Fibroids (uterine myomatosis, leiomyomas)

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ABSTRACT

INTRODUCTION: Between 5–77% of women may have fibroids, depending on the method of diagnosis used. Fibroids may be asymptomatic, or may present with menorrhagia, pain, infertility, or recurrent pregnancy loss. Risk factors for fibroids include obesity, having no children, and no long-term use of the oral contraceptive pill. Fibroids tend to shrink or fibrose after the menopause. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of: medical treatment alone; preoperative medical treatments for women scheduled for surgery; and surgical treatments in women with fibroids? We searched: Medline, Embase, The Cochrane Library and other important databases up to November 2006 (BMJ Clinical Evidence reviews are updated periodically, please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found 41 systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review we present information relating to the effectiveness and safety of the following interventions: gonadorelin analogues (with progestogen, raloxifene, tibolone, or combined oestrogen–progestogen); hysterectomy (plus oophorectomy); hysteroscopic resonance-focused ultrasound; laparoscopic myomectomy; laparoscopically assisted vaginal hysterectomy; rollerball endometrial ablation; thermal balloon ablation; thermal myolysis with laser; total abdominal hysterectomy; total abdominal myomectomy; total laparoscopic hysterectomy; total vaginal hysterectomy.

QUESTIONS

INTERVENTIONS

EFFECTS OF MEDICAL TREATMENT ALONE

Likely to be beneficial

Trade off between benefits and harms

Unknown effectiveness

EFFECTS OF PREOPERATIVE DRUGS

Likely to be beneficial

EFFECTS OF SURGICAL TREATMENTS

Beneficial

Likely to be beneficial

Unknown effectiveness

Covered elsewhere in Clinical Evidence

Menorrhagia (many women with fibroids experience symptoms of heavy menstrual bleeding). See menorrhagia.

To be covered in future updates

Different types of total abdominal myomectomy versus each other

Uterine embolisation

Footnote

*Based on consensus; RCTs unlikely to be conducted.

Key points

- Between 5–77% of women may have fibroids, depending on the method of diagnosis used. Fibroids may be asymptomatic, or may present with menorrhagia, pain, infertility, or recurrent pregnancy loss.

  Risk factors for fibroids include obesity, having no children, and no long-term use of the oral contraceptive pill. Fibroids tend to shrink or fibrose after the menopause.
- Gonadorelin analogues reduce bleeding compared with placebo, but can cause menopausal symptoms and bone loss, which may limit their long-term use.

  Adding progesterone, tibolone, or raloxifene to gonadorelin analogues may prevent these adverse effects, but their addition doesn't produce any greater effect on fibroid symptoms than gonadorelin analogues alone.
- We don't know whether NSAIDs or the levonorgestrel intrauterine system improve symptoms of fibroids.
- Gonadorelin analogues given before fibroid surgery reduce bleeding, and increase the likelihood of having a vaginal rather than abdominal hysterectomy, but increase anti-oestrogenic adverse effects (such as hot flushes, change in breast size, vaginal symptoms).
- Total abdominal hysterectomy is considered to be beneficial in reducing fibroid-related symptoms, but total vaginal hysterectomy and total laparoscopic hysterectomy may have lower risks of complications, and shorter recovery times.

  Laparoscopically assisted vaginal hysterectomy may increase operative times and blood loss compared with total vaginal hysterectomy.
- Myomectomy maintains fertility, but we don't know whether it is better at reducing fibroid symptoms compared with hysterectomy.

  Laparoscopic myomectomy reduces complications and recovery time compared with abdominal myomectomy.

  We don't know whether thermal myolysis with laser, hysteroscopic resection, thermal balloon ablation, or rollerball ablation, or magnetic resonance-guided focused ultrasound surgery are beneficial in women with fibroids compared with hysterectomy, as we found no studies.

DEFINITION

Fibroids (uterine leiomyomas) are benign tumours of the smooth muscle cells of the uterus. Women with fibroids can be asymptomatic, or may present with menorrhagia (30%), pelvic pain with or without dysmenorrhoea or pressure symptoms (34%), infertility (27%), and recurrent pregnancy loss (3%). [1] Much of the data describing the relationship between the presence of fibroids and symptoms are based on uncontrolled studies that have assessed the effect of myomectomy on the presenting symptoms. [2] One observational study (142 women) undertaken in the USA suggested that the prevalence of fibroids in infertile women can be as high as 13%, but no direct causal relationship between fibroids and infertility has been established. [3]

INCIDENCE/ PREVALENCE

The reported incidence of fibroids varies from 5.4–77.0%, depending on the method of diagnosis used (the gold standard is histological evidence). It is not possible to state the actual incidence of fibroids, because some women with fibroids will not have symptoms, and will therefore not be tested for fibroids. Observational evidence suggests that, in premenopausal women, the incidence of fibroids increases with age, reducing during menopause. [4] [5] Based on postmortem examination, 50% of women were found to have these tumours. [6] Gross serial sectioning at 2 mm intervals of 100 consecutive hysterectomy specimens revealed the presence of fibroids in 50/68 (73%) premenopausal women and 27/32 (84%) postmenopausal women. These women were having hysterectomies for reasons other than fibroids. [7] The incidence of fibroids in black women is three times greater than that in white women, based on ultrasound or hysterectomy diagnosis. [8] Submucosal fibroids have been diagnosed in 6–34% of women having a hysteroscopy for abnormal bleeding, and in 2–7% of women having infertility investigations. [9]

AETIOLOGY/ RISK FACTORS

The cause of fibroids is unknown. Each fibroid is of monoclonal origin and arises independently. [10] [11] Factors thought to be involved include the sex steroid hormones oestrogen and proges-

terone, as well as the insulin-like growth factors, epidermal growth factor, and transforming growth factor. Risk factors for fibroid growth include nulliparity, and obesity. Risk also reduces consistently with increasing number of term pregnancies; women with five term pregnancies have a quarter of the risk of nulliparous women (P less than 0.001). [5] Obesity increases the risk of fibroid development by 21% with each 10 kg weight gain (P = 0.008). [5] The combined oral contraceptive pill also reduces the risk of fibroids with increasing duration of use (women who have taken oral contraceptives for 4–6 years compared with women who have never taken oral contraceptives: OR 0.8, 95% CI 0.5 to 1.2; women who have taken oral contraceptives for at least 7 years compared with women who have never taken oral contraceptives: OR 0.5, 95% CI 0.3 to 0.9). [12] Women who have had injections containing 150 mg depot medroxyprogesterone acetate also have a reduced incidence compared with women who have never had injections of this drug (OR 0.44, 95% CI 0.36 to 0.55). [13]

PROGNOSIS

There are few data on the long-term untreated prognosis of these tumours, particularly in women asymptomatic at diagnosis. One small case control study reported that, in a group of 106 women treated with observation alone over 1 year, there was no significant change in symptoms and quality of life over that time. [14] Fibroids tend to shrink or fibrose after the menopause. [5]

AIMS OF INTERVENTION

To reduce menstrual bleeding; reduce pressure symptoms; reduce pelvic pain; and induce a change in fertility status, with minimal adverse effects.

OUTCOMES

Menstrual blood flow (assessed objectively [mL/cycle] or subjectively); haemoglobin concentration and haematocrit; pelvic pain, pressure, or both (measured by a validated scale or subjective report); reduction in fibroid and uterine volume; pregnancy rate; quality of life; adverse effects. Some of the outcomes relate to surgery: ease of surgery as assessed by the surgeon; complication rates during and after surgery; blood loss during surgery; duration of surgery; length of hospital stay; rate of blood transfusions; probability of transverse versus vertical incisions during surgery; probability of vaginal versus abdominal hysterectomy; recurrence rate; patient satisfaction rate.

METHODS

BMJ Clinical Evidence search and appraisal November 2006. The following databases were used to identify studies for this review: Medline 1966 to November 2006, Embase 1980 to November 2006, and The Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Clinical Trials 2006, Issue 4. Additional searches were carried out using these websites: NHS Centre for Reviews and Dissemination (CRD) — for Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA), Turning Research into Practice (TRIP), and National Institute for Health and Clinical Excellence (NICE). Abstracts of the studies retrieved from the initial search were assessed by an information specialist. Selected studies were then sent to the author for additional assessment, using predetermined criteria to identify relevant studies. Study design criteria for evaluation in this review were: published systematic reviews and RCTs in any language, and containing more than 20 individuals of whom more than 80% were followed up. There was no minimum length of follow up required to evaluate studies. We excluded all studies described as “open”, “open label”, or not blinded unless blinding was impossible. We also did a search for cohort studies on specific harms of named interventions. In addition, we use a regular surveillance protocol to capture harms alerts from organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA), which are added to the chapter as required. We compared all listed medical interventions versus all listed surgical interventions and included all RCTs of sufficient quality. We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 24).

QUESTION What are the effects of medical treatment alone in women with fibroids?

OPTION GONADORELIN ANALOGUES PLUS PROGESTOGEN VERSUS GONADORELIN ANALOGUES ALONE

Menstrual blood flow

Compared wth gonadorelin analogues alone Gonadorelin analogues (leuprorelin [leuprolide] acetate) plus progestogen may be no more effective at reducing heavy bleeding at 12 months compared with gonadorelin analogues alone (low-quality evidence).

Adverse effects

Gonadorelin analogues plus progestogen may reduce vasomotor symptoms over 6–12 months compared with gonadorelin analogues alone (moderate-quality evidence).

Note

We found no direct information about whether gonadorelin analogues plus progestogen are better than no active treatment.

For GRADE evaluation of interventions for fibroids

, see table, p 24 .

