Menorrhagia

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ABSTRACT

INTRODUCTION: Menorrhagia limits normal activities, and causes anaemia in two thirds of women with objective menorrhagia (loss of 80 mL blood per cycle). Prostaglandin disorders may be associated with idiopathic menorrhagia, and with heavy bleeding due to fibroids, adenomyosis, or use of intrauterine devices (IUDs). Fibroids have been found in 10% of women with menorrhagia overall, and in 40% of women with severe menorrhagia; but half of women having a hysterectomy for menorrhagia are found to have a normal uterus. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of medical treatments for menorrhagia? What are the effects of surgical treatments for menorrhagia? What are the effects of endometrial thinning before endometrial destruction in treating menorrhagia? We searched: Medline, Embase, The Cochrane Library, and other important databases up to October 2007 (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 39 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 medical interventions: combined pill, danazol, etamsylate, gonadorelin analogues, intrauterine progesterone, non-steroidal inflammatory drugs (NSAIDs), progestogens, and the following surgical interventions: dilatation and curretage, endometrial destruction, and hysterectomy.

QUESTIONS

INTERVENTIONS

Key points

- Menorrhagia limits normal activities, and causes anaemia in two thirds of women with objective menorrhagia (blood loss of more than 80 mL blood per cycle).

  Prostaglandin disorders may be associated with idiopathic menorrhagia, and with heavy bleeding caused by fibroids, adenomyosis, or use of IUDs.

  Fibroids have been found in 10% of women with menorrhagia overall, and in 40% of women with severe menorrhagia; but half of women having a hysterectomy for menorrhagia are found to have a normal uterus.

- NSAIDs, tranexamic acid, and danazol all reduce blood loss compared with placebo.

Tranexamic acid and danazol may be more effective than NSAIDs, etamsylate, and oral progestogens at reducing blood loss, but any benefits of danazol must be weighed against the high risk of adverse effects.

NSAIDs reduce dysmenorrhoea, and may be as effective at reducing menstrual blood loss as oral progestogens given in the luteal phase, but we don't know how they compare with etamsylate, combined oral contraceptives, intrauterine progestogens, or gonadorelin analogues.

We don't know whether combined oral contraceptives, levonorgestrel-releasing intrauterine devices, or gonadorelin analogues are effective at reducing menorrhagia, as few studies were found.

- Hysterectomy reduces blood loss, and reduces the need for further surgery compared with medical treatments or endometrial destruction, but can lead to complications in up to a third of women.

  Endometrial destruction is more effective at reducing menorrhagia compared with medical treatment, but complications can include infection, haemorrhage, and uterine perforation.

  We don't know whether any one type of endometrial destruction is superior, or whether dilatation and curettage has any effect on menstrual blood loss.

- Preoperative gonadorelin analogues reduce long-term postoperative moderate or heavy blood loss, and increase amenorrhoea compared with placebo, but we don't know whether oral progestogens or danazol are also beneficial when used preoperatively.

DEFINITION

Menorrhagia is defined as heavy but regular menstrual bleeding. **Idiopathic ovulatory menorrhagia** is regular heavy bleeding in the absence of recognisable pelvic pathology or a general bleeding disorder. **Objective menorrhagia** is taken to be a total menstrual blood loss of 80 mL or more in each menstruation. [1] Subjectively, menorrhagia may be defined as a complaint of regular excessive menstrual blood loss occurring over several consecutive cycles in a woman of reproductive age.

INCIDENCE/ PREVALENCE

In the UK, 5% of women aged 30–49 years consult their general practitioners each year with menorrhagia. [2] In New Zealand, 2–4% of primary-care consultations by premenopausal women are for menstrual problems. [3]

AETIOLOGY/ RISK FACTORS

Idiopathic ovulatory menorrhagia is thought to be caused by disordered prostaglandin production within the endometrium. [4] Prostaglandins may also be implicated in menorrhagia associated with uterine fibroids, adenomyosis, or the presence of an IUD. Fibroids have been reported in 10% of women with menorrhagia (80–100 mL/cycle), and in 40% of women with severe menorrhagia (at least 200 mL/cycle). [5]

PROGNOSIS

Menorrhagia limits normal activities and causes iron-deficiency anaemia in two thirds of women proven to have objective menorrhagia. [1] [6] [7] One in five women in the UK and one in three in the USA have a hysterectomy before the age of 60 years; menorrhagia is the main presenting problem in at least half of these women. [8] [9] [10] About half of women who have a hysterectomy for menorrhagia are found to have an anatomically normal uterus. [11]

AIMS OF INTERVENTION

To reduce menstrual bleeding; improve quality of life; and prevent or correct iron-deficiency anaemia, with minimum adverse effects. Women may regard amenorrhea as a benefit or a harm of treatment, depending on their perspective.

OUTCOMES

Menstrual blood flow (assessed objectively [mL/cycle] or subjectively); haemoglobin concentration; quality of life; patient satisfaction; incidence of adverse drug effects; and incidence of postoperative complications. Whether a particular percentage reduction in menstrual blood loss is considered clinically important will depend on pretreatment menstrual loss and on individual women's perceptions of acceptable menstrual loss.

METHODS

BMJ Clinical Evidence search and appraisal October 2007. The following databases were used to identify studies for this review: Medline 1966 to October 2007, Embase 1980 to October 2007, and The Cochrane Database of Systematic Reviews 2007, Issue 3. 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 NICE clinical guidelines. Abstracts of the studies retrieved were assessed independently by two information specialists using predetermined criteria to identify relevant studies. Study design criteria for evaluation in this review were: published systematic reviews and RCTs in any language, containing more than 20 individuals of whom more than 80% were followed up. There was no minimum length of follow-up required to include studies. We excluded all studies described as “open”, “open label”, or not blinded, unless blinding was impossible. In addition, we use a regular surveillance protocol to capture harms alerts from organisations such as the FDA and the UK Medicines and Healthcare products Regulatory Agency (MHRA), which

are added to the review as required. The authors also hand-searched reference lists of non-systematic reviews and studies obtained from the initial search, and recent issues of key journals. We found several systematic reviews that assessed the same RCTs in relation to different treatment options. When presenting comparative data regarding an option, we have reported the data from the review that presented the most data on that option. We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 22).

QUESTION What are the effects of medical treatments for menorrhagia?

OPTION NSAIDS

Mean menstrual blood loss
Compared with placebo NSAIDs are more effective at reducing menstrual blood loss (moderate-quality evidence).

Comparing different NSAIDs Different NSAIDs may be equally effective at reducing mean menstrual blood loss, based on a comparison between mefenamic acid and naproxen (low-quality evidence).

Compared with tranexamic acid NSAIDs may be less effective at reducing mean blood loss (very low-quality evidence).

Compared with etamsylate NSAIDs may be more effective at reducing mean blood loss (very low-quality evidence).

Compared with danazol NSAIDs are less effective at reducing mean blood loss (moderate-quality evidence).

Compared with combined oral contraceptives NSAIDs and oral contraceptives may be equally effective at reducing mean blood loss (moderate-quality evidence).

Compared with oral progestogens (luteal phase) NSAIDs and oral progestogens given in the luteal phase are equally effective at reducing mean blood loss (moderate-quality evidence).

Compared with progestogen-releasing IUD We don't know how effective NSAIDs are at reducing mean blood loss compared with progestogen-releasing IUD (very low-quality evidence).

Adverse effects
NSAIDs have fewer adverse effects than danazol.

Note
We found no clinically important results about the effects of NSAIDs compared with gonadorelin analogues.

For GRADE evaluation of interventions for menorrhagia, see table, p 22 .

Benefits:

NSAIDs versus placebo:
We found one systematic review (search date 1996, 12 RCTs, 313 women) comparing NSAIDs (mefenamic acid, naproxen, meclofenamic acid, ibuprofen, and diclofenac) versus placebo. [3] Treatment was taken only during menstruation, and doses varied depending on the drug used. The review found that NSAIDs significantly reduced mean menstrual blood loss compared with placebo (WMD for blood loss for all NSAIDs *v* placebo –35 mL, 95% CI –43 mL to –27 mL).

NSAIDs versus each other:
We found one systematic review (search date 2001, 2 RCTs, 61 women), which found no significant difference in menstrual blood loss between mefenamic acid and naproxen (WMD for blood loss +21.0 mL, 95% CI –5.9 mL to +47.9 mL; see comment below). [12]

NSAIDs versus tranexamic acid:
See benefits of tranexamic acid, p 4 .

NSAIDs versus etamsylate:
See benefits of etamsylate, p 6 .

NSAIDs versus danazol:
We found two systematic reviews (search dates 2001), both of which identified the same three RCTs (79 women). [12] [13] The first review found that NSAIDs were significantly less effective than danazol in reducing menstrual blood loss (WMD for blood loss 45.1 mL, 95% CI 18.7 mL to 71.4 mL; see comment below). [12]

NSAIDs versus combined oral contraceptives:
See benefits of combined oral contraceptives, p 8 .

NSAIDs versus oral progestogens (luteal phase):
We found one systematic review (search date 2001, 2 RCTs, 48 women), which found no significant difference in menstrual blood loss between NSAIDs and oral progestogens given in the luteal phase (WMD for blood loss –23.0 mL, 95% CI –46.6 mL to +0.625 mL). [12]

NSAIDs versus progestogen-releasing IUD:
See benefits of intrauterine progestogens, p 10 .

NSAIDs versus gonadorelin analogues:
We found no RCTs.

