{published data only}*

Wang D, Fan LX. [Treatment of 32 cases of myoma of uterus by Xiao Ji Pills]. *Shaanxi Journal of Traditional Chinese Medicine* 2000;**21**(5): 199.

Wang JH 2002 *{published data only}*

Wang JH. [Chinese medicine for treatment of 67 cases of uterine fibroids]. *Liaoning Journal of Traditional Chinese Medicine* 2002;**29** (6):335.

Wang JH 2007 *{published data only}*

Wang JH. [Clinical study on Hua Zheng Dan for treatment of uterine leiomyoma]. *Liaoning Journal of Traditional Chinese Medicine* 2007; **34**(6):782–3.

Wang MD 1999 *{published data only}*

Wang MD. [Clinical observation of 112 cases of uterine leiomyoma treated by Tripterygium Wilfordii Hook]. *Journal of Zhejiang University of Traditional Chinese Medicine* 1999;**23**(6):29.

Wang P 2005 *{published data only}*

Wang P, Wang LM, Li L. [Therapeutic effect observation of 74 cases of uterine myoma treated by integration internal and external body]. *Guiding Joumal of Traditional Chinese Medicine* 2005;**11**(5):31–3.

Wang YH 2006 *{published data only}*

Wang YH, Han N. [Clinical observation of 40 cases of hysteromyoma treated by Huayu Xiaozheng decoction]. *Chinese Journal of the Practical Chinese with Modern Medicine* 2006;**19**(24):2947–9.

Wang YL 2004 *{published data only}*

Wang YL. [Clinical observation of 64 cases of hysteromyoma in perimenopause women treated with integrated traditional Chinese and western medicine]. *Jilin Journal of Traditional Chinese Medicine* 2004;**25**(1):38–9.

Wen Q 2005 *{published data only}*

Wen Q. [Therapeutic observation on effect of Tripterygium Wilfordii Hook and mifepristone in treatment of uterine leiomyoma]. *Clinical Medicine of China* 2005;**21**(3):277–9.

Wen XL 2007 *{published data only}*

Wen XL. [Xiao Liu Fang for treatment of 42 cases of uterine fibroids]. *Shaanxi Journal of Traditional Chinese Medicine* 2007;**28**(3):298–9.

Wu N 2002 *{published data only}*

Wu N. [Clinical observation on treatment of 55 cases of hysteromyoma by reinforcing kidney and regulating menstrual cycle]. *Jiangsu Journal of Traditional Chinese Medicine* 2002;**23**(6):21–2.

Wu XM 2007 *{published data only}*

Wu XM, Liu F, Liu QZ. [Observation of hysteromyoma treated by combination of traditional Chinese medicine and western medicine]. *Hei Long Jiang Medical Journal* 2007;**31**(8):610–1.

Xiao CC 1990 *{published data only}*

Xiao CC, Yang BY, Huangpu X, Guo Y, Zhang SM. [Clinical observation on Jiliu Neixiao Wan for treatment of 125 cases of uterine fibroids]. *China Journal of Traditional Chinese Medicine and Pharmacy* 1990;**5**(2):39–41.

Xiong DM 2006 *{published data only}*

Xiong DM, Zhang XL. [Clinical therapeutic observation of 68 cases of hysteromyoma treated with integrated traditional Chinese and western medicine]. *Shenzhen Journal of Integrated Traditional Chinese and Western Medicine* 2006;**16**(1):38–40.

Xiong DM, Zhao L, Zhang XL. [Treatment of 38 cases of uterine fibroids by Guizhi Fuling capsules]. *Shaanxi Journal of Traditional Chinese Medicine* 2006;**27**(6):679–80.

Xu H 2005 *{published data only}*

Xu H, Xu ZX. [Xiao Zheng Tang for treatment of 38 cases of uterine fibroids]. *Liaoning Journal of Traditional Chinese Medicine* 2005;**32** (10):1045.

Xu Y 2007 *{published data only}*

Xu Y. [Effect observation of integrated Chinese and western medicine for treatment of uterine fibroids]. *Clinical Misdiagnosis and Mistherapy* 2007;**20**(7):60–1.

Yan H 1994 *{published data only}*

Yan H, Wang J. [Clinical study on acupuncture for treatment of hysteromyoma]. *Acupuncture Research* 1994;**19**(2):14–6.

Yan LQ 2000 *{published data only}*

Yan LQ. [Clinical study on uterine fibroids treated by traditional Chinese medicine]. *Journal of Changzhi Medical College* 2000;**14**(4): 304–5.

Yan Y 2001 *{published data only}*

Yan Y. [Clinical observation of Guizhi Fuling capsules combined with mifepristone for the treatment of uterine fibroids]. *Acta Academiae Medicinae Xuzhou* 2001;**21**(5):428–9.

Yang JL 2001 *{published data only}*

Yang JL, Yan XP. [Clinical observation of 300 cases of hysteromyoma treated with Gong Liu Qing capsule]. *Journal of Chengdu University of Traditional Chinese Medicine* 2001;**24**(1):10–3.

Yang YX 2005 *{published data only}*

Yang YX, Huang BZ, Wang MJ, Li RR. [Clinical observation of 148 cases of hysteromyoma treated with integrated traditional Chinese and western medicine]. *Modern Journal of Integrated Traditional Chinese and Western Medicine* 2005;**14**(24):3233–4.

Ye JF 2001 *{published data only}*

Ye JF, Wang YX. [Ingredient added "Tumor-Reducing Prescription" for hysteromyoma in 45 cases]. *Shanghai Journal of Traditional Chinese Medicine* 2001;**35**(2):33–4.

Ye TH 2002 *{published data only}*

Ye TH. [Clinical observation of 60 cases of hysteromyoma treated with Gong Liu Xiao capsule]. *Journal of Sichuan of Traditional Chinese Medicine* 2002;**20**(1):53–4.

Yu JY 2004 *{published data only}*

Yu JY. [Xiao Liu Wan for treatment of 60 cases of uterine fibroids]. *Nei Mongol Journal of Traditional Chinese Medicine* 2004;**23**(4):9.

Yu QL 2003 *{published data only}*

Yu QL. [Clinical observation of 30 cases of hysteromyoma treated by Wanying Xiaoliu San]. *Chinese Journal of Current Clinical Medicine* 2003;**1**(8):724–5.

Yu T 2002 *{published data only}*

Yu T, Cao SW, Zhi N. [Clinical observation of 30 cases of hysteromyoma treated by Huashi Sanjie Decoction]. *Jiangxi Journal of Traditional Chinese Medicine* 2002;**33**(5):23–4.

Zhan YR 2007 *{published data only}*
Zhan YR. [Analysis of mifepristone and Guizhi Fuling capsule for treatment of uterine fibroids]. *International Medicine and Health Guidance News* 2007;**13**(2):63–5.

Zhang H 2005 *{published data only}*
Zhang H. [Chinese herbal medicine combined with transcatheter arterial embolization for treatment of 21 cases of uterine fibroids]. *Shandong Journal of Traditional Chinese Medicine* 2005;**24**(12):725–6.

Zhang M 2004 *{published data only}*
Zhang M. [Use of worms for treatment of uterine fibroids]. *Liaoning Journal of Traditional Chinese Medicine* 2004;**31**(1):61.

Zhang QM 2007 *{published data only}*
Zhang QM, Chen X, Sun ZY, Yuan JL. [Clinical observation on curative effect of Yuan Xiao Liu decoction for treatment of hysteromyoma]. *Liaoning Journal of Traditional Chinese Medicine* 2007;**34**(9): 1272–3.

Zhang WL 2005 *{published data only}*
Zhang WL, Shen J. [Clinical observation of mifepristone alone or in combination of Chinese medicine for treatment of uterine fibroids]. *Chinese Journal of Clinical Medicine Research* 2005;**11**(17):2463–4.