Benefits:

GnRHa plus progestogen versus GnRHa alone:
We found no systematic review but found one RCT (41 women). [15] It found no significant difference between leuprorelin (leuprolide) acetate plus medroxyprogesterone acetate and leuprorelin acetate plus placebo in heavy bleeding at 12 months (proportion of women with bleeding for less-than or equal to 7 days/month or self reported improvement in bleeding assessed by menstrual calendar: 8/21 [38%] with added progestogen *v* 11/20 [55%] with added placebo; RR 0.69, 95% CI 0.35 to 1.36). We found two RCTs that did not assess effects on fibroid related symptoms, but studied whether adding progestogen to GnRHa reduced the harms associated with giving GnRHa alone (see harms). [16] [17]

Harms:

GnRHa plus progestogen versus GnRHa alone:
The first RCT gave no information on adverse effects. [15] We found two RCTs that did not assess effects on fibroid related symptoms, but studied whether adding progestogen to GnRHa reduced the harms associated with giving GnRHa alone. [16] [17] The first RCT (24 women) assessing harms found that goserelin acetate plus medroxyprogesterone acetate significantly reduced vasomotor symptoms over 12 months compared with GnRHa alone ($P < 0.05$; absolute numbers not reported). [16] The second RCT (16 women) found that leuprorelin acetate plus progestogen hormone replacement (in the form of medroxyprogesterone acetate) significantly reduced the proportion of women with hot flushes over 24 weeks compared with leuprorelin acetate alone (1/9 [11%] with leuprorelin acetate plus progestogen *v* 6/7 [86%] with leuprorelin acetate alone; RR 0.13, 95% CI 0.02 to 0.84). [17] See harms of HRT in review on menopausal symptoms. See also harms of GnRHa alone, p 6 .

Comment:

Most of the RCTs combining GnRHa plus hormone replacement were small (see other options combining GnRHa plus hormone replacement).

Clinical guide:
There is insufficient evidence to determine the optimum hormone replacement regimen that minimises the adverse effects of GnRHa. The RCTs did not assess effects on pregnancy rates.

OPTION GONADORELIN ANALOGUES PLUS RALOXIFENE VERSUS GONADORELIN ANALOGUES ALONE

Fibroid size
Compared with gonadorelin analogues alone Adding raloxifene to gonadorelin analogues may reduce fibroid size compared with gonadorelin analogues alone (low-quality evidence).

Fibroid-related symptoms
Compared with gonadorelin analogues alone Adding raloxifene may not reduce fibroid-related symptoms (low-quality evidence).

Note
We found no direct information about whether gonadorelin analogues plus raloxifene are better than no active treatment.

For GRADE evaluation of interventions for fibroids

, see table, p 24 .

Benefits:

GnRHa plus raloxifene versus GnRHa alone:
We found one RCT (100 women), which compared adding raloxifene to leuprolide acetate versus leuprolide acetate alone for 6 months. [18] It found that both treatments were associated with a reduction in both uterine and fibroid size from baseline, and found that raloxifene plus leuprolide acetate caused a significantly greater reduction in fibroid size at 6 months compared with leuprolide acetate alone (reduction 7% with raloxifene plus leuprolide acetate *v* 4% with leuprolide acetate alone, absolute data read from graph; $P < 0.05$). It found no significant difference between groups in fibroid related symptoms (menorrhagia or constipation: no women in either group; pelvic pressure: 6.7% with raloxifene plus leuprolide acetate *v* 6.5% with leuprolide acetate alone; pelvic pain: 4.4% with raloxifene plus leuprolide acetate *v* 6.5% with leuprolide acetate alone; urinary frequency: 6.7% with raloxifene plus leuprolide acetate *v* 4.3% with leuprolide acetate alone; reported as non-

significant, CI not reported). [18] The same RCT assessed effects on cognition, mood, and overall quality of life at 6 months in 74 of the women in the trial (reported in a separate publication). [19] It found no significant difference between GnRHa plus raloxifene and GnRHa alone in cognition (measured by a memory scale and Mini-Mental State Examination), mood (measured by the Self Rating Anxiety Scale), or overall quality of life (measured by Short Form Healthy Survey and the Women's Health Questionnaire; reported as non-significant for all outcomes, absolute results tabulated). [19]

Harms:

GnRHa plus raloxifene versus GnRHa alone:
The RCT found that both leuprolide acetate alone and raloxifene plus leuprolide acetate significantly increased the mean number of hot flushes a day after 15 days' treatment (mean 3–6 flushes a day; $P < 0.05$). However, it found no significant difference between groups (reported as non-significant, CI not reported). [18] It found that leuprolide acetate plus raloxifene significantly reduced bone mineral density loss from the lumbar spine, trochanter, and femoral neck at 6 months compared with leuprolide acetate alone (results presented graphically; lumbar spine: 1.3% with raloxifene plus leuprolide acetate *v* 5.5% with leuprolide acetate alone, $P < 0.0001$; trochanter: 1.0% with raloxifene plus leuprolide acetate *v* 4.5% with leuprolide acetate alone, $P < 0.0001$; femoral neck: 0.9% with raloxifene plus leuprolide acetate *v* 3.4% with leuprolide acetate alone, $P < 0.001$). [20]
See harms of HRT in review on menopausal symptoms. See also harms of GnRHa alone, p 6 .

Comment:

See comment on GnRHa plus progestogen versus GnRHa alone, p 3 .

OPTION GONADORELIN ANALOGUES PLUS TIBOLONE VERSUS GONADORELIN ANALOGUES ALONE

Fibroid size
Compared with gonadorelin analogues alone Adding tibolone to gonadorelin analogues may not reduce fibroid and uterine size compared with gonadorelin analogues alone (low-quality evidence).

Fibroid-related symptoms
Compared with gonadorelin analogues alone Adding tibolone to gonadorelin analogues may not improve fibroid-related symptoms compared with gonadorelin analogues alone (low-quality evidence).

Adverse effects
Adding tibolone reduces adverse effects of gonadorelin analogues such as hot flushes, vaginal dryness, and night sweats, and prevents loss in bone mineral density (low-quality evidence).

Note
We found no direct information about whether gonadorelin analogues plus tibolone are better than no active treatment.

For GRADE evaluation of interventions for fibroids

, see table, p 24 .

Benefits:

GnRHa plus tibolone versus GnRHa alone:
We found two RCTs. [21] [22] Both RCTs found no significant difference in symptoms at 6 months between adding tibolone to GnRHa and GnRHa alone. The first RCT (50 women) found no significant difference between leuprolide acetate plus tibolone and leuprolide acetate plus placebo in uterine and fibroid size or fibroid related symptoms at 6 months (mean uterine volume 415 cm^3 with added tibolone *v* 386 cm^3 with added placebo; mean fibroid volume 139 cm^3 with added tibolone *v* 133 cm^3 with added placebo; symptom intensity on a visual analogue scale from 0–10: 3.3 with added tibolone *v* 3.5 with added placebo for pelvic pressure; 2.0 with added tibolone *v* 2.5 with added placebo for pelvic pain; 3.0 in both groups for urinary frequency; P value for all comparisons reported as non-significant). [21] The second RCT (20 women) comparing triptorelin plus tibolone versus triptorelin alone also found no significant difference in fibroid volume at 6 months (reduction in volume 64% with triptorelin plus tibolone *v* 60% with triptorelin alone; reported as non-significant, CI not reported). [22] The RCT is likely to have been too small to detect a clinically important difference.

Harms:

GnRHa plus tibolone versus GnRHa alone:
The first RCT found that, after 6 months' treatment, leuprolide acetate plus tibolone significantly reduced the mean number of hot flushes each day compared with leuprolide acetate alone (1.5 with added tibolone *v* 4.6 with added placebo; $P < 0.01$; absolute data read from graph). [21] The RCT also found that the significant reduction in bone mineral density after 6 months' treatment with gonadorelin alone was prevented with the concurrent administration of tibolone (1.035 g/cm^2 with tibolone *v* 1.002 g/cm^2 with GnRHa alone; $P < 0.01$). [21] The risk of fractures was not assessed. The second RCT found that fewer women taking tibolone plus triptorelin had hot flushes (30% with triptorelin plus tibolone *v* 80% with triptorelin alone), vaginal dryness (20% with triptorelin plus ti-

bolone *v* 50% with triptorelin alone), and night sweats (20% with triptorelin plus tibolone *v* 30% with triptorelin alone) compared with women taking triptorelin alone. [22] The RCT did not assess the significance of the difference between groups. See harms of HRT in review on menopausal symptoms. See also harms of GnRHa alone, p 6 .

Drug safety alert:
A drug safety alert has been issued on the increased risk of breast cancer recurrence associated with tibolone (http://www.mhra.gov.uk).

Comment: See comment on GnRHa plus progestogen versus GnRHa alone, p 3 .

OPTION GONADORELIN ANALOGUES ALONE

Menstrual blood loss (amenorrhoea)
Compared with placebo Gonadorelin analogues may increase the proportion of women with amenorrhoea compared with placebo after about 3 months (low-quality evidence).

Intranasal route compared with subcutaneous Intranasal gonadorelin analogues may be as effective as subcutaneous gonadorelin analogues at reducing menorrhagia (very low-quality evidence).

Fibroid size
Intranasal route compared with subcutaneous Intranasal gonadorelin analogues may be as effective as subcutaneous gonadorelin analogues at reducing fibroid size (very low-quality evidence).

Adverse effects
Gonadorelin analogues are associated with menopausal symptoms and bone loss, which may make them unsuitable for long-term use.

Note
We found no clinically important results about how different gonadorelin analogues compare with each other, or comparing gonadorelin analogues with surgical treatment.

For GRADE evaluation of interventions for fibroids

, see table, p 24 .