Harms:

The reviews found that commonly reported adverse effects included headaches, and gastrointestinal disturbances such as indigestion, nausea, vomiting, and diarrhoea. [3] [12] These occurred in at least 50% of women taking NSAIDs in the RCTs that reported data on adverse effects, but similar levels of adverse effects were found in placebo cycles (see review on NSAIDs).

Comment:

The comparisons of NSAIDs versus other drugs may have lacked power to exclude clinically important differences between treatments. [12] Both reviews comparing NSAIDs versus danazol found that NSAIDs were less effective than danazol in reducing blood loss, but the second review [13] did not perform a meta-analysis for this comparison.

Clinical guide:
NSAIDs have the additional benefit of relieving dysmenorrhoea (see review on dysmenorrhoea).

OPTION TRANEXAMIC ACID

Mean menstrual blood loss
Compared with placebo Tranexamic acid may be more effective at reducing blood loss (low-quality evidence).

Compared with NSAIDs Tranexamic acid may be more effective at reducing blood loss (very low-quality evidence).

Compared with etamsylate Tranexamic acid may be more effective at reducing blood loss (very low-quality evidence).

Compared with oral progestogens (luteal phase) Tranexamic acid may be more effective at reducing blood loss (low-quality evidence).

Compared with endometrial resection Tranexamic acid may be less effective at reducing menstrual blood loss at 4 months and 2 years (low-quality evidence).

Adverse effects
Tranexamic acid may increase the proportion of women with adverse effects over 4 months compared with endometrial resection. Adverse effects of tranexamic acid include leg cramps and nausea, which occur in about a third of women using this drug.

Note
We found no clinically important information about the effects of tranexamic acid compared with danazol, combined oral contraceptives, or gonadorelin analogues.

For GRADE evaluation of interventions for menorrhagia, see table, p 22 .

Benefits:

Tranexamic acid versus placebo:
We found two systematic reviews. [3] [14] The first review (search date 1996, 5 RCTs, 153 women) found that tranexamic acid (250–500 mg 4 times daily during menstruation) significantly reduced mean menstrual blood loss compared with placebo (WMD –52 mL; other results and significance presented graphically). [3] Few RCTs in the review measured patient satisfaction. The second review (search date 1997, 7 RCTs) identified two RCTs comparing tranexamic acid (1 g 4 times daily) or a prodrug of tranexamic acid (Kabi 2161; 1.2 g twice daily) versus placebo. [14] It found that either active drug significantly reduced mean menstrual blood loss compared with placebo (WMD –94 mL, 95% CI –151 mL to –37 mL). One of the RCTs identified by the second review found limited evidence from indirect comparisons that tranexamic acid significantly reduced limitations in social activities compared with placebo, and increased the proportion of women with improved sex life (proportion of women who reported reduced limitation in social activities when taking tranexamic acid compared with when taking placebo: 67%, reported as significant, CI not reported; proportion reporting improved sex life when taking tranexamic acid compared with when taking placebo: 46% with tranexamic acid; P = 0.029). [15]

Tranexamic acid versus NSAIDs:
We found three systematic reviews (search date 1997, [14] search date 1996, [3] search date not reported [16]). Two of the reviews [3] [14] identified the same RCT (49 women) comparing tranexamic acid versus mefenamic acid. The RCT found that tranexamic acid significantly reduced mean menstrual blood loss compared with mefenamic acid (WMD –73 mL, 95% CI –123 mL to –23 mL). [14] The second review [3] identified two further RCTs comparing tranexamic acid versus flurbiprofen (15 women) or diclofenac (19 women). [3] Both RCTs found that tranexamic acid improved outcomes compared with flurbiprofen or diclofenac. The third review [16] identified one RCT [17] (81 women) comparing three interventions: tranexamic acid, mefenamic acid, and etamsylate (see comment below). [16] The RCT found that tranexamic acid significantly reduced mean menstrual blood loss compared with mefenamic acid (WMD –56 mL, 95% CI –90 mL to –2 mL).

Tranexamic acid versus etamsylate:
We found two systematic reviews (search date 1996, [3] search date not reported [16]) that identified the same RCT (81 women). [17] The RCT compared three interventions: tranexamic acid, etamsylate, and mefenamic acid (see comment below). It found that tranexamic acid significantly reduced mean menstrual blood loss compared with etamsylate (WMD –97 mL, 95% CI –140 mL to –54 mL). [17]

Tranexamic acid versus danazol:
We found no RCTs.

Tranexamic acid versus combined oral contraceptives:
We found no RCTs.

Tranexamic acid versus oral progestogens (luteal phase):
We found three systematic reviews (search date 1996, [3] search date 1997, [14] search date 2003 [18]). All the reviews identified the same single RCT [15] (46 women). The RCT did not compare the difference in menstrual blood loss between groups directly. [15] One of the reviews performed an analysis comparing tranexamic acid versus norethisterone directly. [14] It found that tranexamic acid significantly reduced mean menstrual blood loss compared with norethisterone (WMD –111 mL, 95% CI –179 mL to –44 mL). [14] We found one subsequent RCT (100 women with dysfunctional uterine bleeding), which compared tranexamic acid (500 mg 4 times daily for 5 days during menstruation) with medroxyprogesterone acetate (10 mg twice daily from day 5 to day 25 of the cycle). [19] A total of 80 women finished the 3-month treatment period. Menstural blood loss before and after treatment was measured with a pictorial blood loss assessment chart scale (PBAC). However the RCT did not directly compare differences between groups, but only reported baseline changes in menstrual blood loss. The RCT found that both treatments significantly reduced menstrual blood loss from baseline at 3 months (PBAC scale: 356.9 pre-treatment to 141.6 post-treatment with tranexamic acid, 60.3% reduction, P less than 0.005; 370.9 pre-treatment to 156.6 post-treatment with medroxyprogeterone acetate, 57.7% reduction, P less than 0.005). [19]

Tranexamic acid versus intrauterine progestogens:
See benefits of intrauterine progestogens, p 10 .

Tranexamic acid versus gonadorelin analogues:
We found no RCTs.

Tranexamic acid versus endometrial destruction:
See benefits of endometrial destruction, p 14 .

Harms:

Nausea and leg cramps occur in a third of women taking tranexamic acid. Isolated case reports have suggested a risk of thromboembolism associated with tranexamic acid, but a large population-based study conducted over 19 years found no evidence that this was higher than expected in the general population. [20]

Tranexamic acid versus placebo or other drugs:
One systematic review (search date 1997) found no increase in gastrointestinal adverse effects compared with either placebo or other drugs. [14] The subsequent RCT reported that 8/49 (16%) of women in the tranexamic-acid group suffered from adverse effects: one allergic reaction, three headaches, three gastrointestinal upsets, and one woman with giddiness. [19]

Tranexamic acid versus endometrial destruction:
See harms of endometrial destruction, p 14 .

Comment:

The RCT comparing tranexamic acid, etamsylate, and mefenamic acid reported that 27% of women withdrew from the study before its end, and made no adjustment for the multiple treatment comparisons involved. [17]

Clinical guide:
Unlike NSAIDs, tranexamic acid has no effect on dysmenorrhoea.

OPTION ETAMSYLATE

Mean menstrual blood loss
Compared with NSAIDs Etamsylate may be less effective at reducing blood loss (very low-quality evidence).

Compared with tranexamic acid Etamsylate may be less effective at reducing blood loss (very low-quality evidence).

Note
We found no clinically important results about the effects of etamsylate compared with danazol, combined oral contraceptives, oral progestogens, intrauterine progestogens, or gonadorelin analogues.

For GRADE evaluation of interventions for menorrhagia, **see table, p 22 .**

Benefits:

We found one systematic review (search date not reported, 4 RCTs) of etamsylate. [16] The results were presented as a comparison versus baseline rather than as direct comparisons of etamsylate versus placebo or other drugs. The review found that etamsylate achieved an overall reduction in menstrual blood loss compared with baseline of 13% (95% CI 11% to 15%), which may not be clinically important. [16]

Etamsylate versus NSAIDs:
The review [16] identified one RCT (double blind, 81 women; see comment below) comparing three treatments: etamsylate, tranexamic acid, and mefenamic acid. [17] The RCT found that etamsylate was significantly less effective in reducing mean menstrual blood loss compared with mefenamic acid (WMD –51 mL, 95% CI –96 mL to –6 mL; see comments below).

Etamsylate versus tranexamic acid:
See benefits of tranexamic acid, p 4 .

Etamsylate versus other drugs:
We found no RCTs.

Harms:

The review found no significant difference between different drug regimens in the rate of adverse effects (nausea, headaches, and dizziness), and these adverse effects seldom caused women to withdraw from studies. [16]

Comment:

The RCT comparing tranexamic acid, etamsylate, and mefenamic acid reported that 27% of women withdrew from the study before its completion, and made no adjustment for the multiple treatment comparisons involved. [17]

OPTION DANAZOL

Mean menstrual blood loss
Compared with placebo Danazol may be more effective at reducing blood loss (very low-quality evidence).

Compared with NSAIDs Danazol is more effective at reducing mean blood loss (moderate-quality evidence).

Compared with the combined oral contraceptive pill We don't know how effective danazol is at reducing mean blood loss compared with the combined oral contraceptive pill (moderate-quality evidence).

Compared with oral progestogens (luteal phase) Danazol is more effective than oral progestogens in the luteal phase at reducing blood loss (moderate-quality evidence).