Zhang XW 1997 *{published data only}*
Zhang XW, Hao SZ. [The clinical analysis of thirty-eight cases of hysteromyoma treated with Hai Kun decoction]. *Chinese Journal of Marine Drugs* 1997;**16**(2):43–5.

Zhang Z 2006 *{published data only}*
Zhang Z. [Jiawei Guizhi Fuling Wan for treatment of 62 cases of uterine fibroids]. *Journal of Sichuan of Traditional Chinese Medicine* 2006;**24**(1):88.

Zhao LX 2003 *{published data only}*
Zhang WL, Shen J. [Clinical observation of hysteromyoma treated by mifepristone with or without traditional Chinese medicine]. *Chinese Journal of Clinical Medicine Research* 2005;**11**(17):2463–4.
Zhao LX. [Treatment of 64 cases of uterine fibroids treated by Tripterygium Wilfordii Hook]. *Chinese Journal of Integrated Traditional and Western Medicine* 2003;**23**(10):787–8.

Zheng CY 2003 *{published data only}*
Zheng CY, Zhong QL. [Dahuang Zhechong Wan Jiawei for treatment of 60 cases of uterine fibroids]. *Guangxi Journal of Traditional Chinese Medicine* 2003;**26**(5):33.

Zhong Q 2006 *{published data only}*
Zhong Q, Fen JY, Liang SX, Xu YJ. [Clinical observation of hysteromyoma in perimenopause women by conservative treatment of integrated traditional Chinese and western medicine]. *Chinese Journal of Clinical Medicine Research* 2006;**12**(7):964–5.

Zhou J 1997 *{published data only}*
Zhou J, Zhu M, Li YX, Shi JR, Yuan MF, Shen ZL, et al.[Clinical and experimental study on improving cellular immunological function of uterine myoma patients by Xiaoliu tablet]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 1997;**17**(5):277–9.

Zhou MY 2003 *{published data only}*
Zhou MY, Wang JJ, Cao LP, Chen CL, Liu P. [Observation on therapeutic effect of Da Huang Tang combined with uterine artery embolization for treatment of uterine fibroids]. *Liaoning Journal of Traditional Chinese Medicine* 2003;**30**(7):561–2.

Zhou YJ 2006 *{published data only}*
Zhou YJ, Gao J. [Treatment of 30 cases of hysteromyoma with Guizhi Fuling capsules]. *China Journal of Clinical Medicine Hygiene* 2006;**4** (10):66–7.

Zhou YR 1999 *{published data only}*
Zhou YR, Sun FL, Wang CX. [Clinical observation of 48 cases of hysteromyoma treated with Bushen, Poyu and Huatan recipe]. *Chinese Journal of Primary Medicine and Pharmacy* 1999;**6**(5):282.

Zhu FH 2006 *{published data only}*
Zhu FH. [35 cases of hysteromyoma treated with mifepristone and Eleng Xiaozheng Decoction]. *Fujian Journal of Traditional Chinese Medicine* 2006;**37**(3):37.

Zhu JY 1997 *{published data only}*
Zhu JY, Chen M, Zhuang CS, Luo ZH. [Treatment of 80 cases of hysteromyoma with LIzhong Sanjie Pills]. *New Journal of Traditional Chinese Medicine* 1997;**29**(1):34.

Zou DH 1993 *{published data only}*
Zou DH. [Clinical observation on practitioner Gong Zi Fu's differentiation of syndrome for treatment of 93 cases of uterine fibroids]. *Jiangxi Journal of Traditional Chinese Medicine* 1993;**24**(6):13–4.

Additional references

Cramer 1990
Cramer SF, Patel A. The frequency of uterine leiomyomas. *American Journal of Clinical Pathology* 1990;**94**:435–8.

Egger 1997
Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;**315**:629–34.

Egger 2003
Egger M, Juni P, Bartlett C, Holenstein F, Sterne J. How important are comprehensive literature searches and the assessment of trial quality in systematic reviews? Empirical study. *Health Technology Assessment* 2003;**7**(1):1–76.

Falcone 2002
Falcone T, Bedaiwy MA. Minimally invasive management of uterine fibroids. *Current Opinion of Obstetrics and Gynecology* 2002;**14**:401–7.

Farquhar 2002
Farquhar CM, Steiner CA. Hysterectomy rates in the United States 1990-1997. *Obstetrics and Gynecology* 2002;**99**(2):229–34.

Fiscella 2006
Fiscella K, Eisinger SH, Meldrum S, Feng C, Fisher SG, Guzick DS. Effect of mifepristone for symptomatic leiomyomata on quality of life and uterine size: a randomized controlled trial. *Obstetrics and Gynecology* 2006;**108**(6):1381–7.

Fugh-Berman 2004
Fugh-Berman A, Balick MJ, Kronenberg F, Ososki AL, O'Connor B, Reiff M, et al.Treatment of fibroids: the use of beets (Beta vulgaris) and molasses (Saccharum officinarum) as an herbal therapy by Dominican healers in New York City. *Journal of Ethnopharmacology* 2004;**92**(2-3):337–9.

Griffiths 2006
Griffiths A, D'Angelo A, Amso N. Surgical treatment of fibroids for subfertility. *Cochrane Database of Systematic Reviews* 2006, Issue 3. [DOI: 10.1002/14651858.CD003857]

Grigorieva 2003

Grigorieva V, Chen-Mok M, Tarasova M, Mikhailov A. Use of a levonorgestrel-releasing intrauterine system to treat bleeding related to uterine leiomyomas. *Fertility and Sterility* 2003;**79**(5):1194–8.

Gupta 2006

Gupta JK, Sinha AS, Lumsden MA, Hickey M. Uterine artery embolization for symptomatic uterine fibroids. *Cochrane Database of Systematic Reviews* 2006, Issue 1. [Art. No.: CD005073. DOI: 10.1002/14651858.CD005073.pub2]

Huang 2003

Huang YY. [Research advance and prospects of traditional Chinese medicine and western medicine for treatment of uterine fibroids]. *Tianjin Journal of Traditional Chinese Medicine* 2003;**20**(6):78–80.

Jadad 1996

Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, et al.Assessing the quality of reports of randomized clinical trials: is blinding necessary?. *Controlled Clinical Trials* 1996;**17**(1): 1–12.

Kjaergard 2001

Kjaergard LL, Villumsen J, Gluud C. Reported methodologic quality and discrepancies between large and small randomized trials in meta-analyses. *Annals of Internal Medicine* 2001;**135**(11):982–9.

Klatsky 2008

Klatsky PC, Tran ND, Caughey AB, Fujimoto VY. Fibroids and reproductive outcomes: a systematic literature review from conception to delivery. *American Journal of Obstetrics and Gynecology* 2008;**198** (4):357–66.

Lethaby 2001

Lethaby A, Vollenhoven B, Sowter M. Pre-operative GnRH analogue therapy before hysterectomy or myomectomy for uterine fibroids. *Cochrane Database of Systematic Reviews* 2001, Issue 2. [DOI: 10.1002/14651858.CD000547]

Marshall 1997

Marshall LM, Spiegelman D, Barbieri RL, Goldman MB, Manson JE, Colditz GA, et al.Variation in the incidence of uterine leiomyoma among premenopausal women by age and race. *Obstetrics and Gynecology* 1997;**90**(6):967–73.

Maruo 2004

Maruo T, Ohara N, Wang J, Matsuo H. Sex steroidal regulation of uterine leiomyoma growth and apoptosis. *Human Reproduction Update* 2004;**10**(3):207–20.

