Menorrhagia

Search date June 2011

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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 June 2011 (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 anti-inflammatory drugs (NSAIDs), progestogens, and the following surgical interventions: dilatation and curettage, 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 80 mL or more 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 trials were found.

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

  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 to 49 years consult their general practitioners each year with menorrhagia. [2] In New Zealand, 2% to 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 shown 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.

OUTCOMES

Anaemia, primarily measured by haemoglobin concentration; **intraoperative and postoperative complications**; **menstrual blood loss** (assessed objectively [mL/cycle] or subjectively), including rates of amenorrhoea; **patient satisfaction**; **postoperative recovery**; **quality of life**; and **adverse drug effects**. 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. Women may regard amenorrhoea as a benefit or a harm of treatment, depending on their perspective.

METHODS

Clinical Evidence search and appraisal June 2011. The following databases were used to identify studies for this systematic review: Medline 1966 to June 2011, Embase 1980 to June 2011, and The Cochrane Database of Systematic Reviews, May 2011 [online] (1966 to date of issue). An additional search within The Cochrane Library was carried out for the Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA) database. We also searched for retractions of studies included in the review. Abstracts of the studies retrieved from the initial search were assessed by an information specialist. Selected studies were then sent to the contributor for additional assessment, using predetermined criteria to identify relevant studies. Study design criteria for inclusion in this review were: published systematic reviews of RCTs and RCTs in any language, at least single blinded, where possible, because blinding is difficult when comparing

different modalities such as IUDs versus tablets or medical versus surgical. Therefore, open studies were included in these scenarios. Studies contained >20 individuals of whom >80% were followed up. There was no minimum length of follow-up required to include studies. We included systematic reviews of RCTs and RCTs where harms of an included intervention were studied applying the same study design criteria for inclusion as we did for benefits. In addition we use a regular surveillance protocol to capture harms alerts from organisations such as the FDA and the MHRA, which are added to the reviews as required. To aid readability of the numerical data in our reviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 66). The categorisation of the quality of the evidence (high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the Clinical Evidence population and outcome of choice may represent only a small subset of the total outcomes reported, and population included, in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicalevidence.com).

QUESTION What are the effects of medical treatments for menorrhagia?

OPTION NSAIDS

- For GRADE evaluation of interventions for Menorrhagia, see table, p 66 .
- NSAIDs reduce blood loss compared with placebo.
- 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.
- NSAIDs have fewer adverse effects than danazol.

Benefits and harms

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.

Menstrual blood loss

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

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Mean menstrual blood loss					
[3] Systematic review	313 women 12 RCTs in this analysis	**Mean menstrual blood loss** with NSAIDs with placebo Absolute results not reported	WMD for blood loss –35 mL 95% CI –43 mL to –27 mL	○○○	NSAIDs

Patient satisfaction

No data from the following reference on this outcome. [3]

Quality of life

No data from the following reference on this outcome. [3]

Anaemia

No data from the following reference on this outcome. [3]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse drug effects					
[3] Systematic review	313 women 12 RCTs in this analysis	**Adverse effects** with NSAIDs with placebo Absolute results not reported The review found that commonly reported adverse effects associated with NSAIDs included headaches and gastrointestinal disturbances, such as indigestion, nausea, vomiting, and diarrhoea. For full details, see further information on studies			

NSAIDs versus each other:

We found one systematic review (search date 2001, 2 RCTs, 61 women). [12]

Menstrual blood loss

Different NSAIDs compared with each other We don't know how mefenamic acid and naproxen compare at reducing mean menstrual blood loss (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Mean menstrual blood loss					
[12] Systematic review	61 women 2 RCTs in this analysis	**Mean menstrual blood loss** with mefenamic acid with naproxen Absolute results not reported	WMD for blood loss +21.0 mL 95% CI –5.9 mL to +47.9 mL Analysis may have been underpowered to detect clinically important differences between treatments	⟷	Not significant

Patient satisfaction

No data from the following reference on this outcome. [12]

Quality of life

No data from the following reference on this outcome. [12]

Anaemia

No data from the following reference on this outcome. [12]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse drug effects					
[12] Systematic review	61 women 2 RCTs in this analysis	**Adverse effects** with mefenamic acid with naproxen Absolute results not reported The review found that commonly reported adverse effects associated with NSAIDs included headaches and gastrointestinal disturbances, such as indigestion, nausea, vomiting, and diarrhoea. For full details, see further information on studies			

NSAIDs versus tranexamic acid:
See option on tranexamic acid, p 8 .

NSAIDs versus etamsylate:
See option on etamsylate, p 14 .

NSAIDs versus danazol:
We found two systematic reviews (search dates 2001 [12] and 2007 [13]), both of which identified the same three RCTs.

Menstrual blood loss

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

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Mean menstrual blood loss					
[12] [13] Systematic review	79 women 3 RCTs in this analysis	**Mean menstrual blood loss** with NSAIDs with danazol Absolute results not reported	WMD for blood loss 45.1 mL 95% CI 18.7 mL to 71.4 mL Analysis may have been underpowered to detect a clinically important difference between treatments	◌◌◌	danazol

Patient satisfaction

No data from the following reference on this outcome. [12] [13]

Quality of life

No data from the following reference on this outcome. [12] [13]

Anaemia

No data from the following reference on this outcome. [12] [13]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse drug effects					
[13] [12] Systematic review	79 women 3 RCTs in this analysis	**Adverse effects** with NSAIDs with danazol Absolute results not reported The reviews found that commonly reported adverse effects associated with NSAIDs included headaches and gastrointestinal disturbances, such as indigestion, nausea, vomiting, and diarrhoea. For full details, see further information on studies			
[13] [12] Systematic review	40 women Data from 1 RCT	**Adverse effects** with mefenamic acid with danazol Absolute results not reported Adverse effects included musculoskeletal pains, dizziness, flushes, acne, behavioural changes, tiredness, and hirsutism	OR 7.0 95% CI 1.7 to 28.2	●●●	mefenamic acid

NSAIDs versus combined oral contraceptives:
See option on combined oral contraceptives, p 18 .