Benefits:

Gonadorelin analogues (GnRHa) alone versus placebo:
We found one systematic review [23] of nafarelin (search date 1997, 1 RCT, 101 women) and one subsequent RCT [24] of goserelin. The RCT identified by the review found that intranasal nafarelin (200 µg twice daily) significantly increased the proportion of women with amenorrhoea at 3 months compared with placebo (33/64 [51%] amenorrhoeic with nafarelin *v* 3/37 [8%] with placebo; P less-than or equal to 0.05). [23] The subsequent RCT (307 women awaiting surgery for fibroids) compared three treatments: goserelin, fulvestrant, and placebo. [24] It found that more women taking goserelin (3.6 mg every 4 weeks) than placebo had amenorrhoea at 13 weeks (AR of amenorrhoea: 0.18% at baseline to 92.5% with goserelin *v* no change from baseline with placebo; P value not reported). [24] We found four additional RCTs (154 women) comparing GnRHa versus placebo. [25] [26] [27] [28] All had important methodological weaknesses. The first RCT (13 participating centres, 128 women, 24 weeks' treatment) had high withdrawal rates, precluding reliable comparison of the benefits of treatments (see harms below). [25] The second RCT (38 premenopausal women) did not assess clinical outcomes. [26] The other two RCTs were too small to yield reliable results (12 women [27] and 15 women [28]). Two of these RCTs found that fibroids returned to their previous size after stopping treatment. [25] [26]

GnRHa alone versus each other:
We found one systematic review (search date 1997), which identified one RCT (211 women) comparing intranasal nafarelin (200 µg twice daily) versus intranasal buserelin (300 µg 3 times daily). [23] The RCT found that nafarelin significantly increased haemoglobin at 16 weeks compared with buserelin (haemoglobin 12.8 g/dL with nafarelin *v* 12.3 g/dL with buserelin; P = 0.03). However, the RCT did not describe the clinical importance of this difference. We also found two additional small RCTs. [29] [30] The first RCT (67 women) compared buserelin (1.8 mg every 4 weeks) versus leuprorelin (1.88 mg every 4 weeks) by subcutaneous injection. [29] The second RCT (27 women) compared triptorelin standard dose treatment plus three different types of dosage regimen. [30] Neither of the RCTs compared clinical outcomes among treatment groups.

Different doses of GnRHa:
We found one systematic review (search date 1997), which identified one RCT (257 women) comparing different doses of nafarelin (50, 100, 200, and 400 µg twice daily). [23] The RCT found that higher doses of nafarelin significantly increased the proportion of women who were amenor-

rhoeic at 16 weeks compared with lower doses (women amenorrhoeic 41/59 [69.5%] with 50 µg *v* 46/54 [85.2%] with 100 µg *v* 40/48 [83.3%] with 200 µg *v* 52/57 [91.2%] with 400 µg; P = 0.0053 for dose–response effect). We also found three small RCTs. [31] [32] [33] Two RCTs (77 women) compared two different doses of leuprorelin (leuprolide) acetate (1.88 mg *v* 3.75 mg every 4 weeks for 24 weeks). [31] [32] Neither of the RCTs compared clinical outcomes among treatment groups, but one RCT reported that all women experienced partial or complete relief from symptoms throughout their treatment. [31] The third RCT (45 women) compared doses of goserelin delivered in a different format (3 subcutaneous 3.6 mg doses monthly for 3 months versus a single subcutaneous injection of 10.8 mg). [33] The RCT did not assess clinical outcomes. It found similar improvements in haemoglobin level in both groups, but found that a single higher dose of goserelin significantly reduced uterine volume compared with three lower doses (54% with single dose *v* 43% with 3 doses; P < 0.001). [33]

Different modes of administration of GnRHa:
We found three RCTs (96 women) comparing intranasal versus subcutaneous GnRHa, none of which reported quantitative results for clinical outcomes. [34] [35] [36] One RCT reported that all women had a subjective improvement in menstrual symptoms after 6 months' treatment, especially menorrhagia and dysmenorrhoea, but no figures were reported. [34] The RCTs found no differences in uterine and fibroid shrinkage between the different modes of GnRHa administration. [34] [35] [36]

GnRHa alone versus GnRHa plus hormonal treatment:
See benefits of GnRHa plus HRT versus surgical treatment, p 8 .

GnRHa alone versus surgical interventions:
We found no systematic review or RCTs.

Harms:

GnRHa alone:
The systematic review identified five RCTs assessing adverse effects. [23] Two RCTs found that intranasal nafarelin (200 µg twice daily) reduced bone density by 2.5% from baseline after 16 weeks' treatment compared with placebo. [23] Six months after treatment was withdrawn, bone density had increased to values not significantly different from baseline. Many women reported hot flushes during nafarelin treatment (rates ranged from 39% to 100% across 5 RCTs in the review). One RCT found that nafarelin significantly increased the proportion of women who had hot flushes compared with placebo (61% with nafarelin *v* 36% with placebo; P = 0.02). [23] The subsequent RCT found that adverse effects, mainly hot flushes and sweating, were more common with goserelin than with placebo (63.3% with goserelin *v* 28.3% with placebo, P value not reported). [24] The first additional RCT found that leuprorelin was associated with vasomotor flushes, vaginitis, arthralgia/myalgia, asthenia, peripheral oedema, insomnia, nausea, and nervousness compared with placebo (see table 1, p 23). [25] It found no significant difference between nafarelin and placebo in the risk of developing emotional lability/nervousness, depression, headaches, or decreased libido, although sample size may have been insufficient to rule out clinically important differences in these outcomes (see table 1, p 23). [25]

GnRHa alone versus each other:
The RCT identified by the review found that nafarelin significantly increased the proportion of women who had hot flushes compared with buserelin (38.5% with nafarelin *v* 23.4% with buserelin; P = 0.025), but few women discontinued treatment (data not reported). [23]

GnRHa alone versus GnRHa plus hormonal treatment:
See harms of GnRHa plus progestogen versus GnRHa alone, p 3 . See harms of GnRHa plus raloxifene versus GnRHa alone, p 4 . See harms of GnRHa plus tibolone versus GnHRa alone, p 5 . See harms of GnRHa plus combined oestrogen–progestogen versus gonadorelin analogues plus progestogen alone, p 7 . See harms of GnRHa plus HRT versus surgical treatment, p 8 .

GnRHa alone versus surgical interventions:
We found no systematic review or RCTs.

Comment:

Clinical guide:
The RCTs did not assess effects on pregnancy rates. GnRHa control bleeding, reduce some fibroid related symptoms, and reduce fibroid and uterine size. However, they may cause menopausal symptoms and bone loss, which make them unacceptable for long term use.

OPTION GONADORELIN ANALOGUES PLUS COMBINED OESTROGEN–PROGESTOGEN VERSUS GONADORELIN ANALOGUES PLUS PROGESTOGEN ALONE

Uterus size

Compared with gonadorelin analogues plus progestogen The gonadorelin analogue leuprorelin plus combined oestrogen–progestogen HRT may reduce uterine size compared with leuprorelin plus progestogen-only HRT (low-quality evidence).

Menstrual blood loss
Compared with gonadorelin analogues plus progestogen The effects on menorrhagia of gonadorelin analogue leuprorelin plus combined oestrogen–progestogen HRT compared with leuprorelin plus progestogen-only HRT are unknown (very low-quality evidence).

For GRADE evaluation of interventions for fibroids

, see table, p 24 .

Benefits: **GnRHa plus progestogen versus GnRHa plus combined oestrogen–progestogen:**
We found one RCT (51 women), which compared leuprorelin plus progestogen hormone replacement versus leuprorelin plus combined oestrogen–progestogen hormone replacement over a 2 year period. [37] After 3 months of leuprorelin treatment, it found a decrease in the mean uterine volume in both groups compared with baseline estimates (mean uterine volume: 416 cm^3 with oestrogen–progestogen *v* 440 cm^3 with progestogen alone; CI of the difference between groups not reported). After 21 months of treatment, the mean uterine volume was reduced only in women taking oestrogen–progestogen hormone replacement (mean uterine volume: 414 cm^3 with oestrogen–progestogen *v* 647 cm^3 with progestogen alone; CI not reported). Most women experienced a reduction in fibroid related symptoms. Menorrhagia reduced or resolved in 85%, pelvic pressure in 63%, and pelvic pain in 100% of women; comparison of results between groups not reported).

Harms: **GnRHa plus progestogen versus GnRHa plus combined oestrogen–progestogen:**
The RCT comparing leuprorelin plus progestogen hormone replacement versus leuprorelin plus combined oestrogen–progestogen hormone replacement found similar rates of adverse effects, including hot flushes, insomnia, vaginal dryness, and mood swings, between groups (absolute results tabulated, P value not reported). [37] See harms of HRT in review on menopausal symptoms. See also harms of GnRHa alone, p 6 .

Comment: See comment on GnRHa plus progestogen versus GnRHa alone, p 3 .

OPTION GONADORELIN ANALOGUES PLUS HORMONE REPLACEMENT VERSUS SURGICAL TREATMENT

We found no clinically important results about the effects of gonadorelin analogues plus tibolone compared with hysterectomy plus bilateral oophorectomy in women with fibroids.

For GRADE evaluation of interventions for fibroids

, see table, p 24 .

Benefits: **GnRHa plus hormone replacement versus surgical treatment:**
We found one RCT (120 women) comparing bone mineral density and bone turnover markers in women 12 months after treatment with GnRHa plus tibolone or hysterectomy plus bilateral oophorectomy, where surgical menopause is induced. [38] The RCT did not assess benefits of treatment (see harms below). [38]

Harms: **GnRHa plus hormone replacement versus surgical treatment:**
We found one RCT (120 women) assessing the effects of GnRHa plus tibolone compared with hysterectomy plus bilateral oophorectomy on bone mineral density and bone turnover markers. [38] In those women who became menopausal (85%), the RCT found no significant difference between groups in bone loss at 12 months after stopping treatment (percentage change in bone mineral density: 5.7 with GnRHa plus tibolone *v* 6.4 with hysterectomy, reported as non-significant, P value not reported). In both groups, there was a significant decrease in these outcomes from baseline ($P < 0.05$ *v* baseline in both groups). See harms of HRT in review on menopausal symptoms. See also harms of GnRHa alone, p 6 .

Comment: See comment on GnRHa plus progestogen versus GnRHa alone, p 3 .

OPTION LEVONORGESTREL INTRAUTERINE SYSTEM

We found no direct information about the effects of the levonorgestrel intrauterine system in women with fibroids.

For GRADE evaluation of interventions for fibroids

, see table, p 24 .

Benefits:

Levonorgestrel intrauterine system versus no treatment:
One systematic review (search date 2000) identified no RCTs. [39] We found no additional RCTs.