McLucas 2001

McLucas B, Goodwin S, Adler L, Rappaport A, Reed R, Perrella R. Pregnancy following uterine fibroid embolization. *International Journal of Gynaecology and Obstetrics* 2001;**74**(1):1–7.

Moher 1998

Moher D, Pham B, Jones A, Cook DJ, Jadad AR, Moher M, et al.Does quality of reports of randomised trials affect estimates of intervention efficacy reported in meta-analyses?. *The Lancet* 1998;**352**:609–13.

Newbold 2000

Newbold RR, DiAugustine RP, Risinger JI, Everitt JI, Walmer DK, Parrott EC, et al.Advances in uterine leiomyoma research: conference overview, summary, and future research recommendations. *Environmental Health Perspectives* 2000;**108**(Suppl 5):769–73.

Schulz 1995

Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *JAMA* 1995;**273**(5):408–12.

Steinauer 2004

Steinauer J, Pritts EA, Jackson R, Jacoby AF. Systematic review of mifepristone for the treatment of uterine leiomyomata. *Obstetrics and Gynecology* 2004;**103**(6):1331–6.

Stewart 2001

Stewart EA. Uterine fibroids. *The Lancet* 2001;**357**:293–8.

Tranquart 2002

Tranquart F, Brunereau L, Cottier JP, Marret H, Gallas S, Lebrun JL, et al.Prospective sonographic assessment of uterine artery embolization for the treatment of fibroids. *Ultrasound in Obstetrics and Gynecology* 2002;**19**(1):81–7.

Vickers 1998

Vickers A, Goyal N, Harland R, Rees R. Do certain countries produce only positive results? A systematic review of controlled trials. *Controlled Clinical Trials* 1998;**19**:159–66.

Watson 2002

Watson GM, Walker WJ. Uterine artery embolization for the treatment of symptomatic fibroids in 114 women: reduction in size of the fibroids and women's views of the success of the treatment. *British Journal of Obstetrics and Gynecology* 2002;**109**(2):129–35.

Xiong 2002

Xiong JH, Xiong CY. [Current status of treatment of uterine fibroids by traditional Chinese medicine]. *Journal of Jiangxi College of Traditional Chinese Medicine* 2002;**14**(4):61–3.

Yuan 2000

Yuan R, Lin Y. Traditional Chinese medicine: an approach to scientific proof and clinical validation. *Pharmacology and Therapeutics* 2000;**86**:191–8.

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Hazlina 2005

Methods	Generation of allocation sequence: adequate Blinding: single blind Withdrawal/loss to follow up: 1 participant was withdrawn from the study due to hypersensitivity to GnRH agonist, and 1 participant became pregnant during the 4th visit. The 2 participants were excluded from the study. Follow up was for 6 months after the end of the treatment. Intention-to-treat analyses: no Baseline comparability: parity, age, level of education, symptom, duration of diagnosis, BMI, haemoglobin level, number of fibroids (P > 0.05)
Participants	35 participants with uterine fibroids confirmed by ultrasound (18 in herbal group and 17 in GnRH group) Inclusion and exclusion criteria were specified
Interventions	Experimental: Herbal preparation was formulated and manufactured by Mustajab Industry. It contained 10 herbs, given daily orally in semi-liquid form for a total of 6 months. Control: Gonadotrophin releasing hormone (GnRH) agonist 3.75 mg, intramuscular or subcutaneous injection once a month, for a total of 3 months.
Outcomes	Fibroid and uterine volume measured by ultrasound, serum FSH, LH and oestradiol, and adverse effects
Notes	Sample size was calculated by using the Pocok's formula with 90% power of study and 95% confidence interval

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Drawing of papers containing 'A' or 'B' by participants. The operator who did the allocation was blinded
Allocation concealment?	Yes	Independent operator allocated the participants
Blinding? All outcomes	Yes	Single blind (outcome assessor)

Hazlina 2005 (*Continued*)

Incomplete outcome data addressed? All outcomes	Yes	Number of participants with loss to follow up reported
Free of selective reporting?	No	Data collection clearly described and reported in results
Free of other bias?	Unclear	Insufficient information for making judgement

Lu JX 2007

Methods	Generation of allocation sequence: random number table Double blinding: not mentioned Loss to follow up: follow up for 3 months, but loss to follow up was not reported Intention-treat analyses: no Baseline comparability: age, disease duration (no statistical testing)
Participants	115 participants with uterine fibroid, belonging to type of qi-stagnancy and blood stasis by TCM diagnosis. The diagnosis was made by a routine gynaecological examination and type B ultrasonography. 59 in Huoxue Sanjie decoction group and 56 in mifepristone group Exclusion criteria: heart, liver, kidney and blood diseases, endocrinal diseases, the diameter of uterine fibroids > 60 mm, or mifepristone counter indication, postmenopause women
Interventions	Experimental: Huoxue Sanjie decoction (self-prescribed herbal formula), twice daily for 6 months Control: Mifepristone, taken before sleep from the first or second day of menstrual cycle, 10 mg daily for 6 months
Outcomes	Disappearance of uterine fibroids, uterine-volume reduction, volume of uterine fibroids, and adverse events
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Random number table
Allocation concealment?	Unclear	No information about concealment
Blinding? All outcomes	No	Herbal decoction compared with mifepristone tablet

Lu JX 2007 (*Continued*)

Incomplete outcome data addressed? All outcomes	No	Same number of participants randomised and analysed
Free of selective reporting?	Unclear	The study presented the results in accordance with the outcome measures in the method
Free of other bias?	Unclear	Insufficient information for making judgement

UAE = uterine artery embolization

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

Akase 2003	Clinical trial using Kampo medicine to treat anaemia of patients with uterine myoma
An ZR 2005	Case series of 43 patients treated by herbal medicine
Chen QM 2007	Randomised trial comparing herbal preparation Rupi Anxiao capsule plus methyltestosterone with Rupi Anxiao capsule for treatment of 100 patients with hysteromyoma. The intervention and comparison did not meet the criteria for this review
Cuan CL 2002	Case series of 30 patients with uterine fibroids treated by herbal medicine
Du WH 1993	Case series of 40 patients with uterine fibroids treated by herbal medicine
Fang RD 2001	Randomised trial comparing 2 different herbal preparations (Xiao Liu Yin versus Guizhi Fuling capsule) in treatment of 160 cases of uterine fibroids
Feng FQ 2003	According to the telephone interview by the author, the trial was planned as randomised trial, but did not apply randomisation due to treatment preference of patients.
Feng X 2004	Case series of 39 patients with uterine fibroids treated by herbal medicine
Fu 2003	Randomised trial comparing 2 different herbal preparations (self-prescribed herbal formula versus Guizhi Fuling capsules) for treatment of 72 cases of uterine fibroids
Fu P 2004	Randomised trial comparing 2 different herbal preparations (Xuejie Hualiu granules versus Guizhi Fuling capsules) in 72 cases of uterine fibroids

(*Continued*)