Compared with progestogen-releasing IUD We don't know how effective danazol is compared with progestogen-releasing IUDs at reducing mean blood loss (very low-quality evidence).

Compared with endometrial ablation Danazol may be less effective at reducing blood loss at 4 months and at 2 years (low-quality evidence).

Adverse effects
Danazol has more adverse effects compared with NSAIDs, oral progestogens, or endometrial ablation.

Note
We found no clinically important results about the effects of danazol compared with tranexamic acid or gonadorelin analogues.

For GRADE evaluation of interventions for menorrhagia, see table, p 22 .

Benefits:

Danazol versus placebo:
We found two systematic reviews (search date 2007, [13] 1 RCT, 66 women; search date 1996, [3] 3 RCTs, 127 women) comparing danazol versus placebo. The RCT identified by the first review did not compare danazol versus placebo directly, but reported blood-loss scores within each group before and after treatment. It found that danazol significantly improved blood-loss scores from baseline, whereas placebo had no significant effect at 3 months. [13] However, it is unclear how this result was calculated, as blood-loss scores and significance assessments were not reported. The second review found that danazol (200 mg/day continuously for 2–3 months) significantly reduced mean menstrual blood loss compared with placebo (WMD –108 mL; CI presented graphically; see comment below). [3]

Danazol versus NSAIDs:
See benefits of NSAIDs, p 3 .

Danazol versus tranexamic acid:
We found no RCTs.

Danazol versus etamsylate:
We found no RCTs.

Danazol versus combined oral contraceptives:
See benefits of combined oral contraceptives, p 8 .

Danazol versus oral progestogens (luteal phase):
See benefits of oral progestogens in luteal phase, p 8 .

Danazol versus intrauterine progestogens:
See benefits of intrauterine progestogens, p 10 .

Different regimens:
We found one systematic review (search date 2007), which included two small RCTs comparing different danazol regimens: standard dose danazol (200 mg/day), lower dose danazol (100 mg/day), and a reducing-dose regimen. [13] It found no significant difference in blood loss, frequency of adverse events, or duration of menstruation when a dose of 200 mg daily was compared with a reducing-dose regimen (WMD for mean menstrual blood loss +33.5 mL, 95% CI –32.4 mL to +99.4 mL; OR for proportion of women reporting adverse events 1.13, 95% CI 0.14 to 9.07; WMD for duration of menstruation +1.3 days, 95% CI –0.76 days to +3.36 days).

Danazol versus endometrial destruction:
See benefits of endometrial destruction, p 14 .

Harms:

Danazol versus placebo:
RCTs included in the first review reported that danazol may be associated with adverse effects such as: weight gain; androgenic effects such as acne, seborrhoea, hirsutism, and voice changes; and general complaints including irritability, musculoskeletal pains, and tiredness. [13] Hot flushes and breast atrophy can sometimes occur. Most of these adverse effects are reversible on stopping treatment (see harms of hormonal treatments in review on endometriosis, and harms of danazol in review on breast pain). Women using danazol may be advised to use barrier methods of contraception, because of potential virilisation of the fetus if pregnancy occurs during treatment with this drug.

Danazol versus NSAIDs:
One RCT (40 women) identified by the first review found that adverse effects, including musculoskeletal pains, dizziness, flushes, acne, behavioural changes, tiredness, and hirsutism, were significantly more frequent with danazol than with mefenamic acid (OR 7.0, 95% CI 1.7 to 28.2). [13] However, the RCT found no significant difference in adherence to treatment (OR 1.11, 95% CI 0.32 to 3.90).

Danazol versus oral progestogens (luteal phase):
See harms of oral progestogens in luteal phase, p 8 .

Danazol versus endometrial destruction:
See harms of endometrial destruction, p 14 .

Comment: **Danazol versus placebo:**
The second systematic review comparing danazol versus placebo had less-rigorous inclusion criteria, and included two RCTs excluded by the first review. [3]

OPTION CONTRACEPTIVES (COMBINED ORAL)

Mean menstrual blood loss
Compared with NSAIDs We don't know how effective combined oral contraceptives are at reducing mean blood loss compared with NSAIDs (moderate-quality evidence).

Compared with danazol We don't know how effective combined oral contraceptives are at reducing mean blood loss compared with danazol (moderate-quality evidence).

Compared with endometrial resection Oral contraceptives may be less effective at reducing menstrual blood loss at 4 months and at 2 years (low-quality evidence).

Note
We found no clinically important results about the effects of combined oral contraceptives compared with other drugs.

For GRADE evaluation of interventions for menorrhagia, see table, p 22 .

Benefits: **Combined oral contraceptives versus placebo:**
We found no RCTs.

Combined oral contraceptives versus NSAIDs or danazol:
We found three systematic reviews (search dates 2001, [12] [13] search date 1997 [21]), all of which identified the same small RCT (38 women) comparing four interventions: a combined oral contraceptive, mefenamic acid, naproxen, and danazol (doses not reported). It found no significant difference in menstrual blood loss between any of the treatments, but was too small to rule out a clinically important difference (WMD for oral contraceptive *v* mefenamic acid: –17.5 mL, 95% CI –22.5 mL to +47.5 mL; WMD for oral contraceptive *v* naproxen: +8.37 mL, 95% CI –27.3 mL to +44.0 mL; WMD for oral contraceptive *v* danazol: +19.3 mL, 95% CI –24.47 mL to +63.01 mL).

Combined oral contraceptives versus other drugs:
We found no RCTs.

Combined oral contraceptives versus endometrial destruction:
See benefits of endometrial destruction, p 14 .

Harms: Minor adverse effects are common, and include nausea, headache, breast tenderness, changes in body weight, hypertension, changes in libido. Contraceptives can also cause depression.

Combined oral contraceptives versus endometrial destruction:
See harms of endometrial destruction, p 14 .

Comment: One non-RCT (164 women) found that a 50 mg oral contraceptive pill led to a 53% reduction in menstrual blood loss from baseline. [22] Two longitudinal case control studies found that women taking the contraceptive pill were less likely than those not taking the pill to experience heavy menstrual bleeding or anaemia. [23] [24]

OPTION PROGESTOGENS (ORAL) IN LUTEAL PHASE

Mean menstrual blood loss
Compared with NSAIDs Oral progestogens given in the luteal phase and NSAIDs may be equally effective at reducing blood loss (moderate-quality evidence).

Compared with danazol Oral progestogens given in the luteal phase are less effective at reducing blood loss (moderate-quality evidence).

Compared with tranexamic acid Oral progestogens given in the luteal phase may be less effective at reducing blood loss (low-quality evidence).

Compared with endometrial resection Oral progestogens given in the luteal phase may be less effective at reducing blood loss at 4 months and at 2 years (low-quality evidence).

Note
We found no direct information about whether oral progestogens are better than no active treatment.

For GRADE evaluation of interventions for menorrhagia, see table, p 22 .

Benefits:

Progestogens (oral) in the luteal phase versus placebo:
We found no RCTs.

Progestogens (oral) in the luteal phase versus NSAIDs:
See benefits of NSAIDs, p 3 .

Progestogens (oral) in the luteal phase versus tranexamic acid:
See benefits of tranexamic acid, p 4 .

Progestogens (oral) in the luteal phase versus etamsylate:
We found no RCTs.

Progestogens (oral) in the luteal phase versus danazol:
We found one systematic review (search date not reported; 2 RCTs, 51 women), which found that oral progestogens were significantly less effective compared with danazol at reducing menstrual blood loss (WMD –56 mL, 95% CI –96 mL to –15 mL). [18] The review also found that luteal phase oral progestogens significantly increased the proportion of women who reported a greater self-assessed menstrual blood loss after treatment compared with danazol (2 RCTs: 19/28 [68%] with luteal phase progestogens *v* 8/26 [31%] with danazol; RR 2.2, 95% CI 1.2 to 4.1; NNH 2, 95% CI 1 to 9).

Progestogens (oral) in the luteal phase versus combined oral contraceptives:
We found no RCTs.

Progestogens (oral) in the luteal phase versus intrauterine progestogens:
See benefits of intrauterine progestogens, p 10 .

Progestogens (oral) in the luteal phase versus endometrial destruction:
See benefits of endometrial destruction, p 14 . See benefits of oral progestogens (longer cycle), p 10 .

Harms:

The review found that adverse effects (including headache, breast tenderness, premenstrual symptoms, and gastrointestinal disturbances) were reported in between a third and a half of the women taking oral progestogens. [18]

Progestogens (oral) in the luteal phase versus placebo:
We found no RCTs.

Progestogens (oral) in the luteal phase versus NSAIDs:
See harms of NSAIDs, p 3 .

Progestogens (oral) in the luteal phase versus tranexamic acid:
See harms of tranexamic acid, p 4 .

Progestogens (oral) in the luteal phase versus etamsylate:
We found no RCTs.

Progestogens (oral) in the luteal phase versus danazol:
The review found that oral progestogens were associated with significantly fewer adverse effects compared with danazol (OR 4.05, 95% CI 1.60 to 10.20). [18]

Progestogens (oral) in the luteal phase versus combined oral contraceptives:
We found no RCTs.

Progestogens (oral) in the luteal phase versus intrauterine progestogens:
See harms of intrauterine progestogens, p 10 .

Progestogens (oral) in the luteal phase versus endometrial destruction:
See harms of endometrial destruction, p 14 . See harms of oral progestogens (longer cycle), p 10 .

Comment:

None.