Levonorgestrel intrauterine system versus surgical interventions:
We found no systematic review or RCTs.

Harms: We found no RCTs.

Comment: None.

OPTION NSAIDS

We found no direct information about NSAIDs in women with fibroids.

For GRADE evaluation of interventions for fibroids

, see table, p 24 .

Benefits: We found no systematic review or RCTs.

Harms: See harms in review on NSAIDs.

Comment:

Clinical guide:
The RCTs did not assess effects on pregnancy rates.

QUESTION In women scheduled for fibroid surgery, what are the effects of preoperative medical treatments?

OPTION GONADORELIN ANALOGUES

Pelvic symptoms
Compared with placebo Gonadorelin analogues taken for at least 3 months before fibroid surgery improve preoperative pelvic symptoms compared with placebo or no preoperative treatment (moderate-quality evidence).

Pregnancy rate
Compared with placebo Gonadorelin analogues may increase pregnancy rates after myomectomy compared with placebo or no treatment (low-quality evidence).

Recurrence of fibroids
Compared with placebo Women treated with gonadorelin analogues preoperatively may be more likely to have recurrence of their fibroids compared with placebo or no pretreatment (moderate-quality evidence).

Need for further treatment
Gonadorelin analogues plus surgery compared with gonadorelin analogues alone Gonadorelin analogues plus surgery may reduce the need for further medical or surgical treatment compared with gonadorelin analogues alone (moderate-quality evidence).

Adverse effects
Preoperative gonadorelin analogues are associated with adverse hypo-oestrogenic effects, such as hot flushes, vaginal symptoms, and sweating, and women receiving gonadorelin analogue may be more likely to withdraw from treatment because of adverse effects.

For GRADE evaluation of interventions for fibroids

, see table, p 24 .

Benefits:

Gonadorelin analogues (GnRHa) versus placebo or no preoperative treatment:
We found one systematic review (search date 2000, 21 RCTs, 1886 women) [40] and one subsequent RCT. [41] The systematic review assessed GnRHa pretreatment (given at least 3 months before surgery) compared with placebo or no treatment, in separate categories: before, during, and after myomectomy or hysterectomy. The review found that, compared with placebo or no treatment, pretreatment with GnRHa significantly improved preoperative haemoglobin concentration (9 RCTs, 541 women: WMD 0.98 g/dL, 95% CI 0.74 g/dL to 1.22 g/dL) and haematocrit (4 RCTs, 138

women: WMD 3.14%, 95% CI 1.78% to 4.51%). It also found that GnRHa significantly improved preoperative pelvic symptoms when measured on a symptom scale (pelvic symptom score: 3 RCTs, 372 women: WMD –2.12, 95% CI –2.38 to –1.87). It found that significantly fewer women receiving GnRHa pretreatment had no improvement in pelvic symptoms compared with women receiving no pretreatment (1 RCT: OR 0.38, 95% CI 0.22 to 0.60). It found that pretreatment with GnRHa significantly reduced intraoperative blood loss (estimated by measuring the weight of swabs and the volume of blood collected in receptacles) compared with placebo or no treatment (8 RCTs, 263 women: WMD 67 mL, 95% CI 44 mL to 91 mL during myomectomy; 6 RCTs, 419 women: WMD 58 mL, 95% CI 40 mL to 76 mL during hysterectomy), although these differences may not be clinically important. The review also found that GnRHa significantly reduced the duration of operation in women having hysterectomy (8 RCTs, 748 women: WMD 5.2 minutes, 95% CI 1.8 minutes to 8.6 minutes) and reduced hospital stay compared with placebo or no treatment (4 RCTs, 392 women: WMD 1.0 day, 95% CI 0.9 days to 1.2 days). GnRHa pretreatment significantly reduced vertical incision rate in women having laparotomy compared with placebo or no treatment (vertical incision rate with myomectomy, 1 RCT, 28 women: OR 0.11, 95% CI 0.02 to 0.75; hysterectomy, 4 RCTs, 529 women: OR 0.36, 95% CI 0.23 to 0.55). There was also a suggestion that hysterectomy was subjectively graded by the surgeons as "not as difficult" in the pretreated women (2 RCTs: OR 0.73, 95% CI 0.25 to 0.97). A significantly higher proportion of these women also converted to a vaginal procedure (3 RCTs: OR 4.7, 95% CI 3.0 to 7.5). The review found that pretreated compared with non-pretreated women maintained marginally but significantly higher postoperative blood counts (postoperative haemoglobin; 3 RCTs, 240 women: WMD 0.8 g/dL, 95% CI 0.5 g/dL to 1.1 g/dL) for both types of surgery and higher haematocrit levels after hysterectomy (2 RCTs, 173 women: WMD 1.8%, 95% CI 1.1% to 2.4%), although the clinical importance of these results is unclear. One small RCT (60 women, 18 infertile, 6 with recurrent abortion) identified by the review [40] assessed the pregnancy rate in infertile women who had had myomectomy for fibroids at a mean follow up of 13 months. [42] The pregnancy rate was higher for pretreated versus non-pretreated women, although the difference was not significant (AR 7/11 [64%] for pretreated *v* 6/13 [46%] for non-pretreated; RR 1.4, 95% CI 0.7 to 2.9). The RCT may have been too small to detect a clinically important difference. The subsequent RCT (100 women) comparing 2 months of pretreatment with triptorelin versus immediate surgery (myomectomy) found no significant difference in blood loss during surgery between the two groups (mean blood loss 265 mL in the pretreated group *v* 296 mL in the immediate surgery group, WMD –31 mL, 95% CI –108 mL to 46 mL). [41]

Surgery plus GnRHa versus GnRHa alone:
We found one RCT (25 women) comparing goserelin acetate plus endometrial resection versus goserelin acetate alone. [43] It found that, compared with goserelin acetate alone, combined treatment reduced the proportion of women who required further treatment (either medical or surgical) over 1 year (17% with combined treatment *v* 69% with goserelin acetate alone; RR 4.3, 95% CI 1.1 to 15.4).

Harms:

GnRHa versus placebo or no preoperative treatment:
The review found that women pretreated with GnRHa versus placebo or no treatment were significantly more likely to experience hypo-oestrogenic symptoms, such as hot flushes (534 women: OR 6.5, 95% CI 4.6 to 9.2), change in breast size (261 women: OR 7.7, 95% CI 2.4 to 24.9), and vaginal symptoms (534 women: OR 4.0, 95% CI 2.1 to 7.6). [40] Women receiving GnRHa were also more likely to withdraw from treatment because of adverse effects (4 RCTs, 628 women: OR 2.5, 95% CI 1.0 to 5.9). The systematic review identified two small RCTs, which evaluated long term follow up in women receiving pretreatment with GnRHa before myomectomy. In one of these, all 24 women were checked for fibroid recurrence at 6 months, and 63% of the pretreated group had a recurrence of their fibroids compared with 13% of the control group. Fibroid recurrence 2–3 years after surgery was over 50% in the 18 women from the second RCT, but no significant difference was found between pretreated and non-pretreated women. No other adverse effects were assessed. One subsequent RCT also found that GnRHa pretreatment increased fibroid recurrence compared with no pretreatment at 6 months, although this difference was not significant (OR 4.10, 95% CI 0.44 to 38.25). [41]

Surgery plus GnRHa versus GnRHa alone:
The RCT gave no information on harms. [43]

Comment:

Only one of the RCTs [42] assessed effects on pregnancy rates. One RCT was not included in the systematic review because the outcome of avoiding scheduled hysterectomy was assessed in the GnRHa group only. [44]

QUESTION What are the effects of surgical treatments in women with fibroids?

OPTION LAPAROSCOPIC MYOMECTOMY

Postoperative recovery
Compared with abdominal myomectomy Recovery times and duration of hospital stay are shorter following laparoscopic myomectomy compared with abdominal myomectomy (moderate-quality evidence).

Compared with minilaparotomy Laparoscopic myomectomy reduces recovery time compared with minilaparotomy (moderate-quality evidence).

Pregnancy rate
Compared with abdominal myomectomy There seems to be no significant difference in pregnancy rates after laparoscopic myomectomy compared with abdominal myomectomy (low-quality evidence).

Recurrence of fibroids
Compared with abdominal myomectomy There seems to be no significant difference in recurrence rates after laparoscopic myomectomy compared with abdominal myomectomy (low-quality evidence).

Note
We found no clinically important results about laparoscopic myomectomy compared with total abdominal, vaginal, or laparoscopic hysterectomy. The main benefit of myomectomy compared with hysterectomy is that it maintains fertility. We found no clinically important information about the effects of total laparoscopic myomectomy compared with medical treatments.

For GRADE evaluation of interventions for fibroids

, see table, p 24 .

Benefits: We found no systematic review.

Laparoscopic myomectomy versus no intervention or sham surgery:
We found no RCTs.