Fu WJ 2005	Randomised trial was included originally, but the trial authors refused to answer questions in the phone by review author for three times.
Gao SM 2006	Randomised trial comparing two different herbal preparations (self-prescribed herbal formula versus Guizhi Fuling pills) in treatment of 60 cases of uterine fibroids.
Gao XL 2001	Randomised trial comparing herbal preparation with methyltestosterone in treatment of 134 cases of uterine fibroids. However, there was obvious skew in the numbers of patients between the two groups (104 versus 30), which could not be explained by randomisation.
Gao YP 2000	Randomised trial comparing herbal preparation with mifepristone in treatment of 85 cases of uterine fibroids. However, there was obvious skew in the numbers of patients between the two groups (65 versus 20), which could not be explained by randomisation.
Gu H 1992	Case series of 35 patients with uterine fibroids treated by herbal medicine
Guo AQ 2000	Randomised trial was originally included, but according to telephone interview to the hospital personnel office on 6 Jan 2009, the trial author left the hospital and could not be contacted and randomisation method is not confirmed.
Han HL 1992	Case series of 118 patients with uterine fibroids treated by herbal medicine
Han MX 2002	Case series of 32 patients with uterine fibroids treated by herbal medicine
He H 2003	Randomised trial was originally included, but review author failed to confirm the randomisation process through phone calls (both to the department of the trial author and hospital personnel office, they said there was no named person working in the hospital. 29 Dec 2008).
Hu WD 2007	The trial was claimed as randomised, but our phone interview (29 Dec 2008) confirmed that it was allocated according to patient preference to treatment.
Ji CW 2004	Randomised trial comparing 2o different herbal preparations (self-prescribed herbal formula versus Bai Xiao Dan) in treatment of 300 cases of uterine fibroids.
Jiang JF 2002	Randomised trial comparing 2 different herbal preparations (Eleng Xiaoliu decoction versus Guizhi Fuling capsules) in treatment of 180 cases of uterine fibroids
Jiang LG 2006	Randomised trial comparing 2 different herbal preparations (self-prescribed herbal formula versus Guizhi Fuling capsules) in treatment of 54 cases of uterine fibroids
Jiang P 2003	Randomised trial was included originally, but the author refused to answer questions about confirmation of the 'randomisation' when in a telehpone interviewing (6 Jan 2009).
Jiang XJ 2007	Quasi-randomised trial comparing mifepristone plus Guizhi Fuling capsules with mifepristone alone in 118 cases of uterine fibroids

(*Continued*)

Jiang Y 2003	Case series of 186 patients with uterine fibroids treated by herbal medicine
Jiao ML 2005	Randomised trial comparing 2 different herbal preparations (Gong Ji Ning pills versus Guizhi Fuling capsules) in treatment of 108 cases of uterine fibroids
Kang YP 2005	Randomised trial originally was included, but failed to acquire additional information about randomisation process and other required data through phone interview (6 and 13 Jan 2009).
Lai HH 2004	Randomised trial comparing 2 different herbal preparations (self-prescribed herbal formula Pu Gui Wan versus Gong Liu Qing capsules) in treatment of 50 cases of uterine fibroids
Li CY 2004	Randomised trial comparing 2 different herbal preparations (self-prescribed herbal formula plus ear acupoint pressing versus Guizhi Fuling capsules) in treatment of 120 cases of uterine fibroids
Li DM 1998	Randomised trial comparing 2 different herbal preparations (self-prescribed Xiao Zheng Yin versus Guizhi Fuling pills) in treatment of 68 cases of uterine fibroids
Li FY 1993	Case series of 40 patients with uterine fibroids treated by herbal medicine
Li JX 2005	Randomised trial comparing 2 different herbal preparations (self-prescribed Zigong Xiaoliu tablets versus Guizhi Fuling pills) in treatment of 125 cases of uterine fibroids
Li JX 2006	Randomised trial originally was included, but failed to acquire additional information about randomisation process and other required data through phone interview (7 Jan 2009).
Li KY 2005	Case-control study of the effect of Lizhi Sanjie pill on oestrogen and progestin levels in uterine fibroids
Li LZ 2003	Randomised trial comparing 2 different herbal preparations (Sanjie Xiaoliu Tang versus Guizhi Fuling capsules) in treatment of 120 cases of uterine fibroids
Li WY 1999	Randomised trial comparing 2 different herbal preparations (Xiao Zheng Wan versus Guizhi Fuling capsules) in treatment of 150 cases of uterine fibroids
Li WY 2002	Randomised trial comparing 2 different herbal preparations (Xiao Zheng Wan versus Guizhi Fuling capsules) in treatment of 300 cases of uterine fibroids
Li Y 2003	Randomised trial comparing 2 different herbal preparations (Danqi Huazheng capsules versus Guizhi Fuling capsules) in treatment of 240 cases of uterine fibroids
Li YY 2002	Case series of 98 patients with uterine fibroids treated by herbal medicine
Liang YY 2006	Case series of 42 patients with uterine fibroids treated by herbal medicine
Liu DX 2005	Randomised trial comparing 2 different herbal preparations (Xiao Zheng Wan versus Guizhi Fuling pills) in treatment of 80 cases of uterine fibroids

(*Continued*)

Liu GY 2005	Randomised trial comparing 2 different herbal preparations (Zhechong Siwu Tang versus Guizhi Fuling pills) in treatment of 75 cases of uterine fibroids
Liu JY 2002	Randomised trial originally was included, but failed to acquire information about randomisation from the trial authors due to change of job (first author) or not aware of the information through phone interview (30 Dec 2008).
Liu QP 2001	Case series of 37 patients with uterine fibroids treated by herbal medicine
Lu M 2007	Randomised trial comparing 2 different herbal preparations (Yiqi Huayu Xiaozheng Tang versus Guizhi Fuling capsules) in treatment of 120 cases of uterine fibroids
Lu SQ 2000	Randomised trial comparing 2 different herbal preparations (Xiaozheng Sanjie tablets versus Bai Xiao Dan) in treatment of 160 cases of uterine fibroids
Lu Y 2005	Randomised trial comparing 2 different herbal preparations (Hua Zheng Tang versus Guizhi Fuling capsules) in treatment of 60 cases of uterine fibroids
Luo L 2003	Randomised trial comparing 2 different herbal preparations (Qing Gong Liu capsules versus Guizhi Fuling capsules) in treatment of 165 cases of uterine fibroids
Lv 2007	Randomised trial comparing 2 different herbal preparations (Yiqi Huayu Xiaozheng Tang versus Guizhi Fuling capsules) in treatment of 120 cases of uterine fibroids
Ma WX 2003	Case series of 42 patients with uterine fibroids treated by herbal medicine
Miao XL 2002	Controlled clinical study comparing 2 herbal medicines for treatment of 130 cases of uterine fibroids
Min XL 2007	Randomised trial comparing 2 different herbal preparations (Xiao Liu formula versus Guizhi Fuling capsules) in treatment of 84 cases of uterine fibroids
Miu XY 2003	Randomised trial comparing 2 different herbal preparations (Ji Liu powder versus Guizhi Fuling decoction) in treatment of 400 cases of uterine fibroids
Miu XY 2007	Replicated publication with Miu XY 2003
Peng XJ 2007	Randomised trial was originally included in this review, but no further information about randomisation method was acquired through phone calls to the trial author (6 Jan 2009).
Qi C 2003	Randomised trial comparing 2 different herbal preparations (Bushen Huoxue formula versus Guizhi Fuling capsules) in treatment of 93 cases of uterine fibroids
Qian L 2007	Randomised trial comparing 2 different herbal preparations (Bushen Xiaoliu formula versus Guizhi Fuling capsules) in treatment of 80 cases of uterine fibroids

(*Continued*)