OPTION PROGESTOGENS (ORAL) FOR LONGER CYCLE

Mean menstrual blood loss
Compared with progestogen-releasing IUDs We don't know how oral progestogens compare with progestogen-releasing IUDs (very low-quality evidence).

Adverse effects
Half of the women taking oral progestogens may feel unwell.

Note
We found no direct information about whether oral progestogens are better than no active treatment.

For GRADE evaluation of interventions for menorrhagia, see table, p 22 .

Benefits:

Progestogens (oral) for longer cycle versus placebo:
We found no RCTs.

Progestogens (oral) for longer cycle versus progestogen-releasing IUD:
See benefits of intrauterine progestogens, p 10 .

Harms:

Progestogens (oral) for longer cycle versus progestogen-releasing IUD:
See harms of intrauterine progestogens, p 10 .

Comment: None.

OPTION INTRAUTERINE PROGESTOGENS

Mean menstrual blood loss
Compared with other drugs We don't know how progestogen-releasing IUDs compare with other drugs (very low-quality evidence).

Compared with endometrial ablation Intrauterine progestogens may be less effective at reducing pictorial blood loss assessment (PBAC) scores (low-quality evidence).

Quality of life
Compared with hysterectomy progestogen-releasing IUDs and hysterectomy are equally effective at improving quality of live and patient satisfaction at 1 year (moderate-quality evidence).

Adverse effects
The risk of serious adverse effects is lower with intrauterine progestogens compared with hysterectomy.

Note
We found no direct information about whether intrauterine progestogens are better than no active treatment.

For GRADE evaluation of interventions for menorrhagia, see table, p 22 .

Benefits:

We found no systematic review or RCTs comparing intrauterine progestogens versus placebo.

We found three systematic reviews (search date not reported, 1 RCT; [18] search date 2005, 10 RCTs; [25] search date 2005, 8 RCTs; [26] with 6 RCTs common to all) and two subsequent RCTs [27] [28] comparing intrauterine progestogens versus other drugs or versus surgical treatment.

Progestogen-releasing IUD versus other drugs:
The reviews identified four RCTs. The first RCT (30 women) compared four interventions: a progesterone-releasing IUD (65 µg/day), an NSAID (mefenamic acid), danazol, and a long-cycle oral progestogen (norethisterone). [25] The RCT did not compare treatments versus each other, and menstrual blood loss at baseline was not comparable between groups. The groups in this study were small, but all treatments reduced menstrual blood loss compared with baseline values. [25] In the second RCT (44 women) comparing the progestogen-releasing IUD versus long-cycle oral progestogen (norethisterone), there was a marked reduction in median blood loss from baseline in both groups, although there was no significant difference between groups in this median reduction (median reduction in menstrual blood loss: 104 mL with progestogen-releasing IUD *v* 94 mL with oral norethisterone; P = 0.56). [25] [18] A significantly greater proportion of women in the progestogen-releasing IUD group were willing to continue with their treatment compared with the long-cycle oral-progestogen group (77% *v* 22%; P value not reported). In the third RCT (51 women) comparing the levonorgestrol IUD with mefenamic acid, reductions in menstrual blood loss, total menstrual fluid loss, and pictorial blood loss assessment chart (PBAC) scores after six cycles were significantly

greater with the levonorgestrol IUD compared with mefenamic acid (figures not provided). In the fourth RCT (56 women) that randomised women on a waiting list for hysterectomy to either a levonorgestrol IUD or their existing medical treatment (not defined), quality-of-life scores were significantly higher in the levonorgestrol IUD group, and women in this group were significantly more likely to cancel their hysterectomy after 6 months of treatment. [25] However, details of the existing medical treatments were not reported by the RCT. [25]

Progestogen-releasing IUD versus surgery:
The systematic reviews identified six RCTs comparing a progestogen-releasing IUD versus transcervical endometrial resection (2 RCTs), thermal balloon ablation (3 RCTs), or hysterectomy (1 RCT). [25] [26] The reviews had similar findings. When both types of endometrial ablation were compared with levonorgestrol IUD, endometrial ablation was significantly more likely to lead to a successful treatment (as measured by a pictorial blood loss assessment (PBAC) score less than 75) at 12 months compared with levonorgestrol IUD (3 RCTs, 210 women, OR 0.28, 95% CI 0.14 to 0.58); but there was no significant difference between groups in amenorrhoea at 12, 24, or 36 months (12 months: OR 0.75, 95% CI 0.36 to 1.54; 24 months: OR 1.3, 95% CI 0.48 to 3.53; 36 months: OR 0.6, 95% CI 0.14 to 2.57). [25] The review found no significant difference between treatments in the proportion of women satisfied with treatment (2 RCTs,136 women, OR 0.61, 95% CI 0.26 to 1.46), or in the likelihood of needing further surgical treatment for their heavy bleeding (2 RCTs, 110 women, OR 1.33, 95% CI 0.47 to 3.81). [25] When compared with hysterectomy, the health-related quality-of-life scores had improved in both groups after 1 year, and patient satisfaction was high, and not significantly different between groups (1 RCT, 232 women, OR 1.17, 95% CI 0.41 to 3.34). [25] However, after 12 months, the levonorgestrol IUD was in place in only 68% of the women, and 20% had undergone hysterectomy. [25] After 5 years, the levonorgestrol IUD was in place in only 48% of the women (8 of whom had had a replacement IUD), 42% had undergone hysterectomy, and one woman had undergone endometrial ablation. [25] After 1 year, no women with hysterectomy had any menstrual bleeding. [26] The review found that haemoglobin levels after 12 months' follow-up were significantly higher in the group of women with a levonorgestrol IUD (1 RCT, 228 women, WMD 3 units, 95% CI 0.1 to 5.9 units). [25] The first subsequent RCT (44 women with menorrhagia) compared thermal balloon ablation versus a levonorgestrol IUD. [27] The RCT found that all women in the thermal balloon ablation group had decreased blood flow at 1 year, whereas 5/18 (33%) of the women in the levonorgestrol IUD group remained menorrhagic (statistical analysis between groups not reported). It found that haemoglobin levels improved in both groups, but the mean haemoglobin was significantly higher with thermal balloon ablation compared with IUD (12.6 g/dL with ablation *v* 10.3 g/dL with IUD; P = 0.018), and iron deficiency persisted in two women with thermal balloon ablation, and in nine women with the levonorgestrol IUD (13% *v* 50%; P = 0.026). [27] Of 44 women initially randomised in the RCT, the results are based on 33 (75%) women who actually received the allocated treatment, the rest either having refused treatment, defaulted, had an endometrial polyp or submucosal fibroid, or had a large uterine cavity. The second subsequent RCT (63 women with PBAC scores greater than 120) compared a progestogen-releasing IUD with thermal balloon ablation at 12-month follow-up. [28] The RCT found that the progestogen-releasing IUD significantly reduced PBAC scores compared with thermal balloon ablation (median PBAC score 26 [range 0–68] with progestogen-releasing IUD *v* 62 [range 0–142] with thermal balloon ablation; P less than 0.001) at 12 months. However, at 24 months, more women from the progestogen-releasing IUD group underwent hysterectomy compared with the thermal balloon ablation group (8/33 [21%] with progestogen-releasing IUD *v* 4/30 [13%] with thermal balloon ablation, P greater than 0.05) owing to either continued heavy bleeding or frequent light bleeding. [28]

Harms:

There are concerns that progestogen-releasing IUDs increase rates of ectopic pregnancy, although the RCT identified by the first systematic review did not report this adverse effect. [25] RCTs looking at the contraceptive effect of progestogen-releasing IUD in younger women found that, during the first few months of use, the total number of bleeding days (including menstrual bleeding, intermenstrual bleeding, and spotting) increased in most women. [29] However, most women bled lightly for only 1 day a month, and about 15% were amenorrhoeic after 12 months. [30]

Progestogen-releasing IUD versus other drugs:
The first systematic review found that most adverse effects in women using a progestogen-releasing IUD were typical of progestogens (bloating, weight gain, and breast tenderness). [25] One RCT identified by the reviews found that a progestogen-releasing IUD significantly increased the proportion of women who were amenorrhoeic after 3 months of treatment compared with norethisterone (32% with a progestogen-releasing IUD *v* 0% with norethisterone). [25] The RCT also found that 56% of women taking oral progestogens did not feel "well" or "very well" and only 22% elected to continue treatment with oral progestogens after the 3 months of the study. [18]

Progestogen-releasing IUD versus surgery:
The second systematic review found that surgery was significantly less likely to cause adverse effects compared with the progestogen-releasing IUD at 1 year (2 RCTs, 141 women; OR 0.24, 95% CI

0.11 to 0.49). [26] However, the adverse effects in the RCT that assessed hysterectomy were much more serious than those reported in the progestogen-releasing IUD group. Adverse effects in women having hysterectomy included bladder and bowel perforation, vesicovaginal fistula, urinary retention, intestinal obstruction, postoperative bleeding, severe postoperative pain, peritonitis, fever, wound infection, wound rupture, and infected pelvic haematoma. In women using a progestogen-releasing IUD, the adverse effects were failure of insertion, intermenstrual bleeding, hormonal symptoms, and expulsion. Significantly more women developed ovarian cysts in the levonorgestrol IUD group compared with women undergoing hysterectomy, both at 6 and 12 months (at 6 months: 1 RCT, 198 women, OR 4.93, 95% CI 1.96 to12.39; at 12 months: 1 RCT, 180 women, OR 3.10, 95% CI 1.33 to 7.24). [25] The second subsequent RCT reported the expulsion rate for the progestogen-releasing IUD to be 6% over 2 years. [28]

Comment: Long-term follow-up in women with menorrhagia is required to assess continuation rates, satisfaction, and whether surgical treatment is avoided or just postponed. The trials that considered long-term bleeding patterns were mainly in women under 40 years of age. It is not yet known whether these results can be extrapolated to older women with menorrhagia.