Laparoscopic myomectomy versus total abdominal myomectomy:
We found five RCTs comparing laparoscopic versus abdominal myomectomy, one of which compared laparoscopic myomectomy with a less invasive form of abdominal myomectomy, "minilaparotomy". [45] [46] [47] [48] [49]

Peri- and postoperative outcomes:
The first RCT (40 women with < 5 myomas and the size of the largest myoma < 7 cm) found no significant difference in length of surgery, blood loss, or postoperative complications (fever) between laparoscopic and abdominal myomectomy (P > 0.05 for all outcomes). [45] Women having laparoscopic myomectomy reported a lower intensity of postoperative pain (unlabelled scale), required less analgesia, and had a shorter recovery time than women having abdominal myomectomy by laparotomy. Two days after surgery, a significantly smaller proportion of women required analgesia with laparoscopic myomectomy than with abdominal myomectomy (analgesia free women: 17/20 [85%] with laparoscopic myomectomy *v* 3/20 [15%] with abdominal myomectomy; RR 5.7, 95% CI 2.0 to 16.4; NNT 2, 95% CI 1 to 3), and by day 15 more women were fully recovered after laparoscopic myomectomy (18/20 [90%] with laparoscopic *v* 1/20 [5%] with abdominal myomectomy; RR 18.0, 95% CI 2.7 to 122.0; NNT 2, 95% CI 1 to 2). [45] The second RCT (131 women with at least 1 myoma greater-than or equal to 5 cm) found a similar length of surgery with laparoscopic and abdominal myomectomy (100 minutes with laparoscopic *v* 88 minutes with abdominal myomectomy, reported as non-significant, P value not reported). [46] However, it found a significantly greater reduction in haemoglobin with abdominal than with laparoscopic myomectomy (1.33 g/dL with laparoscopic *v* 2.17 g/dL with abdominal myomectomy; P < 0.001). Women who had laparoscopic myomectomy were significantly less likely than women who had abdominal myomectomy to experience postoperative fever (8/66 [12%] with laparoscopic *v* 17/65 [26%] with abdominal myomectomy; RR 0.46, 95% CI 0.22 to 1.00; NNT 9, 95% CI 4 to 116), and were more likely to have a shorter hospital stay (75.6 hours with laparoscopic myomectomy *v* 142.8 hours with abdominal myomectomy; CI not reported; P < 0.001). [46] The third RCT did not assess peri- or postoperative outcomes. [47] The fourth RCT (148 women) compared laparoscopic myomectomy versus minilaparotomy (which has an incision only half the length of full abdominal myomectomy). [48] It found that the mean duration of surgery was significantly shorter with minilaparotomy compared with laparoscopic myomectomy (85 minutes with minilaparotomy *v* 98 minutes with laparoscopic myomectomy; P < 0.001). [48] The RCT found that laparoscopic myomectomy significantly reduced the mean decline in

haemoglobin, duration of ileus, and time to hospital discharge, compared with minilaparotomy (decline in haemoglobin: 1.1 g/dL with laparoscopic myomectomy *v* 2.2 g/dL with minilaprotomy, P < 0.001; postoperative ileus: 28 hours *v* 45 hours, P < 0.001; time to hospital discharge: 38 hours *v* 48 hours, P < 0.001). [48] The RCT found that, compared with minilaparotomy, laparoscopic myomectomy significantly reduced both mean pain intensity 6 hours after surgery (measured on visual analogue score scale: 4.1 units with laparoscopic myomectomy *v* 6.5 units with minilaparotomy; P < 0.001), and the percentage of women requesting analgesics (34.7% *v* 73%; P < 0.001). [48] It found that women having laparoscopic myomectomy were significantly more likely to be fully recuperated on the 15th postoperative day compared with minilaparotomy (P = 0.012). The fifth RCT (40 women with both women and observers blinded) compared postoperative pain levels between women having laparoscopic or open abdominal myomectomy. [49] The RCT found that laparoscopic myomectomy significantly reduced mean postoperative pain compared with open abdominal myomectomy (mean overall visual analogue scale score at 24, 48, and 72 hours after surgery: 2.28 units with laparoscopic myomectomy *v* 4.03 units with open; P < 0.01) and significantly reduced blood loss (71 mL *v* 115 mL; P < 0.05). [49] It found that length of surgery was significantly greater with laparoscopic myomectomy compared with abdominal myomectomy (99 minutes *v* 68 minutes; P < 0.01). [49]

Pregnancy rate:
The second RCT found no significant difference in pregnancy rate after surgery between laparoscopic and abdominal myomectomy (53.6% with laparoscopic *v* 55.9% with abdominal myomectomy; reported as non-significant, CI not reported).

Recurrence rate:
The third RCT (81 women with infertility and less-than or equal to 7 fibroids) found no significant difference between laparoscopic and abdominal myomectomy in recurrence of fibroids at 3.3 years (27% with laparoscopic *v* 23% with abdominal; reported as non-significant, figures not reported). [47]

Laparoscopic myomectomy versus total abdominal, vaginal, or laparoscopic hysterectomy:
We found no systematic review or RCTs (see comment below).

Laparoscopic myomectomy versus medical interventions:
We found no systematic review or RCTs.

Harms:

Laparoscopic myomectomy versus no intervention or sham surgery:
We found no RCTs.

Laparoscopic myomectomy versus total abdominal myomectomy:
No major complications were reported in the RCTs. [45] [46] [47] [48] [49] The second RCT found that more women having abdominal compared with laparoscopic myomectomy required blood transfusions (transfusion risk: 3/65 [5%] with abdominal *v* 0/66 [0%] with laparoscopic myomectomy; P value and CI not reported). [46] In the fourth RCT, two women having laparoscopic myomectomy had complications compared with none in the minilaparotomy group. [48] One woman had laparoconversion caused by difficulties of haemostasis, and another woman had acute peritonitis which required abdominal surgery 10 days after laparoscopic myomectomy. [48] Two out of four RCTs found that length of surgery with abdominal myomectomy was significantly shorter than with laparoscopic myomectomy (see benefits above). [48] [49] The other two RCTs found no evidence of a difference in the length of surgery. [45] [46]

Laparoscopic myomectomy versus total abdominal, vaginal, or laparoscopic hysterectomy:
We found no RCTs.

Laparoscopic myomectomy versus medical interventions:
We found no RCTs.

Comment:

Clinical guide:
We found no RCTs comparing laparoscopic myomectomy versus hysterectomy.

Clinical guide:
The main benefit of myomectomy compared with hysterectomy is that it maintains fertility.

OPTION LAPAROSCOPICALLY ASSISTED VAGINAL HYSTERECTOMY

Postoperative recovery
Compared with total abdominal hysterectomy Postoperative recovery times are reduced after laparoscopically assisted vaginal hysterectomy compared with total abdominal hysterectomy (moderate-quality evidence).

Compared with total vaginal hysterectomy Postoperative recovery rates are similar for laparoscopically assisted vaginal hysterectomy compared with total vaginal hysterectomy (moderate-quality evidence).

Note
We found no clinically important results about total laparoscopically assisted vaginal hysterectomy compared with laparoscopic or total abdominal myomectomy or compared with medical treatments. The main benefit of myomectomy compared with hysterectomy is that it maintains fertility.

For GRADE evaluation of interventions for fibroids

, see table, p 24 .

Benefits:

We found no systematic review. We found no RCTs comparing laparoscopically assisted vaginal hysterectomy (LAVH) versus no intervention or sham surgery.

LAVH versus total abdominal hysterectomy (TAH) or total vaginal hysterectomy:
We found two RCTs in women with symptomatic fibroids scheduled for hysterectomy comparing the effects of LAVH versus TAH on operating time, blood loss, complications (not clearly specified), febrile morbidity, postoperative analgesic requirement, and hospital stay. [50] [51] Both RCTs found that LAVH improved intraoperative and postoperative outcomes compared with TAH. The first RCT (90 women) compared three interventions: LAVH, total vaginal hysterectomy, and TAH. [50] There was no significant difference in age, weight, or other relevant demographic characteristics among groups. The RCT found that, compared with either LAVH or TAH, total vaginal hysterectomy significantly reduced intraoperative blood loss (343 mL with LAVH *v* 215 mL with vaginal hysterectomy *v* 293 mL with TAH; P = 0.04). It found that, compared with TAH, both LAVH and total vaginal hysterectomy significantly reduced postoperative pain scores at 24 hours (measured on a scale from 0–10; 4 with LAVH *v* 3 with total vaginal hysterectomy *v* 6 with TAH; P < 0.001), and the number of days of postoperative antibiotic use (1.3 days with LAVH *v* 1.3 days with total vaginal hysterectomy *v* 1.7 days with TAH; P < 0.001). It also found that both LAVH and total vaginal hysterectomy significantly reduced the time to return to work (mean 30 days with LAVH *v* 29 days with vaginal hysterectomy *v* 41 days with TAH; P < 0.001), reduced the proportion of women with febrile morbidity (3% with LAVH *v* 13% with total vaginal hysterectomy *v* 27% with TAH; P < 0.05), and reduced mean hospital stay (4.7 days with LAVH *v* 4.7 days with vaginal hysterectomy *v* 5.0 days with TAH; P = 0.003). It found no significant difference in postoperative pain, time to return to work, or febrile morbidity between LAVH and vaginal hysterectomy. [50] The second RCT (62 women) found that LAVH significantly reduced hospital stay and analgesic use compared with TAH (mean hospital stay 3.8 days with LAVH *v* 5.8 days with TAH, P < 0.001; analgesic use for > 24 hours postoperatively 23% with LAVH *v* 77% with TAH, CI not reported). [51] *Post hoc* subgroup analyses found limited evidence that the relative effects of LAVH and TAH depended on uterine weight. [51]

In women with a uterus estimated to weigh 500 g or less:
Subgroup analysis in 41 women with a uterus estimated to weigh 500 g or less in the preoperative assessment found that LAVH and TAH required comparable operating times (130 minutes on average with LAVH *v* 120 minutes with TAH). [51] Women in the LAVH group had less postoperative pain and shorter recovery times compared with the TAH group. Sonograms were used to estimate uterine weight. Analgesia requirement was reduced with LAVH (1/20 [5%] with LAVH *v* 6/11 [55%] with TAH; RR 0.09, 95% CI 0.01 to 0.67; NNT 2, 95% CI 1 to 6). Hospital stay was also reduced with LAVH (3.8 days, 95% CI 3.2 days to 4.0 days with LAVH *v* 5.8 days, 95% CI 5.0 days to 6.4 days with TAH; P < 0.0001).

In women with a uterus estimated to weigh more than 500 g:
Subgroup analysis in 21 women with a uterus weighing more than 500 g found that LAVH was associated with a shorter recovery time, but a longer operating time compared with TAH. [51] About 27% of women randomised to LAVH converted to TAH. Mean operating time was significantly increased with LAVH (mean 150 minutes with LAVH *v* 108 minutes with TAH; P = 0.002). Mean hospital stay was also significantly reduced with LAVH (4.0 days with LAVH *v* 6.0 days with TAH; P = 0.03).