Qiu HN 2006	Randomised trial comparing mifepristone plus Guizhi Fuling capsules with Guizhi Fuling capsules in treatment of 108 pre-menopausal women with uterine fibroids. The intervention did not meet our inclusion criteria
Sakamoto 1992	Case series
Sakamoto 1998	Case series
Sang H 2004	Clinical study comparing Kangfu Xiaozheng tablet with Guizhi Fuling pill in 120 cases of hysteromyoma
Sang HL 2002	Randomised trial comparing 2 different herbal preparations (Kangfu Xiaozheng tablets versus Guizhi Fuling pills) in treatment of 250 cases of uterine fibroids
Sang HL 2003	Randomised trial comparing 2 different herbal preparations (Kangfu Xiaozheng tablets versus Guizhi Fuling pills) in treatment of 220 cases of uterine fibroids
Shen D 2006	Randomised trial was originally included, but trial author was not able to confirm the randomisation method through phone call (16 Jan 2009).
Shu S 2001	Randomised trial comparing hormone and vitamins plus herbal preparation during menstrual period with hormone plus herbal medicine Guizhi Fuling decoction in treatment of 50 cases of uterine fibroids. The interventions did not meet our inclusion criteria
Song SM 2006	Randomised trial comparing 2 different herbal preparations (Guizhi Fuling capsules versus Jin Gang Teng Liquid) in treatment of 252 cases of uterine fibroids
Su GH 2005	Case series of 43 patients with uterine fibroids treated by herbal medicine
Su XC 2005	Randomised trial comparing 2 different herbal preparations (Zi Bao Kang capsules versus Guizhi Fuling capsules) in treatment of 100 cases of uterine fibroids
Sun DJ 2007	Case series
Sun L 1995	Case series
Tan SY 2003	Randomised trial was originally included, but trial author was not able to confirm the randomisation method through phone call (6 Jan 2009).
Tian LJ 2005	Randomised trial comparing 2 different herbal preparations (Fu Liu Qing No.1 decoction versus Guizhi Fuling capsules) in treatment of 120 cases of uterine fibroids
Wang D 2000	Randomised trial was originally included, but trial author was not able to confirm the randomisation method and blinding through phone call (14 Jan 2009).
Wang JH 2002	Case series of 67 cases of uterine fibroids treated by herbal medicine

(*Continued*)

Wang JH 2007	Randomised trial comparing 2 different herbal preparations (Hua Zheng Dan versus Guizhi Fuling capsules) in treatment of 110 cases of uterine fibroids
Wang MD 1999	Randomised trial comparing herbal preparation with methyltestosterone in treatment of 149 cases of uterine fibroids. However, there was obvious skew in the numbers of patients between the 2 groups (112 versus 37), which could not be explained by randomisation
Wang P 2005	Randomised trial comparing a self-prescribed herbal formula (oral and enema) plus external use of another herbal formula with the same self-prescribed herbal formula (oral) in treatment of 123 cases of uterine fibroids
Wang YH 2006	Randomised trial comparing 2different herbal preparations (Huayu Xiaozheng decoction versus Guizhi Fuling capsules) in treatment of 80 cases of uterine fibroids
Wang YL 2004	Plagiarism of another study (Liu JY 2002)
Wen Q 2005	Randomised trial was originally included, but trial author was not able to confirm the randomisation method through phone call (13 Jan 2009).
Wen XL 2007	Randomised trial comparing 2 different herbal preparations (Xiao Liu Fang versus Guizhi Fuling capsules) in treatment of 84 cases of uterine fibroids
Wu N 2002	Randomised trial comparing 2 different herbal preparations (Xiao Zheng San plus other herbs versus Xiao Zheng San only in treatment of 87 cases of uterine fibroids
Wu XM 2007	Case series
Xiao CC 1990	Case series of 125 patients with uterine fibroids treated by herbal medicine
Xiong DM 2006	Randomised trial was originally included, but trial author used alternate allocation according to the sequence of patient admission, and it is assessed as quasi-randomised trial through phone call (5 Jan 2009).
Xu H 2005	Case series of 38 patients with uterine fibroids treated by herbal medicine
Xu Y 2007	Case series
Yan H 1994	Controlled clinical study testing acupuncture comparing with methyltestosterone, testosterone, or Guizhi Fuling capsules in treatment of 187 cases of uterine fibroids
Yan LQ 2000	Randomised trial was originally included, but trial author refused to answer questions about the randomisation method through phone call (7 Jan 2009).
Yan Y 2001	Quasi-randomised trial comparing Guizhi Fuling capsules combined with mifepristone versus mifepristone alone in 68 patients with uterine fibroids

(*Continued*)

Yang JL 2001	Randomised trial comparing 2 different herbal preparations (Gong Liu Qing capsules versus Guizhi Fuling capsules) in treatment of 300 cases of uterine fibroids
Yang YX 2005	Three-arm randomised trial comparing 2 different herbal preparations with mifepristone in treatment of 344 cases of uterine fibroids. However, there was obvious skew in the numbers of patients among 3 groups (148 versus 96 versus100), which could not be explained by randomisation
Ye JF 2001	Randomised trial comparing 2 different herbal preparations (Xiao Liu formula versus Guizhi Fuling capsules) in treatment of 90 cases of uterine fibroids
Ye TH 2002	Randomised trial comparing 2 different herbal preparations (Gong Liu Xiao capsules versus Gong Liu Qing capsules) in treatment of 90 cases of uterine fibroids
Yu JY 2004	Case series of 60 patients with uterine fibroids treated by herbal medicine
Yu QL 2003	Randomised trial comparing 2 different herbal preparations (Wanying Xiaoliu powder versus Guizhi Fuling capsules) in treatment of 60 cases of uterine fibroids
Yu T 2002	Randomised trial comparing 2 different herbal preparations (Huashi Sanjie Tang versus Ping Xiao capsules) in treatment of 50 cases of uterine fibroids
Zhan YR 2007	Randomised trial was originally included, but trial author was not confirmed as prospective study through phone call (26 Dec 2008).
Zhang H 2005	Randomised trial comparing herbal preparation with no intervention after transcatheter arterial embolization in treatment of 31 cases of uterine fibroids. However, there was an obvious skew in the numbers of patients between the 2 groups (21 versus10), which could not be explained by randomisation
Zhang M 2004	Case report
Zhang QM 2007	Randomised trial comparing 2 different herbal preparations (Yuanshi Xiaoliu Tang versus Guizhi Fuling capsules) in treatment of 54 cases of uterine fibroids
Zhang WL 2005	Randomised trial was originally included, but trial author was not able to confirm the randomisation method through phone call (16 Jan 2009).
Zhang XW 1997	Randomised trial comparing 2 different herbal preparations (Hai Kun decoction versus Guizhi Fuling pills) in treatment of 38 cases of uterine fibroids
Zhang Z 2006	Case series of 62 patients with uterine fibroids treated by herbal medicine
Zhao LX 2003	Randomised trial was originally included, but trial author used alternate allocation (quasi-randomisation) through phone call (7 Jan 2009).
Zheng CY 2003	Case series of 60 patients with uterine fibroids treated by herbal medicine

(*Continued*)

Zhong Q 2006	Randomised trial comparing mifepristone combined with Guizhi Fuling capsules versus hormone (GnRH-a) in treatment of 104 cases of uterine fibroids. The intervention comparison did not comply with the inclusion criteria of this review
Zhou J 1997	Randomised trial comparing herbal preparation with placebo in treatment of 100 cases of uterine fibroids. However, there was obvious skew in the numbers of patients between the 2 groups (71 versus 29), which could not be explained by randomisation.
Zhou MY 2003	Randomised trial was originally included, but trial author was not able to confirm the randomisation method through phone call (13 Jan 2009).
Zhou YJ 2006	Randomised trial comparing 2 different herbal preparations (Guizhi Fuling capsules versus Xuefu Zhuyu capsules) in treatment of 60 cases of uterine fibroids
Zhou YR 1999	Randomised trial comparing herbal preparation with mifepristone in treatment of 80 cases of uterine fibroids. However, there was obvious in the skew numbers of patients between the 2 groups (48 versus 32), which could not be explained by randomisation.
Zhu FH 2006	Randomised trial was originally included, but trial author was not able to confirm the randomisation method through phone call (16 Jan 2009).
Zhu JY 1997	Randomised trial comparing different formulation of the same herbal medicine (Lichong Sanjie pills versus Lichong Sanjie decoction) in treatment of 110 cases of uterine fibroids
Zou DH 1993	Case series of 93 patients with uterine fibroids treated by herbal medicine