OPTION GONADORELIN ANALOGUES

We found no direct information about the effects of gonadorelin analogues in women with menorrhagia.

For GRADE evaluation of interventions for menorrhagia, **see table, p 22 .**

Benefits: We found no systematic review or RCTs.

Harms: We found no RCTs (see comment below).

Comment: **Clinical guide:**
A few small, non-randomised studies have looked at gonadorelin analogues in menorrhagia. Others have examined their effects in women with fibroids, or on thinning the endometrium before ablation or resection. Adverse effects of gonadorelin analogues are mainly due to reduced oestrogens. Hormone replacement to counteract hypo-oestrogenism has been tried to reduce hot flushes, with limited success. [31] Bone demineralisation occurs in most women after 6 months of treatment, but is reversible after treatment is stopped. [32] Contraception while using these drugs is not guaranteed. [33]

QUESTION What are the effects of surgical treatments for menorrhagia?

OPTION DILATATION AND CURETTAGE

We found no direct information about the effects of dilatation and curettage in women with menorrhagia.

For GRADE evaluation of interventions for menorrhagia, **see table, p 22 .**

Benefits: We found no systematic review or RCTs.

Harms: Observational evidence suggests that dilatation and curettage may cause adverse effects including uterine perforation and cervical laceration, as well as the usual risks of general anaesthesia. [34]

Comment: **Clinical guide:**
Dilatation and curettage still plays a role in the investigation of menorrhagia. We found one uncontrolled cohort study (50 women) that measured blood loss before and after dilatation and curettage. [35] It found a reduction in menstrual blood loss immediately after the procedure, but losses returned to previous levels or higher by the second menstrual period.

OPTION HYSTERECTOMY

Mean menstrual blood loss
Compared with endometrial destruction Hysterectomy is more effective at reducing both menstrual blood loss and the proportion of women requiring further operations (high-quality evidence).

Subtotal compared with total hysterectomy Subtotal hysterectomy is more likely to result in ongoing cyclical bleeding in women with benign gynaecological disease including menorrhagia (moderate-quality evidence).

Quality of life

Compared with progestogen-releasing IUD Hysterectomy and progestogen-releasing IUDs are equally effective at 1 year at improving quality of life and patient satisfaction (moderate-quality evidence).

Postoperative recovery
Abdominal compared with laparoscopic or vaginal hysterectomy Postoperative recovery is faster with vaginal or laparoscopic hysterectomy in women with benign gynaecological disease including menorrhagia (moderate-quality evidence).

Adverse effects
Compared with endometrial destruction Hysterectomy is associated with a higher risk of intraoperative and postoperative complications (moderate-quality evidence).

Subtotal compared with total hysterectomy Complication rates are similar for subtotal compared with total hysterectomy (moderate-quality evidence).

Abdominal compared with vaginal hysterectomy Postoperative mortality may be greater with abdominal hsyterectomy (very low-quality evidence).

Abdominal compared with vaginal and laparoscopic hysterectomy Complications of surgery are greater with abdominal or laparoscopic hysterectomy (moderate-quality evidence).

Compared with progestogen-releasing IUD Serious adverse effects are more likely after hysterectomy (moderate-quality evidence).

For GRADE evaluation of interventions for menorrhagia, see table, p 22 .

Benefits:

Hysterectomy versus intrauterine progestogens:
See benefits of intrauterine progestogens, p 10 .

Hysterectomy versus endometrial destruction:
We found two systematic reviews (search date 1996 [3] and search date not reported [36]), and one subsequent RCT. [37] Both reviews identified the same five RCTs (708 premenopausal women) comparing hysterectomy versus endometrial destruction (transcervical endometrial resection or laser ablation). [3] [36] The reviews found that hysterectomy significantly reduced menstrual blood loss, and significantly increased the proportion of women with a reduction in menstrual blood loss after 12 months (3 RCTs; 220/220 [100%] with hysterectomy *v* 191/220 [87%] with endometrial destruction; NNT 8, 95% CI 6 to 13). However, the reviews reported that the differences in reduction in blood loss between treatments seemed to narrow with longer follow-up, possibly because of re-treatment in the endometrial ablation group, or because of menopause. The reviews also found that women were more satisfied with hysterectomy than with endometrial ablation after 12 months (RR 0.93, 95% CI 0.89 to 0.99), and after 2 years (RR for being "moderately" or "very" satisfied with endometrial ablation *v* hysterectomy: 0.87, 95% CI 0.81 to 0.94). [3] [36] Two RCTs included in the reviews found no significant difference between treatments in satisfaction rates after 3 and 4 years. The reviews found that endometrial destruction significantly increased the proportion of women requiring repeat surgery compared with hysterectomy (after 12 months, 5 RCTs: 1/320 [1%] with hysterectomy *v* 54/386 [14%] with endometrial destruction; RR 44.8, 95% CI 6.2 to 321.8; after 4 years, 1 RCT: 1/95 [1%] with hysterectomy *v* 39/102 [38%] with endometrial destruction; RR 36.3, 95% CI 5.1 to 259.2). They found that, compared with hysterectomy, endometrial destruction significantly reduced the duration of surgery (–23 minutes), duration of hospital stay (–5 days), and time to return to work (–4.5 weeks). The subsequent RCT (181 women) compared laparoscopic supracervical hysterectomy versus transcervical endometrial resection. [37] It found no significant difference between hysterectomy and endometrial resection in intraoperative blood loss, discharge home, and return to normal activity (P value reported as non-significant for all outcomes, no further data reported). It found that hysterectomy significantly increased pain scores at discharge (P less than 0.01), and duration of surgery compared with endometrial resection (mean 71.5 minutes with hysterectomy *v* 41.7 minutes with endometrial resection; P less than 0.01). However, it found that, at 2-year follow-up, endometrial resection significantly increased bleeding recurrence and need for further surgery compared with hysterectomy (bleeding recurrence: 0/92 [0%] with hysterectomy *v* 11/89 [12%] with endometrial resection; P less than 0.01; need for further surgery: 1/92 [1%] with hysterectomy *v* 12/89 [13%] with endometrial resection; P less than 0.01). There was an improvement in all quality-of-life scores after surgery in both groups: general health and social function significantly improved with both endometrial resection and hysterectomy (P less than 0.01), and emotional role and vitality also significantly improved with hysterectomy (P less than 0.01). [37]

Different techniques for performing hysterectomy:
We found two systematic reviews comparing different surgical techniques. [38] [39] The first review (search date 2005, 3 RCTs, 733 women) compared subtotal with total abdominal hysterectomy.

[38] It included women eligible for hysterectomy for benign gynaecological conditions, mostly fibroids or heavy menstrual bleeding. However, it did not report a subgroup analysis for women with menorrhagia alone. It found that subtotal abdominal hysterectomy significantly reduced operating time and blood loss compared with total abdominal hysterectomy (operating time: 2 RCTs, 411 women, WMD 11.4 minutes, 95% CI 6.6 minutes to 16.3 minutes; blood loss: 2 RCTs, 411 women, WMD 85 mL, 95% CI 27 mL to 142 mL), but with no significant difference between groups in the rates of transfusion (2 RCTs, 411 women, OR 1.06, 95% CI 0.45 to 2.5). [38] It found that ongoing cyclical vaginal bleeding was significantly more likely with subtotal hysterectomy compared with total abdominal hysterectomy (OR 11.3, 95% CI 4.1 to 31.2). The second systematic review (search date 2004, 27 RCTs, 3643 women) compared abdominal, vaginal, and laparoscopic approaches. [39] It included women suitable for hysterectomy for benign gynaecological conditions, which also included uterine fibroids. However, it did not report a separate analysis for women with menorrhagia alone. It found that both vaginal and laparoscopic hysterectomy resulted in significantly shorter hospital stays and speedier return to normal activities compared with abdominal hysterectomy (vaginal *v* abdominal hysterectomy: duration of hospital stay, WMD 1.0 day, 95% CI 0.7 to 1.2 days; speedier return to normal activities, WMD 9.5 days, 95% CI 6.4 days to 12.6 days; laparoscopic *v* abdominal: duration of hospital stay, WMD 2 days, 95% CI 1.9 days to 2.2 days; speedier return to normal activities, WMD 13.6 days, 95% CI 11.8 days to 15.4 days). [39] It found no evidence of benefit for laparoscopic compared with vaginal hysterectomy.

Harms:

One large population-based analysis stratified by age found that mortality after hysterectomy for non-malignant conditions is about 1/2000 in women aged under 50 years. [40]

Hysterectomy versus intrauterine progestogens:
See harms of intrauterine progestogens, p 10 .