Laparoscopically assisted vaginal hysterectomy versus laparoscopic or total abdominal myomectomy:
We found no systematic review or RCTs (see comment below).

Laparoscopically assisted vaginal hysterectomy versus medical interventions:
We found no systematic review or RCTs.

Harms:

Laparoscopically assisted vaginal hysterectomy versus total abdominal hysterectomy:
The first RCT also found that LAVH significantly increased mean operating time (without second procedure) and blood loss compared with TAH (mean 109 minutes with LAVH *v* 98 minutes with TAH, P < 0.001; mean blood loss 343 mL with LAVH *v* 293 mL with TAH, P = 0.04). [50] No major complications were reported in either RCT, although there was insufficient information to determine which complications were addressed. The second RCT found that LAVH significantly increased operating time (in women who did not have a second operation [oophorectomy and/or adhesiolysis]) compared with TAH (mean operating time 135 minutes with LAVH *v* 120 minutes with TAH; P = 0.001). [51]

Laparoscopically assisted vaginal hysterectomy versus laparoscopic or total abdominal myomectomy:
We found no RCTs.

Laparoscopically assisted vaginal hysterectomy versus medical interventions:
We found no RCTs.

Comment:

The RCTs did not assess effects on pregnancy rates.

Clinical guide:
Other RCTs have compared different types of hysterectomy in other groups of women, but results from these RCTs are not generalisable to women with fibroids. The main benefit of myomectomy compared with hysterectomy is that it maintains fertility.

OPTION TOTAL ABDOMINAL HYSTERECTOMY

Postoperative recovery
Compared with vaginal hysterectomy Total abdominal hysterectomy leads to slower postoperative recovery, assessed as time in hospital or time to return to work, compared with total vaginal hysterectomy or with laparoscopically assisted vaginal hysterectomy (moderate-quality evidence).

Note
We found no direct information about whether total abdominal hysterectomy is better than no treatment or sham surgery. We found no clinically important results about the effects of total abdominal hysterectomy compared with laparoscopic or total abdominal myomectomy or compared with medical treatments. The main benefit of myomectomy compared with hysterectomy is that it maintains fertility.

For GRADE evaluation of interventions for fibroids

, see table, p 24 .

Benefits:

We found no systematic review. We found no RCTs comparing total abdominal hysterectomy (TAH) versus no intervention or sham surgery (see comment below).

TAH versus total vaginal hysterectomy:
See benefits of total vaginal hysterectomy, p 16 .

TAH versus laparoscopically assisted vaginal hysterectomy:
See benefits of laparoscopically assisted vaginal hysterectomy, p 12 .

TAH versus laparoscopic or total abdominal myomectomy:
We found no systematic review or RCTs (see comment below).

TAH versus medical interventions:
We found no systematic review or RCTs.

Harms:

TAH versus total vaginal hysterectomy:
See harms of total vaginal hysterectomy, p 16 .

TAH versus laparoscopically assisted vaginal hysterectomy:
See harms of laparoscopically assisted vaginal hysterectomy, p 12 .

TAH versus laparoscopic myomectomy:
See harms of laparoscopic myomectomy, p 11 .

TAH versus laparoscopic or total abdominal myomectomy:
We found no RCTs.

TAH versus medical interventions:
We found no RCTs.

Comment:

Clinical guide:
There is consensus that TAH is superior to no treatment in improving fibroid related symptoms. An RCT is unlikely to be conducted. Other RCTs have compared different types of hysterectomy in various groups of women, but results from these RCTs are not generalisable to women with fibroids. The main benefit of myomectomy compared with hysterectomy is that it maintains fertility.

OPTION TOTAL ABDOMINAL MYOMECTOMY

Postoperative recovery
Compared with abdominal myomectomy Recovery times and duration of hospital stay are shorter following laparoscopic myomectomy compared with abdominal myomectomy (moderate-quality evidence).

Compared with minilaparotomy Laparoscopic myomectomy reduces recovery time compared with minilaparotomy (moderate-quality evidence).

Pregnancy rate
Compared with laparoscopic myomectomy There may be no significant difference in pregnancy rates after abdominal myomectomy compared with laparoscopic myomectomy (low-quality evidence).

Recurrence of fibroids
Compared with laparoscopic myomectomy There may be no difference in recurrence rates after laparoscopic myomectomy compared with abdominal myomectomy (low-quality evidence).

Note
We found no clinically important results about the effects of abdominal myomectomy compared with total abdominal, vaginal, or laparoscopic hysterectomy. The main benefit of myomectomy compared with hysterectomy is that it maintains fertility. We also found no clinically important results about myomectomy compared with medical interventions.

For GRADE evaluation of interventions for fibroids

, see table, p 24 .

Benefits:

We found no systematic review.

Total abdominal myomectomy versus no intervention or sham surgery:
We found no RCTs.

Total abdominal myomectomy versus laparoscopic myomectomy:
See benefits of laparoscopic myomectomy, p 11 .

Total abdominal myomectomy versus total abdominal, vaginal, or laparoscopic hysterectomy:
We found no systematic review or RCTs (see comment below).

Total abdominal myomectomy versus medical interventions:
We found no systematic review or RCTs.

Harms:

We found no systematic review.

Total abdominal myomectomy versus no intervention or sham surgery:
We found no RCTs.

Total abdominal myomectomy versus laparoscopic myomectomy:
See harms of laparoscopic myomectomy, p 11 .

Total abdominal myomectomy versus total abdominal, vaginal, or laparoscopic hysterectomy:
We found no RCTs.

Total abdominal myomectomy versus medical interventions:
We found no RCTs.

Comment:

Clinical guide:
The main benefit of myomectomy compared with hysterectomy is that it maintains fertility.

OPTION TOTAL LAPAROSCOPIC HYSTERECTOMY

Postoperative recovery
Compared with total abdominal hysterectomy Postoperative recovery may be shorter after total laparoscopic hysterectomy compared with total abdominal hysterectomy (low-quality evidence).

Note
We found no clinically important results about total laparoscopic hysterectomy compared with laparoscopic or total abdominal myomectomy or compared with medical treatments. The main benefit of myomectomy compared with hysterectomy is that it maintains fertility.

For GRADE evaluation of interventions for fibroids

, see table, p 24 .

Benefits:

We found no systematic review. We found no RCTs comparing total laparoscopic hysterectomy versus no intervention or sham surgery.

Total laparoscopic hysterectomy versus total abdominal hysterectomy:
We found no systematic review but found one RCT (122 women with an enlarged uterus [equivalent to > 14 weeks' gestation] because of fibroids) comparing total laparoscopic hysterectomy versus total abdominal hysterectomy. [52] It found that, compared with total abdominal hysterectomy, total laparoscopic hysterectomy significantly reduced the proportion of women who had postoperative fever (13% with total laparoscopic hysterectomy *v* 29% with total abdominal hysterectomy; P < 0.05), and reduced duration of hospital stay (mean 76.4 hours with total laparoscopic hysterectomy *v* 121.8 hours with total abdominal hysterectomy) and recovery times (mean 22 days with total laparoscopic hysterectomy *v* 36 days with total abdominal hysterectomy; P < 0.001 for both outcomes).

Total laparoscopic hysterectomy versus laparoscopic or total abdominal myomectomy:
We found no systematic review or RCTs.

Total laparoscopic hysterectomy versus medical interventions:
We found no systematic review or RCTs.

Harms:

The RCT reported that one woman randomised to total laparoscopic hysterectomy converted to abdominal hysterectomy because of incidental bowel injury. [52] It found no other major complications associated with laparoscopic or abdominal hysterectomy.

Total laparoscopic hysterectomy versus laparoscopic or total abdominal myomectomy:
We found no RCTs.

Total laparoscopic hysterectomy versus medical interventions:
We found no RCTs.

Comment:

Clinical guide:
Women were only included in the RCT if they had an enlarged uterus. [52] This would usually be a contraindication to total laparoscopic hysterectomy. The RCT did not assess effects on pregnancy rates. [52] Other RCTs have compared different types of hysterectomy in various groups of women, but results from these RCTs are not generalisable to women with fibroids. The main benefit of myomectomy compared with hysterectomy is that it maintains fertility.

OPTION TOTAL VAGINAL HYSTERECTOMY

Postoperative recovery
Compared with total abdominal hysterectomy Total vaginal hysterectomy leads to faster postoperative recovery, assessed as time in hospital or time to return to work, compared with total abdominal hysterectomy (moderate-quality evidence).

Compared with laparoscopically assisted vaginal hysterectomy Recovery times after total vaginal hysterectomy are similar to those after laparoscopically assisted vaginal hysterectomy (moderate-quality evidence).

Note
We found no clinically important results about total vaginal hysterectomy compared with laparoscopic or total abdominal myomectomy, or compared with medical treatments. The main benefit of myomectomy compared with hysterectomy is that it maintains fertility.

For GRADE evaluation of interventions for fibroids

, see table, p 24 .

Benefits:

We found no systematic review. We found no RCTs comparing total vaginal hysterectomy versus no intervention or sham surgery.