DATA AND ANALYSES

Comparison 1. Herbal preparations versus medical treatment

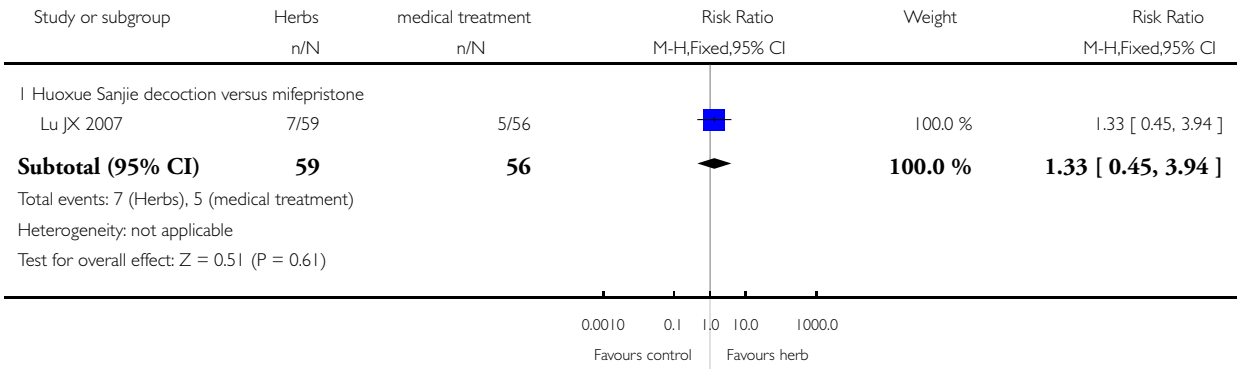
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Disappearance of uterine fibroids	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Huoxue Sanjie decoction versus mifepristone	1	115	Risk Ratio (M-H, Fixed, 95% CI)	1.33 [0.45, 3.94]
2 Number of patients with shrinkage of uterine fibroids	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 Huoxue Sanjie decoction versus mifepristone (shrank > 1/2)	1	115	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.64, 1.54]
2.2 Huoxue Sanjie decoction versus mifepristone (shrank > 1/3)	1	115	Risk Ratio (M-H, Fixed, 95% CI)	1.16 [0.70, 1.92]
3 Average volume of uterine fibroids (cm^3)	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 Huoxue Sanjie decoction versus mifepristone	1	115	Mean Difference (IV, Random, 95% CI)	4.98 [-6.08, 16.04]
3.2 Nona Roguy herbal product versus GnRH agonist	1	35	Mean Difference (IV, Random, 95% CI)	6.74 [-27.43, 40.91]
4 Average size of uterus (cm^3)	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
4.1 Huoxue Sanjie decoction versus mifepristone	1	115	Mean Difference (IV, Fixed, 95% CI)	23.23 [17.85, 28.61]
4.2 Nona Roguy herbal product versus GnRH agonist	1	35	Mean Difference (IV, Fixed, 95% CI)	-23.61 [-223.63, 176.41]

Analysis 1.1. Comparison 1 Herbal preparations versus medical treatment, Outcome 1 Disappearance of uterine fibroids.

Review: Herbal preparations for uterine fibroids

Comparison: 1 Herbal preparations versus medical treatment

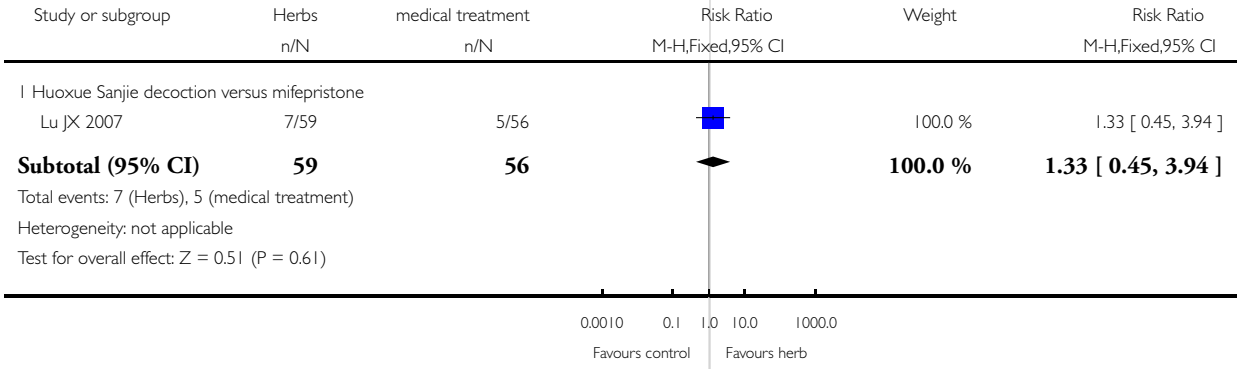
Outcome: 1 Disappearance of uterine fibroids



Review: Herbal preparations for uterine fibroids

Comparison: 1 Herbal preparations versus medical treatment

Outcome: 1 Disappearance of uterine fibroids

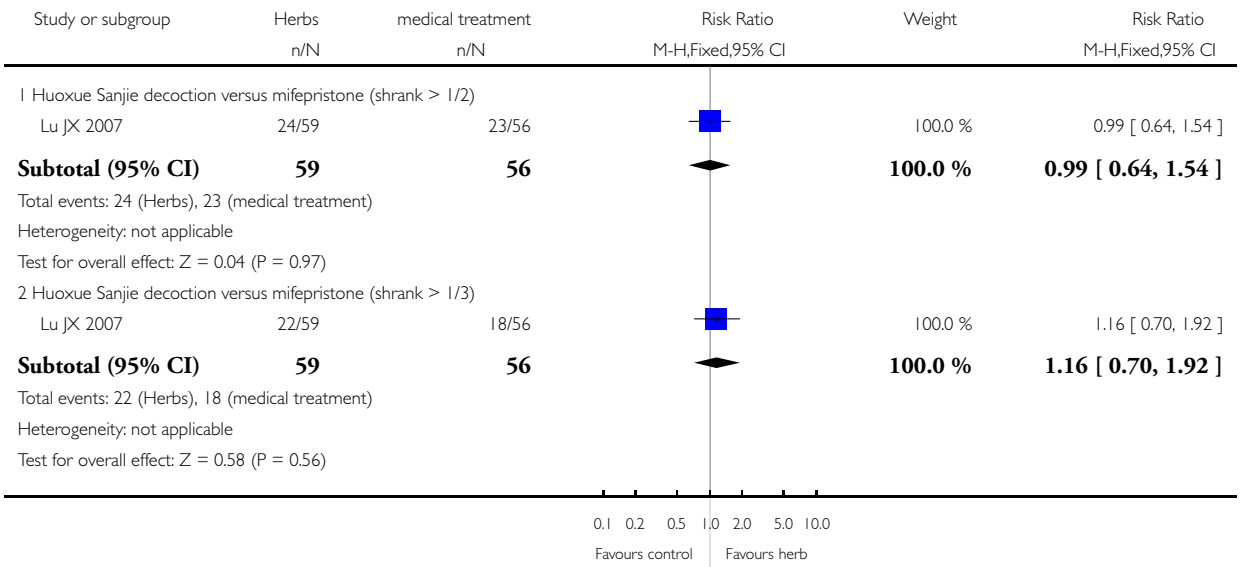


Analysis 1.2. Comparison 1 Herbal preparations versus medical treatment, Outcome 2 Number of patients with shrinkage of uterine fibroids.