Hysterectomy versus endometrial destruction:
The reviews found that, compared with endometrial destruction, hysterectomy increased the risk of sepsis, blood transfusion, urinary retention, anaemia, pyrexia, vault and wound haematoma, and cautery of hypergranulation before hospital discharge. [3] [36] The subsequent RCT found no significant difference in intraoperative and postoperative complications between hysterectomy and endometrial resection (P value reported as non-significant, CI not reported). [37]

Different techniques for performing hysterectomy:
The systematic review comparing subtotal with total hysterectomy did not show any differences between the two procedures in the rates of urinary symptoms, bowel symptoms, or sexual dysfunction. [38] The second systematic review comparing abdominal, vaginal, and laparoscopic hysterectomy found that vaginal and laparoscopic procedures resulted in significantly fewer unspecified infections or febrile episodes compared with abdominal hysterectomy (vaginal *v* abdominal: OR 0.42, 95% CI 0.21 to 0.83: laparoscopic *v* abdominal: OR 0.65, 95% CI 0.49 to 0.87). [39] It found that laparoscopic hysterectomy did, however, involve significantly longer operating time, and resulted in significantly more urinary tract injuries compared with abdominal procedures (operating time: WMD 10.6 minutes, 95% CI 7.4 minutes to 13.8 minutes; OR 2.61, 95% CI 1.22 to 5.60). Operating time was also shown to be significantly longer with laparoscopic compared with vaginal hysterectomy, with no evidence of extra benefit (WMD 41.5 minutes, 95% CI 33.7 minutes to 49.4 minutes). One UK study of 37,928 women with benign disease [41] compared abdominal (24,772 women), vaginal (11,122 women), and laparoscopic (1154 women) hysterectomies performed during 1994 and 1995. It found an overall mortality of 0.38 per 1000 (95% CI 0.25 to 0.64 per 1000). Abdominal hysterectomy had the highest mortality, at 0.75 per 1000 (95% CI 0.31 to 1.80 per 1000), with mortality from vaginal hysterectomy reported as 0.25 per 1000 (95% CI 0.08 to 0.79 per 1000). There were no deaths in the laparoscopic hysterectomy group. However, this may be a reflection of the difference in the size of the three groups.

Comment:

None.

OPTION ENDOMETRIAL DESTRUCTION (RESECTION OR ABLATION)

Mean menstrual blood loss
Compared with intrauterine progestogens Endometrial ablation may be more effective at reducing pictorial blood loss assessment chart (PBAC) scores (low-quality evidence).

Compared with oral drugs Endometrial destruction may be more effective than tranexamic acid, danazol, oral progestogens, or combined oral contraceptives at reducing blood loss (low-quality evidence).

Compared with hysterectomy Endometrial destruction is less effective at reducing menstrual blood loss, and increases the number of women requiring further operations (high-quality evidence).

First-generation compared with second-generation techniques First- and second-generation endometrial ablation techniques are equally effective at reducing blood loss (moderate-quality evidence).

Need for further surgery
First- and second-generation techniques are equally effective at reducing the need for further surgery (high-quality evidence).

Adverse effects
Different techniques of endometrial destruction Different techniques are associated with different adverse effects (moderate-quality evidence).

Compared with hysterectomy Endometrial destruction is associated with a lower risk of intraoperative and postoperative complications (moderate-quality evidence). Recognised complications of endometrial destruction techniques include infection, haemorrhage, and uterine perforation.

For GRADE evaluation of interventions for menorrhagia, see table, p 22 .

Benefits:

Endometrial destruction (resection or ablation) versus intrauterine progestogens:
See benefits of intrauterine progestogens, p 10 .

Endometrial destruction (resection or ablation) versus other drugs:
We found one systematic review (search date 2005, 1 RCT, 187 women) comparing endometrial resection (93 women) versus tranexamic acid (22 women), danazol (15 women), combined oral contraceptives (24 women), oral progestogens (31 women), and HRT plus an NSAID (2 women). [26] It found that surgery significantly reduced menstrual blood loss at 4 months and at 2 years compared with medical treatment (at 4 months: 77/93 [83%] with endometrial resection *v* 29/93 [31%] with medical treatment; RR 2.66, 95% CI 1.94 to 3.64). [26] At 5 years' follow-up, it found no significant difference in menstrual blood loss between groups, but by then 77% of the women randomised to medical treatment had received surgery.

Endometrial destruction (resection or ablation) versus hysterectomy:
See benefits of hysterectomy, p 12 .

First-generation versus second-generation techniques:
We found one systematic review and one subsequent RCT. [42] [43] The review (search date 2004, 11 RCTs, 2040 premenopausal women) compared first-generation techniques (including hysteroscopic methods such as laser ablation, rollerball ablation, transcervical endometrial resection (TCRE), and vaporising electrode ablation) with second-generation techniques (including mostly non-hysteroscopic methods, such as thermal uterine balloon therapy, multielectrode balloon ablation, microwave endometrial ablation, Novasure endometrial ablation, and heated saline). The review found that all methods reduced menstrual blood loss compared with baseline assessment. The review found no significant difference between first- and second-generation techniques in amenorrhoea rates, hysterectomy rates, or the requirement for any additional surgery, at 1 year, 2 years, 3 years, or 5 years, although 25% of participants will have had a hysterectomy after 5 years. [42] It also found that patient satisfaction was similar between both types of techniques at 1 year, 3 years, and 5 years, but was significantly higher at 2 years in the second-generation technique group (5 RCTs, 802 women, OR 1.62, 95% CI 1.13 to 2.33, no absolute figures reported). The subsequent RCT (51 women with menorrhagia unresponsive to medical treatment) compared thermal balloon endometrial ablation with TCRE with 1-year follow-up. [43] However, the RCT did not directly compare differences between groups, but only reported baseline changes. The results of the RCT supported those of the systematic review: both treatments significantly reduced menstrual blood loss compared with baseline (median decrease in Higham score: 377, range 108 to 1300 with balloon; and 255, range –82 to 553 with TCRE, P = 0.006). [43]

First-generation techniques versus each other:
We found one systematic review (search date 2004, 4 RCTs, 605 women). [42] The review found no significant difference at 12 months between laser ablation and transcervical endometrial resection in rates of amenorrhoea or in patient satisfaction (amenorrhoea: 1 RCT, 306 women, OR 1.07, 95% CI 0.63 to 1.83; patient satisfaction: 1 RCT, 321 women, OR 0.88, 95% CI 0.43 to 1.81). The review also found no significant difference after 12 months between vaporising electrode ablation and transcervical endometrial resection in amenorrhoea/hypomenorrhoea (1 RCT, 91 women, OR 0.95, 95% CI 0.35 to 2.60), or in patient satisfaction (1 RCT, 91 women, OR 1.65, 95% CI 0.26 to 10.35). [42] One RCT included in the review (120 women with heavy dysfunctional bleeding) has published a 10-year follow-up. [44] The follow-up found no significant differences at 10 years between rollerball ablation and transcervical endometrial resection for rates of hysterectomy (no absolute figures, RR, CI, or P value reported). The follow-up found that 22% of the women who were ran-

domised had proceeded to hysterectomy in the 10 years after the initial ablation, and 94% stated that they would recommend the surgery to their best female friend. [44]

Harms:

Intraoperative complications of endometrial destruction include uterine perforation, haemorrhage, and fluid overload from the distension medium. Immediate postoperative complications include infection, haemorrhage, and, rarely, bowel injury. One large prospective survey of 10,686 women having endometrial destruction in the UK found an immediate complication rate of 4%. [45] Intraoperative emergency procedures were performed in 1%, and two procedure-related deaths occurred.

Endometrial destruction (resection or ablation) versus intrauterine progestogens:
See harms of intrauterine progestogens, p 10 .

Endometrial destruction (resection or ablation) versus other drugs:
The RCT found that endometrial resection significantly reduced the proportion of women who had adverse effects at 4 months' follow-up compared with oral medication (12/93 [13%] with endometrial resection *v* 46/93 [49%] with medical treatment; RR 0.26, 95% CI 0.15 to 0.46). [26]

Endometrial destruction (resection or ablation) versus hysterectomy:
See harms of hysterectomy, p 12 .

First-generation versus second-generation techniques:
The systematic review found that second-generation techniques significantly reduced the incidence of fluid overload, uterine perforation, cervical lacerations, and haematometra compared with first-generation techniques (fluid overload: 4 RCTs, 0/354 [0%] with second generation *v* 10/327 [3%] with first generation, OR 0.13, 95% CI 0.04 to 0.45; uterine perforation: 8 RCTs, 3/1114 [0.3%] *v* 10/771 [1.3%], OR 0.21, 95% CI 0.07 to 0.65; cervical lacerations: 8 RCTs, 2/1005 [1%] *v* 15/671 [2%], OR 0.12, 95% CI 0.05 to 0.33; haematometra: 5 RCTs, 5/673 [1%] *v* 11/460 [2%], OR 0.25, 95% CI 0.09 to 0.71). However, there was significantly more risk of nausea and vomiting and of uterine cramping with second-generation techniques (nausea and vomiting: 4 RCTs, 120/620 [20%] *v* 29/377 [8%], OR 2.29, 95% CI 1.54 to 3.40; uterine cramping: 2 RCTs, 157/408 [38%] *v* 64/193 [33%], OR 1.80, 95% CI 1.10 to 2.93). There was no significant difference between the two groups for endometritis, UTIs, hydrosalpinx, haemorrhage, fever, myometritis, pelvic inflammatory disease, pelvic abscess, cervical stenosis, severe pelvic pain, external burns, or requirement for blood transfusion. [42] The subsequent RCT reported three minor events, one case of cystitis, and one case of tranisent urinary incontinence in the thermal balloon endometrial ablation group, and one case of vaginal mycosis in the TCRE group. [43]