Total vaginal hysterectomy versus TAH:
We found no systematic review. We found three RCTs (239 women) comparing total vaginal hysterectomy versus TAH. [50] [53] [54] All of the RCTs found that vaginal hysterectomy improved intraoperative and postoperative outcomes compared with abdominal hysterectomy. The first RCT (90 women) compared three interventions: total vaginal hysterectomy; total abdominal hysterectomy; and laparoscopically assisted vaginal hysterectomy (LAVH). [50] The women in each group did not differ significantly in age, weight, or other relevant demographic characteristics. The RCT found that, compared with either TAH or LAVH, total vaginal hysterectomy significantly reduced intraoperative blood loss (215 mL with vaginal hysterectomy *v* 293 mL with TAH *v* 343 mL with LAVH; P = 0.04). It found that, compared with TAH, both total vaginal hysterectomy and LAVH significantly reduced postoperative pain scores at 24 hours (measured on a scale from 0–10; 3 with vaginal hysterectomy *v* 6 with TAH *v* 4 with LAVH; P < 0.001) and the number of days of postoperative antibiotic use (1.3 days with vaginal hysterectomy *v* 1.7 days with TAH *v* 1.3 days with LAVH; P < 0.001). It also found that both total vaginal hysterectomy and LAVH significantly reduced the time to return to work (mean: 29 days with vaginal hysterectomy *v* 41 days TAH *v* 30 days with LAVH; P < 0.001), reduced the proportion of women with febrile morbidity (13% with vaginal hysterectomy *v* 27% with TAH *v* 3% with LAVH; P < 0.05), and reduced mean hospital stay (4.7 days with vaginal hysterectomy *v* 5.0 days with TAH *v* 4.7 days with LAVH; P = 0.003). The second RCT (89 women) found that, compared with TAH, total vaginal hysterectomy significantly reduced the duration of operation (86 minutes with vaginal hysterectomy *v* 102 minutes with TAH; P < 0.001), reduced the proportion of women with postoperative fever (17% with vaginal hysterectomy *v* 30% with TAH; P < 0.05), and reduced the proportion of women who needed postoperative analgesics (66% with vaginal hysterectomy *v* 86% with TAH; P < 0.05). [53] It found that total vaginal hysterectomy significantly reduced hospital stay compared with TAH (3.4 days with vaginal hysterectomy *v* 4.3 days with TAH; P < 0.001). More women having vaginal hysterectomy rated treatment as "good" or "very good" (83% with vaginal hysterectomy *v* 32% with total hysterectomy; P value not reported). The third RCT (60 women) found that women with vaginal hysterectomy had significantly better postoperative quality of life scores than women with TAH. [54] The RCT found that SF-36 scores were significantly improved by vaginal hysterectomy compared with TAH (functional capacity score: 95 with vaginal hysterectomy *v* 72.5 with TAH, P = 0.002; physical aspect score: 100 *v* 37.5, P = 0.008; pain score: 84 *v* 51, P = 0.002). [54] There was no evidence of a difference in the degree of general postoperative satisfaction with surgery (very satisfied: 100% with vaginal hysterectomy *v* 87% with TAH; P = 0.147). The RCT found that the acceptability of the surgical procedure (measured by the proportion who would choose the same modality) was significantly improved by vaginal hysterectomy compared with TAH (90% with vaginal hysterectomy *v* 65.5% with TAH; P = 0.021). It also found that the mean operating time (61.1 minutes *v* 90.5 minutes; P < 0.001) and hospital stay (24.7 hours *v* 51.3 hours; P < 0.001) were significantly shorter with vaginal hysterectomy compared with TAH.

Total vaginal hysterectomy versus laparoscopically assisted vaginal hysterectomy:
See benefits of laparoscopically assisted vaginal hysterectomy, p 12 .

Total vaginal hysterectomy versus laparoscopic or total abdominal myomectomy:
We found no systematic review or RCTs (see comment below).

Total vaginal hysterectomy versus medical interventions:
We found no systematic review or RCTs.

Harms:

Total vaginal hysterectomy versus laparoscopic or total abdominal myomectomy:
We found no RCTs.

Total vaginal hysterectomy versus medical interventions:
We found no RCTs.

Comment:

Clinical guide:
Other RCTs have compared different types of hysterectomy in various groups of women, but results from these RCTs are not generalisable to women with fibroids. The RCTs did not assess effects on pregnancy rates. The main benefit of myomectomy compared with hysterectomy is that it maintains fertility.

OPTION HYSTEROSCOPIC RESECTION

We found no clinically important results about the effects of hysteroscopic resection in women with fibroids.

For GRADE evaluation of interventions for fibroids

, see table, p 24 .

Benefits: We found no systematic review or RCTs.

Harms: We found no systematic review or RCTs.

Comment: None.

OPTION MAGNETIC RESONANCE-GUIDED FOCUSED ULTRASOUND (MAGNETIC RESONANCE IMAGING GUIDED FOCUSED ULTRASOUND SURGERY)

We found no clinically important results about the effects of magnetic resonance imaging-guided focused ultrasound surgery in women with fibroids.

For GRADE evaluation of interventions for fibroids

, see table, p 24 .

Benefits: We found one systematic review (search date 2005). [55] The systematic review identified two observational studies but no RCTs. We found no subsequent RCTs.

Harms: We found no RCTs.

Comment: **Clinical guide:**
No RCTs were identified by the systematic review. [55] The authors of the review concluded that there was insufficient evidence to permit conclusions regarding the effect of this intervention on health outcomes. [55]

OPTION ROLLERBALL ENDOMETRIAL ABLATION

Menstrual blood loss
Compared with thermal balloon ablation There may be no significant difference in postoperative amenorrhoea rates between rollerball endometrial ablation compared with thermal balloon ablation, in women with fibroids smaller than the average size of a 12-week pregnancy, who have been pretreated with gonadorelin analogues (very low-quality evidence).

Need for subsequent hysterectomy
Compared with thermal balloon ablation There may be no difference in rates of subsequent hysterectomy between rollerball endometrial ablation compared with thermal balloon ablation (very low-quality evidence).

Intraoperative complications
Compared with thermal balloon ablation There may be higher intraoperative complication rates with rollerball endometrial ablation compared with thermal balloon ablation (very low-quality evidence).

Note
We found no clinically important results about the effects of rollerball endometrial ablation compared with medical treatment or hysterectomy.

For GRADE evaluation of interventions for fibroids

, see table, p 24 .

Benefits: **Rollerball endometrial ablation versus medical treatment or hysterectomy:**
We found no systematic review or RCTs.

Rollerball endometrial ablation versus thermal balloon ablation:
See benefits of thermal balloon ablation, p 19 .

Harms: **Rollerball endometrial ablation versus medical treatment or hysterectomy:**
We found no RCTs.

Rollerball endometrial ablation versus thermal balloon ablation:
See harms of thermal balloon ablation, p 19 .

Comment: None.

OPTION THERMAL BALLOON ABLATION

Menstrual blood loss
Compared with rollerball endometrial ablation There may be no significant difference in postoperative amenorrhoea rates between thermal balloon ablation compared with rollerball endometrial ablation, in women with fibroids smaller than the average size of a 12-week pregnancy, who have been pretreated with gonadorelin analogues (very low-quality evidence).

Need for subsequent hysterectomy
Compared with rollerball endometrial ablation There may be no significant difference in rates of subsequent hysterectomy between thermal balloon ablation compared with rollerball endometrial ablation (very low-quality evidence).

Intraoperative complications
Compared with rollerball endometrial ablation There may be lower intraoperative complication rates with thermal balloon ablation compared with rollerball endometrial ablation (very low-quality evidence).

Note
We found no clinically important results about the effects of thermal balloon ablation compared with medical treatments or hysterectomy.

For GRADE evaluation of interventions for fibroids

, see table, p 24 .

Benefits:

Thermal balloon ablation versus other surgical treatment:
We found no RCTs comparing thermal balloon ablation versus hysterectomy. We found one RCT (96 women with fibroids smaller than the average size of a 12 week pregnancy who had received 2 months of preoperative treatment with gonadorelin analogues), which compared thermal balloon ablation versus rollerball endometrial ablation. [56] Thermal balloon ablation was performed by staff surgeons or supervised residents under local intracervical and paracervical anaesthesia with intravenous sedation. Rollerball ablation was performed under general anaesthesia by experienced surgeons.

Effects on hysterectomy rates and symptoms:
The RCT found no significant difference between thermal balloon ablation compared with rollerball endometrial ablation in hysterectomy rates, amenorrhoea rates, pictorial bleeding assessment chart score, or haemoglobin at 12 months (women having hysterectomy: 4/45 [9%] with thermal balloon *v* 4/48 [8%] with rollerball; amenorrhoea: 5 women with thermal balloon *v* 8 women with rollerball; mean decrease in pictorial bleeding assessment chart score: 343 with thermal balloon *v* 345 with rollerball; mean increase in haemoglobin: 2.7 g/dL with thermal balloon *v* 3.0 g/dL with rollerball; P values reported as non-significant for all comparisons; CI not reported).

Perioperative outcomes:
Operating time was significantly shorter in the thermal balloon group compared with the rollerball group (11.5 minutes with thermal ball oon *v* 37.3 minutes with rollerball; P < 0.0001). About a third of women in both groups reported that they were “not very satisfied” with their operation (33% with thermal balloon *v* 39% with rollerball). [56]

Thermal balloon ablation versus medical interventions:
We found no systematic review or RCTs.

Harms:

The RCT found that a significantly higher proportion of women had intraoperative complications with rollerball ablation than with thermal balloon ablation (5/45 [11%] with rollerball *v* 0/48 [0%] with thermal balloon; P < 0.05; 2 women had fluid overload, 2 had major bleeding, and 1 had injury to the cervix). [56] It found no significant difference between rollerball ablation and thermal balloon ablation in postoperative complications (3 women in each group) or postoperative pain score at 12 hours.

Thermal balloon ablation versus medical interventions:
We found no RCTs.

Comment: The RCT did not assess effects on pregnancy rates.

OPTION THERMAL MYOLYSIS WITH LASER

We found no clinicaly important results about the effects of thermal myolysis with laser in women with fibroids.

For GRADE evaluation of interventions for fibroids

, see table, p 24 .

Benefits: We found no systematic review or RCTs.

Harms: We found no systematic review or RCTs.

Comment: None.