Review: Herbal preparations for uterine fibroids

Comparison: 1 Herbal preparations versus medical treatment

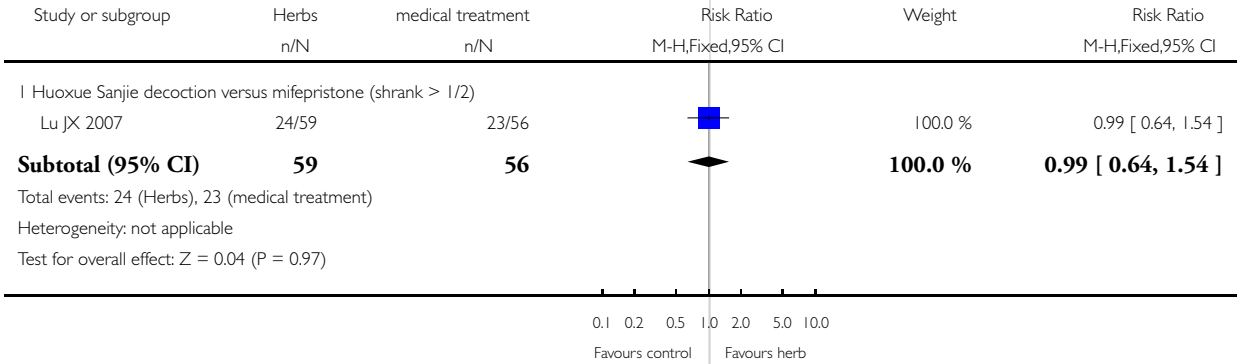
Outcome: 2 Number of patients with shrinkage of uterine fibroids



Review: Herbal preparations for uterine fibroids

Comparison: 1 Herbal preparations versus medical treatment

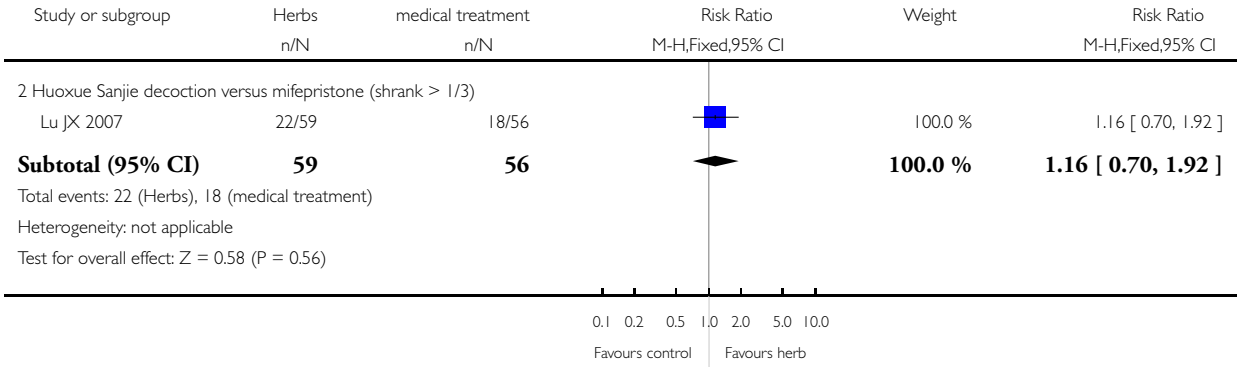
Outcome: 2 Number of patients with shrinkage of uterine fibroids



Review: Herbal preparations for uterine fibroids

Comparison: 1 Herbal preparations versus medical treatment

Outcome: 2 Number of patients with shrinkage of uterine fibroids

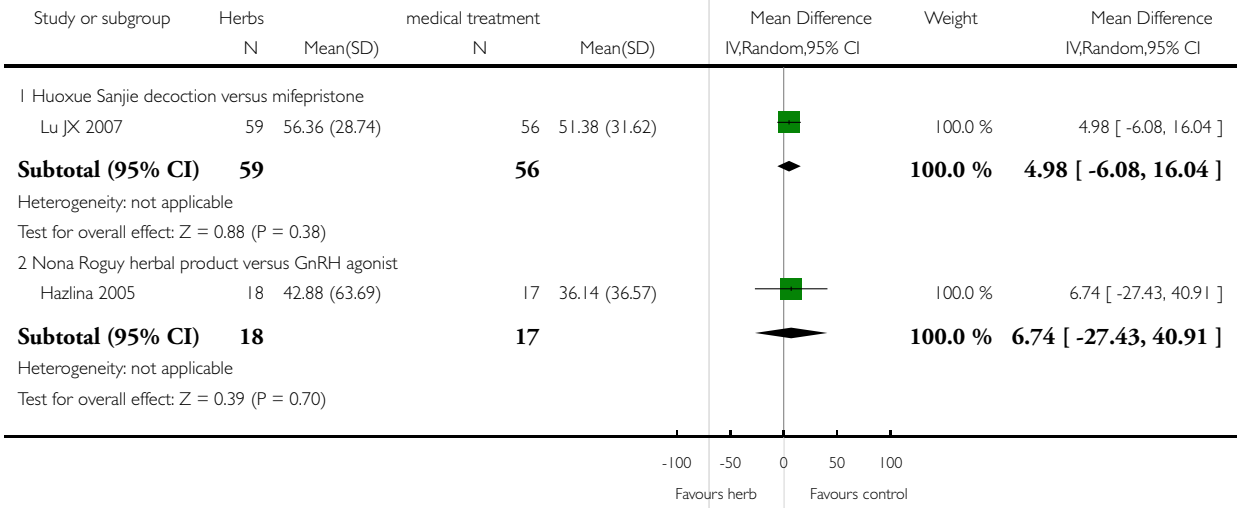


Analysis 1.3. Comparison 1 Herbal preparations versus medical treatment, Outcome 3 Average volume of uterine fibroids (cm^3).

Review: Herbal preparations for uterine fibroids

Comparison: 1 Herbal preparations versus medical treatment

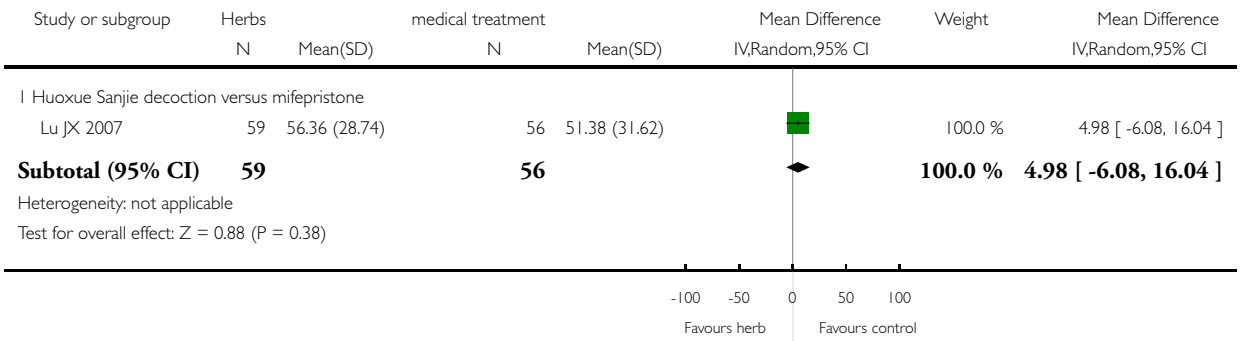
Outcome: 3 Average volume of uterine fibroids (cm^3)