First-generation techniques versus each other:
The review found that the amount of fluid deficit was greater in the group undergoing transcervical endometrial resection compared with the vaporising electrode ablation group (1 RCT, WMD 258 mL, 95% CI 173.9 mL to 342.1 mL). [42] The follow-up study gave no information on adverse effects. [44]

Comment:

First-generation versus-second generation techniques:
The review found that second-generation techniques significantly reduced operating times compared with first-generation techniques (9 RCTs, 988 *v* 774 women, WMD –14.86 minutes, 95% CI –19.68 minutes to –10.05 minutes). [42] It found that operative difficulties were significantly higher in the second-generation technique group (2 RCTs, 13/166 [8%] *v* 3/167 [2%], OR 4.17, 95% CI 1.26 to 13.81), but there was no difference between groups in the proportion of abandoned procedures. Local anaesthetic rather than general anaesthetic was more likely to be used with second-generation techniques (5 RCTs, 544/893 [61%] *v* 94/490 [19%], OR 8.28, 95% CI 3.92 to 17.50), although there was significant heterogeneity in the trials when reporting this outcome. [42] Among hysteroscopic techniques, the review found that laser ablation significantly increased procedural length compared with transcervical endometrial resection (WMD 9.15 minutes, 95% CI 7.20 minutes to 11.10 minutes). When laser ablation was compared with transcervical resection of the endometrium, the rates of equipment failure and of fluid overload were significantly higher in the laser ablation group (equipment failure: OR 6.0, 95% CI 1.7 to 20.9; fluid overload: OR 5.2, 95% CI 1.5 to 18.4). [42]

First-generation techniques versus each other:
One further RCT comparing rollerball ablation versus endometrial destruction is awaiting assessment for possible inclusion in future updates of the review. [46]

QUESTION **What are the effects of endometrial thinning before endometrial destruction in treating menorrhagia?**

OPTION GONADORELIN ANALOGUES

Postoperative amenorrhoea

Compared with placebo Preoperative gonadorelin analogues (GnRHa) are more effective than placebo or no preoperative treatment at reducing postoperative moderate or heavy menstrual blood loss at 6–12 months after surgery, and at increasing amenorrhoea at 24 months after surgery (moderate-quality evidence).

Compared with danazol GnRHa and danazol are equally effective at producing postoperative amenorrhoea at 12 months (high-quality evidence).

Compared with oral progestogens We don't know how effective GnRHa are at increasing postoperative amenorrhoea compared with oral progestogens (low-quality evidence).

For GRADE evaluation of interventions for menorrhagia, see table, p 22 .

Benefits:

We found one systematic review (search date 2001, 11 RCTs, 998 women). [47]

Gonadorelin analogues (GnRHa) versus placebo or no treatment:
Eight RCTs (618 women) identified by the review compared preoperative GnRHa versus placebo or no treatment. The review found that GnRHa significantly increased the rate of postoperative amenorrhoea at 24 months, and significantly reduced the risk of continued moderate or heavy periods after 6–12 months (amenorrhoea, 2 RCTs: RR 1.62, 95% CI 1.04 to 2.52; moderate or heavy periods, 4 RCTs: RR 0.74, 95% CI 0.59 to 0.92). The review found no significant difference in patient satisfaction or in the likelihood of having further surgery.

GnRHa versus danazol:
Three RCTs (340 women) identified by the review compared GnRHa (goserelin or decapeptyl) versus danazol. The review found no significant difference in postoperative amenorrhoea at 12 months between GnRHa and danazol (RR 1.18, 95% CI 0.18 to 1.57). [47]

GnRHa versus other medical treatments:
Two RCTs included in the review (140 women) compared four interventions: preoperative GnRHa, danazol, progestogens, and no treatment. The trials were too small to allow firm conclusions to be drawn. [47]

Harms:

Gonadorelin analogues (GnRHa) versus placebo or no treatment:
The review found no significant difference in intraoperative uterine perforations between goserelin and either placebo or no treatment (2/266 [0.8%] with goserelin *v* 1/275 [0.4%] with no treatment or placebo; RR 2.01, 95% CI 0.19 to 22.67). [47]

GnRHa versus danazol:
The review found that goserelin significantly increased hot flushes, depression, and vaginal dryness, and reduced libido compared with danazol. Oily skin, hirsutism, and weight gain were significantly more common with danazol. The review also found that danazol significantly increased withdrawal due to adverse effects compared with goserelin (11/139 [8%] with danazol *v* 1/566 [1%] with goserelin; RR 44.80, 95% CI 5.83 to 344.00).

Comment:

Gonadorelin analogues (GnRHa) versus placebo or no treatment:
None of the RCTs included in the review used objective measures of postoperative menstrual blood loss. [47] Rates of withdrawal or loss to follow-up were low in all RCTs. One systematic review found that GnRHa significantly reduced both the duration of surgery and operative difficulty compared with placebo or no treatment (duration of surgery, 3 RCTs: WMD –4.8 minutes, 95% CI –6.5 minutes to –3.0 minutes; difficulty during procedure, 2 RCTs: RR 0.32, 95% CI 0.22 to 0.46). [47]

GnRHa versus danazol:
The review found that GnRHa significantly reduced the duration of surgery compared with danazol (3 RCTs: WMD –3.9 minutes, 95% CI –6.1 minutes to –1.7 minutes). It found no significant difference in operative difficulty between GnRHa and danazol (RR 0.68, 95% CI 0.31 to 1.51). [47]

OPTION DANAZOL

Postoperative amenorrhoea

Compared with placebo Danazol may be no more effective at producing postoperative amenorrhoea (low-quality evidence).

Compared with gonadorelin analogues Gonadorelin analogues and danazol are equally effective at producing post-operative amenorrhoea at 12 months (high-quality evidence).

Compared with oral progestogens We don't know how effective danazol is at producing postoperative amenorrhoea compared with oral progestogens (low-quality evidence).

For GRADE evaluation of interventions for menorrhagia, see table, p 22 .

Benefits: We found one systematic review (search date 2001, 3 RCTs, 110 women) [47] and one subsequent RCT. [48]

Danazol versus placebo:
The review [47] identified two small RCTs, and we found one subsequent RCT. [48] Both RCTs identified by the review found no significant difference in amenorrhoea at 12 and 24 months between preoperative danazol and placebo (1 RCT, 50 women: RR 1.31, 95% CI 0.82 to 2.08; 1 RCT, 20 women: RR 3.00, 95% CI 0.79 to 11.44). The subsequent RCT (132 women) found no significant difference in amenorrhoea at 1 year between preoperative danazol and placebo (129 women analysed; amenorrhoea rate: 49% with danazol *v* 52% with placebo; CI and P values not reported). [48] It found that danazol significantly reduced operating time compared with placebo (25.7 minutes with danazol *v* 33.6 minutes with placebo; P less than 0.001).

Danazol versus gonadorelin analogues:
See benefits of gonadorelin analogues, p 17 . [48]

Danazol versus other medical treatments:
Two RCTs included in the review (140 women) compared four interventions: preoperative danazol, gonadorelin analogues, progestogens, and no treatment. [47] The trials were too small to allow firm conclusions to be drawn.

Harms: **Danazol versus placebo:**
The review [47] and subsequent RCT [48] gave no information on adverse effects.

Danazol versus gonadorelin analogues:
See harms of gonadorelin analogues, p 17 .

Comment: None.

OPTION PROGESTOGENS (ORAL)

Postoperative amenorrhoea
Compared with no preoperative treatment Oral progestogens are no more effective at producing postoperative amenorrhoea (moderate-quality evidence).

Compared with danazol We don't know how effective oral progestogens are at producing postoperative amenorrhoea compared with danazol (low-quality evidence).

For GRADE evaluation of interventions for menorrhagia, see table, p 22 .

Benefits: We found one systematic review (search date 2001, 3 RCTs, 110 women). [47]

Oral progestogens versus no treatment:
Two RCTs included in the review (70 women) compared preoperative oral progestogens versus no preoperative treatment. The review found no significant difference between oral progestogens and no preoperative treatment in amenorrhoea at 2 years after endometrial destruction (RR 0.75, 95% CI 0.36 to 1.54). [47]

Oral progestogens versus other medical treatments:
Two RCTs included in the review (140 women) compared four interventions: oral progestogens, gonadorelin analogues, danazol, and no treatment. The trials were too small to allow firm conclusions to be drawn. [47]

Harms: The review gave no information on adverse effects. [47]

Comment: None.