GLOSSARY

Endometrial resection Destruction of the endometrium using a cutting tool.
Myomectomy Removal of fibroids from the uterus. The mode of removal may be abdominal, laparoscopic, or hysteroscopic.
Pelvic symptom score scale An ordinal scale that adds the results of pelvic pain and pelvic pressure. Each symptom is evaluated on a scale ranging from 0–3, where 0 means absence of pain, and increasing numbers represent mild, moderate, and severe pain. Because both results are added, the absence of symptoms is represented by 0 and severe pain and pelvic pressure by 6. We found no data on validation of the scale. However, it is commonly used in studies evaluating pelvic pain.
Pictorial bleeding assessment chart Used to measure menstrual bleeding. Validation studies indicate that a pictorial bleeding assessment chart score of 100–185 is suggestive of menorrhagia (heavy menstrual bleeding), which is objectively defined by the alkaline haematin test as a menstrual blood loss greater than 80 mL. The chart score used as an end point varies between studies.
Rollerball endometrial ablation Destruction of the endometrium using electrical coagulation with a rollerball electrode applied through the cervical os.
Thermal balloon ablation Destruction of the endometrium using pressure from a balloon catheter inserted through the cervical os and then filled with fluid to a pressure of 160–180 mm Hg and heated to about 87 °C.
Total hysterectomy Removal of the uterus. The mode of removal may be through the abdominal wall (total abdominal hysterectomy), through the vagina (total vaginal hysterectomy), partially through the vagina and partially morcellated and removed by laparoscopic incision (laparoscopically assisted vaginal hysterectomy), or entirely by laparoscopic excision (total laparoscopic hysterectomy). In some situations, total abdominal hysterectomy is performed in conjunction with a bilateral salpingo-oophorectomy — the removal of both ovaries and fallopian tubes.
Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Moderate-quality evidence Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Very low-quality evidence Any estimate of effect is very uncertain.

SUBSTANTIVE CHANGES

Laparoscopic myomectomy One RCT comparing laparoscopic myomectomy versus minilaparotomy [48] and one RCT comparing laparoscopic versus open myomectomy [49] added; benefits and harms data enhanced, categorisation unchanged (Beneficial).
Magnetic resonance guided focused ultrasound (magnetic resonance imaging guided focused ultrasound surgery) One systematic review added; [55] benefits and harms data enhanced, categorisation unchanged (Unknown effectiveness).
Total vaginal hysterectomy One RCT comparing total vaginal hysterectomy versus total abdominal hysterectomy added; [54] benefits and harms data enhanced, categorisation unchanged (Likely to be beneficial).

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TABLE 1 **Harms of leuprotelin versus placebo in one RCT (65 women) (see text, p 6).** [25]

Harms	Gonadorelin			Placebo				
	Outcome	Population	%	Outcome	Population	%	RR*	95% CI*
Vasomotor flushes	52	63	83%	5	65	8%	10.7	4.6 to 25.1
Vaginitis	11	63	17%	0	65	0%		
Arthralgia/mialgia	9	63	14%	0	65	0%		
Asthenia	10	63	16%	3	65	5%	3.4	0.97 to 996
Peripheral oedema	7	63	11%	1	65	2%	7.2	0.9 to 57
Insomnia	6	63	10%	0	65	0%		
Nausea	6	63	10%	1	65	2%	6.2	0.8 to 50
Emotional ability /nervousness	5	63	8%	1	65	2%	5.2	0.6 to 42.9
Depression	7	63	11%	2	65	3%	3.6	0.8 to 16.7
Headaches	18	63	29%	13	65	20%	1.4	0.8 to 2.7
Decreased libido	2	63	3%	0	65	0%		

**BMJ Clinical Evidence* recalculation.

TABLE **GRADE evaluation of interventions for fibroids.**

Number of studies (participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
Important outcomes	**Menstrual blood flow; Reduction in fibroid/uterine volume; Pregnancy rate; Pelvic pain/pressure; Postoperative recovery times; Adverse effects/complications**								
What are the effects of medical treatment alone in women with fibroids?									
1 (41) [15]	Heavy bleeding	Gonadorelin analogues plus progestogen *v* gonadorelin analogues alone	4	–2	0	0	0	Low	Quality points deducted for sparse data and subjective outcome assessment
2 (40) [16] [17]	Vasomotor adverse effects	Gonadorelin analogues plus progestogen *v* gonadorelin analogues alone	4	–2	0	0	1	Moderate	Quality points deducted for sparse data and incomplete reporting of results. Effect size point added for RR less than 0.2
1 (100) [18]	Fibroid/uterus size	Gonadorelin analogues plus raloxifene *v* gonadorelin analogues alone	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete presentation of results
1 (100) [18]	Fibroid -related symptoms (menorrhagia, pelvic pain)	Gonadorelin analogues plus raloxifene *v* gonadorelin analogues alone	4	–2	0	0	0	Low	Quality point s deducted for sparse data and incomplete presentation of results
2 (70) [21] [22]	Fibroid/uterine size	Gonadorelin analogues plus tibolone *v* gonadorelin analogues alone	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
1 (50) [21]	Fibroid-related symptoms (menorrhagia, pelvic pain)	Gonadorelin analogues plus tibolone *v* gonadorelin analogues alone	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
2 (70) [21] [22]	Gonadorelin analogue adverse effects	Gonadorelin analogues plus tibolone *v* gonadorelin analogues alone	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
6 (562) [23] [24] [25] [26] [27] [28]	Menstrual blood loss (amenorrhoea)	Gonadorelin analogues *v* placebo	4	–2	+1	0	0	Low	Quality points deducted for poor follow-up and other methodological flaws. Consistency point added for dose response (1 additional RCT, 257 women)
3 (96) [34] [35]	Fibroid size	Intranasal gonadorelin analogues *v* subcutaneous gonadorelin analogues	4	–3	0	0	0	Very low	Quality points deducted for sparse data, incomplete reporting of results, subjective assessment of outcomes
3 (96) [34] [35]	Menorrhagia	Intranasal gonadorelin analogues *v* subcutaneous gonadorelin analogues	4	–3	0	0	0	Very low	Quality points deducted for sparse data, incomplete reporting of results, subjective assessment of outcomes
1 (51) [37]	Uterus size	Gonadorelin analogue plus combined oestrogen-progesterone *v* gonadorelin analogue plus progesterone	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
1 (51) [37]	Menorrhagia	Gonadorelin analogue plus combined oestrogen-progesterone *v* gonadorelin analogue plus progesterone	4	–2	0	–1	0	Very low	Quality points deducted for sparse data and incomplete reporting of results. Directness point deducted for no direct comparison between groups
In women scheduled for fibroid surgery, what are the effects of preoperative medical treatments?									

Important outcomes	Menstrual blood flow; Reduction in fibroid/uterine volume; Pregnancy rate; Pelvic pain/pressure; Postoperative recovery times; Adverse effects/complications								
Number of studies (participants)	**Outcome**	**Comparison**	**Type of evidence**	**Quality**	**Consistency**	**Directness**	**Effect size**	**GRADE**	**Comment**
3 (372) [40]	Improvement in pelvic symptoms	Gonadorelin analogue pre-treatment plus surgery *v* surgery	4	0	0	–1	0	Moderate	Directness point deducted as only preoperative symptoms assessed
1 (60) [42]	Pregnancy rate	Myomectomy plus gonadorelin analogue pretreatment *v* myomectomy alone	4	–1	0	–1	0	Low	Quality point deducted for sparse data. Directness point deducted as not all women had infertility problems
3 (142) [40]	Recurrence of fibroids	Myomectomy plus gonadorelin analogue pretreatment *v* myomectomy alone	4	–1	–1	0	1	Moderate	Quality point deducted for sparse data. Consistency point deducted for conflicting results. Effect size point added for OR less than 5
1 (25) [43]	Need for further treatment	Gonadorelin analogue plus surgery *v* gonadorelin analogue alone	4	–2	0	0	1	Moderate	Quality points deducted for sparse data and no blinding of surgical treatment. Effect size point added for RR less than 5
What are the effects of surgical treatments in women with fibroids?									
2 (171) [45] [46]	Postoperative recovery (and duration of hospital stay)	Laparoscopic myomectomy *v* abdominal myomectomy	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (148) [48]	Postoperative recovery	Laparoscopic myomectomy *v* minilaparotomy	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (131) [46]	Pregnancy rate	Laparoscopic myomectomy *v* abdominal myomectomy	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
1 (87) [47]	Recurrence of fibroids	Laparoscopic myomectomy *v* abdominal myomectomy	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
2 (152) [50] [51]	Postoperative recovery	Laparoscopically assisted vaginal hysterectomy *v* total abdominal hysterectomy	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
3 (239) [50] [53]	Postoperative recovery	Total abdominal hysterectomy *v* total vaginal hysterectomy	4	0	0	–1	0	Moderate	Directness point deducted for range of outcomes included
1 (90) [50]	Postoperative recovery	Laparoscopically assisted vaginal hysterectomy *v* total vaginal hysterectomy	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (122) [52]	Postoperative recovery	Total laparoscopic hysterectomy *v* total abdominal hysterectomy	4	–1	0	–1	0	Low	Quality point deducted for sparse data. Directness point deducted for inclusion criteria reducing generalisability
1 (96) [56]	Menstrual bleeding (amenorrhoea)	Thermal balloon ablation *v* rollerball endometrial ablation	4	–2	0	–1	0	Very low	Quality points deducted for sparse data and incomplete reporting of results. Directness point deducted as all women had pre-treatment with gonadorelin analogues
1 (96) [56]	Need for subsequent treatment (hysterectomy)	Thermal balloon ablation *v* rollerball endometrial ablation	4	–2	0	–1	0	Very low	Quality points deducted for sparse data and incomplete reporting of results. Directness point deducted as all women had pre-treatment with gonadorelin analogues

Important outcomes	Menstrual blood flow; Reduction in fibroid/uterine volume; Pregnancy rate; Pelvic pain/pressure; Postoperative recovery times; Adverse effects/complications								
Number of studies (participants)	**Outcome**	**Comparison**	**Type of evidence**	**Quality**	**Consistency**	**Directness**	**Effect size**	**GRADE**	**Comment**
1 (96) [56]	Intraoperative complications	Thermal balloon ablation *v* rollerball endometrial ablation	4	–2	0	–1	0	Very low	Quality points deducted for sparse data and incomplete reporting of results. Directness point deducted as all women had pre-treatment with gonadorelin analogues

Type of evidence: 4 = RCT; 2 = Observational; 1 = Non-analytical/expert opinion.
Consistency: similarity of results across studies.
Directness: generalisability of population or outcomes.
Effect size: based on relative risk or odds ratio.