Review: Herbal preparations for uterine fibroids

Comparison: 1 Herbal preparations versus medical treatment

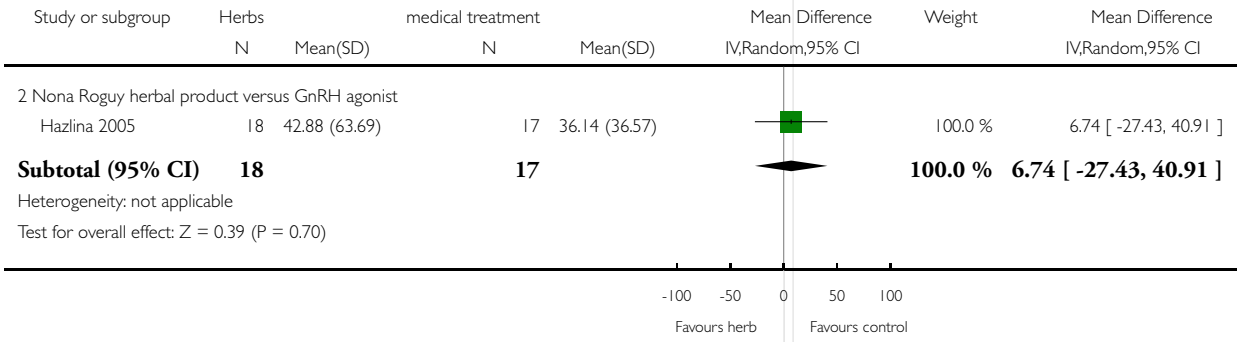
Outcome: 3 Average volume of uterine fibroids (cm^3)



Review: Herbal preparations for uterine fibroids

Comparison: 1 Herbal preparations versus medical treatment

Outcome: 3 Average volume of uterine fibroids (cm^3)

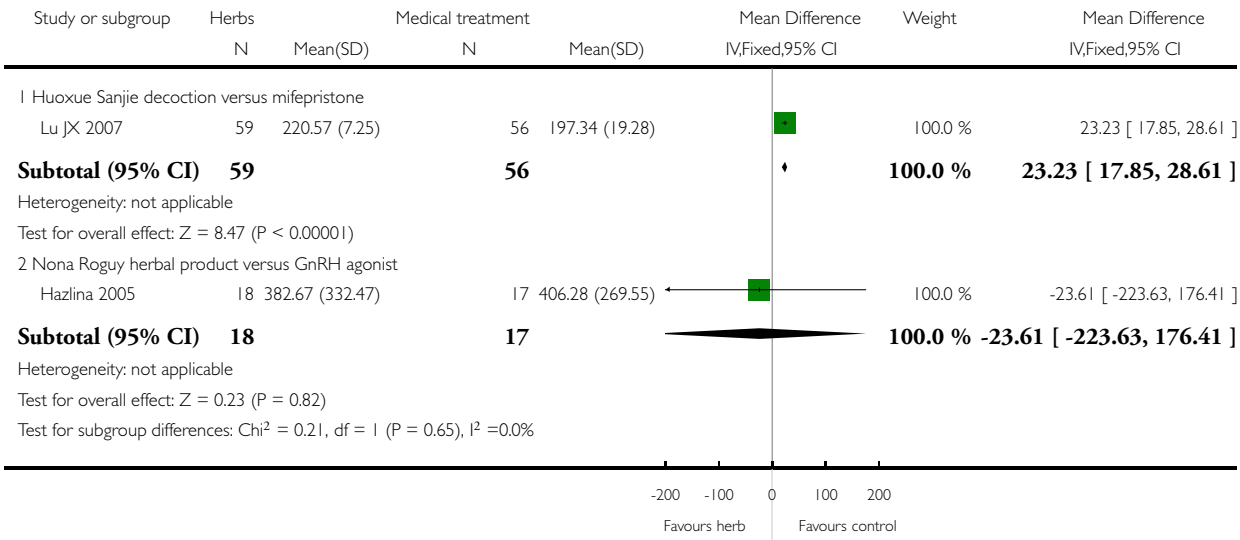


Analysis 1.4. Comparison 1 Herbal preparations versus medical treatment, Outcome 4 Average size of uterus (cm^3).

Review: Herbal preparations for uterine fibroids

Comparison: 1 Herbal preparations versus medical treatment

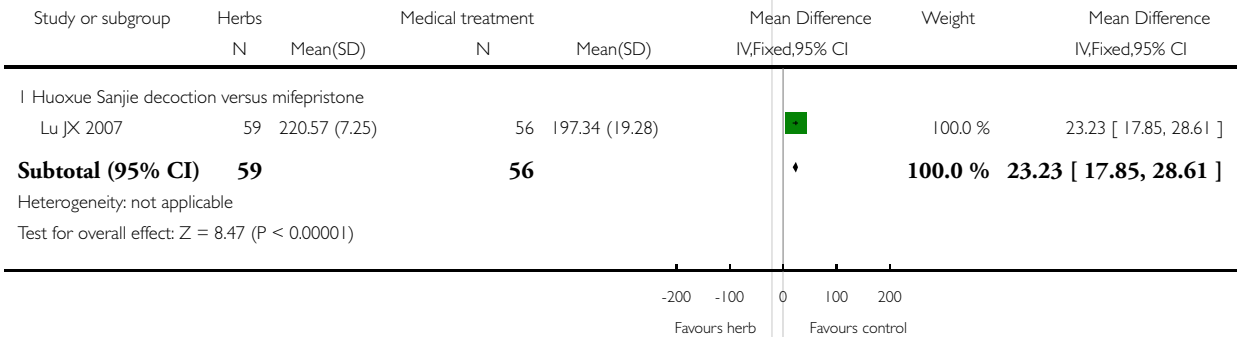
Outcome: 4 Average size of uterus (cm^3)



Review: Herbal preparations for uterine fibroids

Comparison: 1 Herbal preparations versus medical treatment

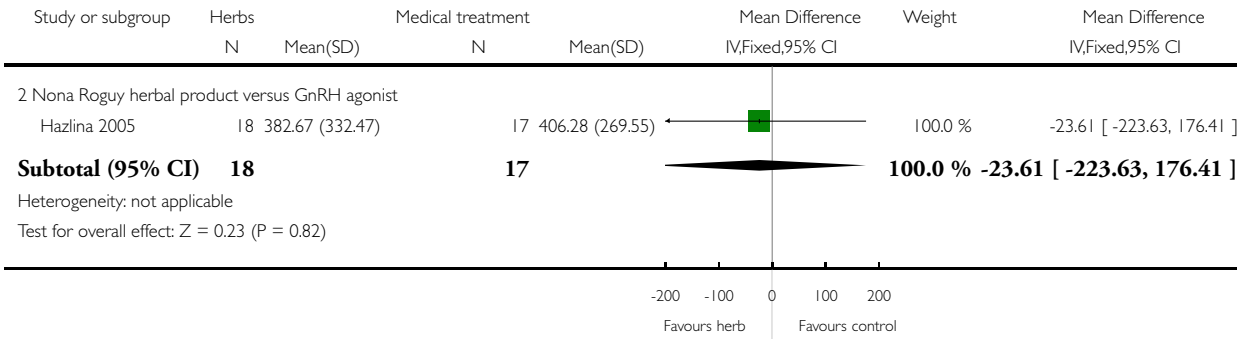
Outcome: 4 Average size of uterus (cm^3)



Review: Herbal preparations for uterine fibroids

Comparison: 1 Herbal preparations versus medical treatment

Outcome: 4 Average size of uterus (cm^3)



WHAT'S NEW

Last assessed as up-to-date: 22 January 2009.

16 April 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 2, 2005

Review first published: Issue 2, 2009

14 April 2008	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Jianping Liu conceived the review, wrote the protocol, performed quality assessment and data analyses, drafted and revised the review.

Hong Yang identified studies, extracted data, performed quality assessment, and analysed data.

Yun Xia contacted with trial authors for confirmation of randomisation and missing data.

Francesco Cardini revised the protocol and the review.

DECLARATIONS OF INTEREST

None known.

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