GLOSSARY

Laparoscopic supracervical hysterectomy A laparoscopic procedure where the uterus, but not the cervix, is removed.
Laser ablation A hysteroscopic procedure in which endometrium is destroyed under direct vision by a laser beam.
Microwave endometrial ablation A procedure in which a microwave probe is passed through the cervix into the uterine cavity. When activated it is moved slowly from side to side over the whole surface of the uterine cavity in order to destroy the endometrium.
Multielectrode balloon ablation A procedure in which an inflatable device with electrodes on the outside is inserted into the uterine cavity through the cervix. The electrodes make contact with the endometrium and cause necrosis.
NovaSure endometrial ablation A procedure in which a disposable, conformable bipolar electrode array mounted on an expandable frame desiccates and coagulates endometrial tissue.
Pictorial blood loss assessment chart (PBAC) A semiquantitative assessment of menstrual blood loss based on women filling in the number and appearances of their sanitary protection and size of blood clots on a pictorial chart. Scores of 100 or more equate to a menstrual blood loss of 80 mL or more. [49]
Rollerball ablation A hysteroscopic procedure in which endometrium is destroyed under direct vision by diathermy applied by a rollerball.
Thermal uterine balloon therapy/thermal ablation A procedure in which a balloon catheter is passed through the cervix into the uterine cavity. The balloon is then filled with fluid, which is heated to about 87 °C, and left for 8 minutes. This causes necrosis of the endometrium.
Transcervical endometrial resection A hysteroscopic procedure in which endometrium is removed under direct vision by using an electrosurgical loop.
Vaporising electrode ablation A hysteroscopic procedure in which a cylindrical, corrugated electrode, or vaporiser is rolled along the endometrium. The bar electrode has three grooves that provide eight edges along which electrons concentrate, allowing immediate cell vaporisation on contact.
High-quality evidence Further research is very unlikely to change our confidence in the estimate of effect.
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

Endometrial destruction Two RCTs added comparing either first- with second-generation techniques, or first-generation techniques with each other. [43] [44] The first RCT compared thermal balloon endometrial ablation with transcervical endometrial resection, and found both treatments reduced menstrual blood loss compared with baseline. [43] The second RCT (10-year follow-up of a trial included in the systematic review) compared rollerball ablation and transcervical endometrial resection. The follow-up found no difference between groups for rates of hysterectomy. [44] Categorisation unchanged (Likely to be beneficial).
Intrauterine progestogens One RCT added comparing progestogen-releasing IUD versus thermal balloon ablation at 12-month follow-up. [28] The RCT found that the progestogen-releasing IUD significantly reduced PBAC scores at 12 months compared with thermal balloon ablation. However, the progestogen-releasing IUD was associated with higher hysterectomy rates at 24 months compared with the thermal balloon. Owing to the small numbers included in the trial, the categorisation remains as Unknown effectiveness.
Tranexamic acid One RCT added comparing tranexamic acid with medroxyproesterone acetate. [19] There was no direct comparison of menstrual blood loss between groups, but the reduction from baseline was reported for both groups. The RCT found that both treatments reduced menstrual blood loss from baseline at 3 months. Categorisation unchanged (Beneficial).

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

Number of studies (participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
What are the effects of medical treatments for menorrhagia?									
12 (313) [3]	Mean menstrual blood loss	NSAIDs *v* placebo	4	0	0	–1	0	Moderate	Directness point deducted for differences in regimens between studies
2 (61) [12]	Mean menstrual blood loss	NSAIDs *v* each other	4	–1	0	–1	0	Low	Quality point deducted for sparse data. Directness point deducted for small number of comparisons
4 (164) [14] [3] [17]	Mean menstrual blood loss	NSAIDs *v* tranexamic acid	4	–3	0	0	0	Very low	Quality points deducted for sparse data, poor follow-up, and other methodological flaws
1 (81) [17]	Mean menstrual blood loss	NSAIDs *v* etamsylate	4	–3	0	0	0	Very low	Quality points deducted for sparse data, poor follow-up, and other methodological flaws
3 (79) [12] [13]	Mean menstrual blood loss	NSAIDs *v* danazol	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (38) [12] [13] [21]	Mean menstrual blood loss	NSAIDs *v* combined oral contraceptives	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
2 (48) [12]	Mean menstrual blood loss	NSAIDs *v* oral progestogens (luteal phase)	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
7 (At least 153 people) [3] [14]	Mean menstrual blood loss	Tranexamic acid *v* placebo	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete presentation of results
1 (81) [17]	Mean menstrual blood loss	Tranexamic acid *v* etamsylate	4	–3	0	0	0	Very low	Quality points deducted for sparse data, poor follow-up, and other methodological flaws
2 (146) [15] [19]	Mean menstrual blood loss	Tranexamic acid *v* oral progestogens (luteal phase)	4	–2	0	0	0	Low	Quality points deducted for sparse data and methodological flaws
1 (187) [26]	Mean menstrual blood loss	Tranexamic acid *v* endometrial resection	4	–1	0	–1	0	Low	Quality point deducted for sparse data. Directness point deducted for range of drugs in comparison
1 (81) [17]	Mean menstrual blood loss	Etamsylate *v* NSAIDs	4	–3	0	0	0	Very low	Quality points deducted for sparse data, poor follow-up, and other methodological flaws
4 (193) [13] [3]	Mean menstrual blood loss	Danazol *v* placebo	4	–2	0	–1	0	Very low	Quality points deducted for sparse data and incomplete presentation of results. Directness point deducted for indirect comparisons
1 (38) [13] [12] [21]	Mean menstrual blood loss	Danazol *v* combined oral contraceptive pill	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
2 (51) [18]	Mean menstrual blood loss	Danazol *v* oral progestogens (luteal phase)	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (187) [26]	Mean menstrual blood loss	Danazol *v* endometrial ablation	4	–1	0	–1	0	Low	Quality point deducted for sparse data. Directness point deducted for range of drugs in comparison

Number of studies (participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
1 (187) [26]	Mean menstrual blood loss	Oral progestogens *v* endometrial resection	4	–1	0	–1	0	Low	Quality point deducted for sparse data. Directness point deducted for range of drugs in comparison
1 (44) [18]	Mean menstrual blood loss	Oral progestogen (longer cycle) *v* progestogen-releasing IUD	4	–1	0	0	0	Moderate	Quality point deducted for sparse data.
4(181) [25] [18]	Mean menstrual blood loss	Progestogen-releasing IUD *v* other drugs	4	–3	0	–2	0	Very low	Quality points deducted for sparse data, incomplete reporting of results, and baseline differences in severity of menorrhagia. Directness points deducted for multiple drugs in comparison and analysis of indirect comparisons
5 (317) [25] [27] [28]	Reduced PBAC score	Progestogen-releasing IUD *v* endometrial ablation	4	0	-1	–1	0	Low	Consistency point deducted for conflicting results. Directness point deducted for study involving mainly younger women
1 (232) [25]	Quality of life	Progestogen-releasing IUD *v* hysterectomy	4	0	0	–1	0	Moderate	Directness point deducted for high switch rates to surgery
What are the effects of surgical treatments for menorrhagia?									
5 (708) [3] [36]	Mean menstrual blood loss	Hysterectomy *v* endometrial destruction	4	0	0	0	0	High	
6 (887) [3] [36] [37]	Need for further surgery	Hysterectomy *v* endometrial destruction	4	0	0	0	0	High	
6 (887) [3] [36] [37]	Complications of surgery	Hysterectomy *v* endometrial destruction	4	0	–1	0	0	Moderate	Directness point deducted for contradictory results
3 (733) [38]	Vaginal bleeding (ongoing after surgery)	Subtotal hysterectomy *v* total hysterectomy	4	0	0	–1	0	Moderate	Directness point deducted for analysis not limited to women with menorrhagia
3 (733) [38]	Complications of surgery	Subtotal hysterectomy *v* total hysterectomy	4	0	0	–1	0	Moderate	Directness point deducted for analysis not limited to women with menorrhagia
27 (3643) [39]	Postoperative recovery	Abdominal hysterectomy *v* vaginal or laparoscopic hsyterectomy	4	0	0	–1	0	Moderate	Directness point deducted for analysis not limited to women with menorrhagia
1 (37928) [41]	Mortality	Abdominal hysterectomy *v* vaginal or laparoscopic hysterectomy	2	–1	0	–1	0	Very low	Quality point deducted for inadequate statistical reporting. Directness point deducted for range of underlying conditions included in the analysis
27 (3643) [39]	Complications of surgery	Abdominal hysterectomy *v* vaginal	4	0	0	–1	0	Moderate	Directness point deducted for analysis not limited to women with menorrhagia
27 (3643) [39]	Complications of surgery	Vaginal hysterectomy *v* laparoscopic hysterectomy	4	0	0	–1	0	Moderate	Directness point deducted for analysis not limited to women with menorrhagia
11 (2040) [42]	Mean menstrual blood loss	First-generation endometrial destruction techniques *v* second-generation techniques	4	0	0	–1	0	Moderate	Directness point deducted for lack of direct comparisons
11 (2040) [42]	Need for further surgery	First-generation endometrial destruction techniques *v* second-generation techniques	4	0	0	0	0	High	

Number of studies (participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
11 (2040) [42]	Complications of procedure	First-generation endometrial destruction techniques *v* second-generation techniques	4	0	–1	0	0	Moderate	Consistency point deducted for conflicting results
What are the effects of endometrial thinning before endometrial destruction in treating menorrhagia?									
8 (618) [47]	Postoperative amenorrhoea	Gonadorelin analogues *v* placebo/no treatment	4	–1	0	0	0	Moderate	Quality point deducted for no objective measure of menorrhagia
3 (340) [47]	Postoperative amenorrhoea	Gonadorelin analogues *v* danazol	4	0	0	0	0	High	
3 (202) [47] [48]	Postoperative amenorrhoea	Danazol *v* placebo	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
2 (140) [47]	Postoperative amenorrhoea	Gonadorelin analogues or danazol *v* oral progestogens	4	–1	–1	0	0	Low	Quality point deducted for sparse data. Consistency point deducted for inconclusive results
2 (70) [47]	Postoeprative amenorrhoea	Oral progestogens *v* no treatment	4	–1	0	0	0	Moderate	Quality point deducted for sparse data

Type of evidence: 4 = RCT; 2 = Observational
Consistency: similarity of results across studies
Directness: generalisability of population or outcomes
Effect size: based on relative risk or odds ratio