NSAIDs versus oral progestogens (luteal phase):
We found one systematic review (search date 2001, 2 RCTs, 48 women). [12]

Menstrual blood loss

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

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Mean menstrual blood loss					
[12] Systematic review	48 women 2 RCTs in this analysis	**Mean menstrual blood loss** with NSAIDs with oral progestogens Absolute results not reported	WMD for blood loss –23.0 mL 95% CI –46.6 mL to +0.625 mL Analysis may have been underpowered to detect clinically important differences between treatments	⟷	Not significant

Patient satisfaction

No data from the following reference on this outcome. [12]

Quality of life

No data from the following reference on this outcome. [12]

Anaemia

No data from the following reference on this outcome. [12]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse drug effects					
[12] Systematic review	48 women 2 RCTs in this analysis	**Adverse effects** with NSAIDs with oral progestogens Absolute results not reported The review found that commonly reported adverse effects included headaches and gastrointestinal disturbances, such as indigestion, nausea, vomiting, and diarrhoea. For full details, see further information about studies			

NSAIDs versus progestogen-releasing IUD:

See option on intrauterine progestogens, p 26 .

NSAIDs versus gonadorelin analogues:

We found no RCTs.

Further information on studies

[3] [12] **Adverse effects** In the RCTs that reported data on adverse effects, the commonly reported adverse effects occurred in at least 50% of women taking NSAIDs, but similar levels of adverse effects were found in placebo cycles (see review on NSAIDs).

Comment: Both reviews comparing NSAIDs versus danazol found that NSAIDs were less effective than danazol in reducing blood loss, [12] [13] 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

- For GRADE evaluation of interventions for Menorrhagia, see table, p 66 .
- Tranexamic acid reduces blood loss compared with placebo.
- Tranexamic acid may be more effective than NSAIDs, etamsylate, and oral progestogens at reducing blood loss.
- 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.

Benefits and harms

Tranexamic acid versus placebo:

We found two systematic reviews (search date 1996, 5 RCTs, 153 women; [3] and search date 1997, 7 RCTs [14]) and one subsequent RCT. [15] The second review also gave information on the outcomes of social activity and improved sex life; see further information on studies for full details. [14] For further information on adverse effects of tranexamic acid from observational studies, see .

Menstrual blood loss

Compared with placebo Tranexamic acid seems more effective at reducing blood loss (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Mean menstrual blood loss					
[3] Systematic review	153 women 5 RCTs in this analysis	**Mean menstrual blood loss** with tranexamic acid (250–500 mg 4 times daily during menstruation) with placebo Absolute results reported graphically	WMD –52 mL Other results and significance presented graphically	○○○	tranexamic acid
[14] Systematic review	Women with menorrhagia (number of women not reported) 2 RCTs in this analysis	**Mean menstrual blood loss** with tranexamic acid (both active forms of drug) with placebo Absolute results not reported	WMD –94 mL 95% CI –151 mL to –37 mL	○○○	tranexamic acid

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[15] RCT	187 women with mean menstrual blood loss 80mL or more per cycle	**Change in mean menstrual blood loss** –69.6 mL with tranexamic acid –12.6 mL with placebo Tranexamic acid (new oral formulation called Lysteda) 1.3 g three times a day for up to 5 days	P <0.001	○○○	tranexamic acid

Patient satisfaction

No data from the following reference on this outcome. [3] [14] [15]

Quality of life

Compared with placebo Tranexamic acid seems to improve social, physical, and work activity scores in women with menorrhagia (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Quality of life					
[15] RCT	187 women with mean menstrual blood loss 80 mL or more per cycle	**Limitation of social or leisure activities score** with tranexamic acid with placebo Absolute results reported graphically Tranexamic acid (new oral formulation called Lysteda) 1.3 g three times a day for up to 5 days	P <0.05	○○○	tranexamic acid
[15] RCT	187 women with mean menstrual blood loss 80 mL or more per cycle	**Limitation of physical activities score** with tranexamic acid with placebo Absolute results reported graphically Tranexamic acid (new oral formulation called Lysteda) 1.3 g three times a day for up to 5 days	P <0.05	○○○	tranexamic acid
[15] RCT	187 women with mean menstrual blood loss 80 mL or more per cycle	**Limitation in work inside or outside the home score** with tranexamic acid with placebo Absolute results reported graphically Tranexamic acid (new oral formulation called Lysteda) 1.3 g three times a day for up to 5 days	P <0.05	○○○	tranexamic acid

No data from the following reference on this outcome. [3] [14] [15]

Anaemia

No data from the following reference on this outcome. [3] [14] [15]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse drug effects					
[14] Systematic review	Women with menorrhagia (number of women not reported)	**Gastrointestinal adverse effects** with tranexamic acid (both active forms of drug) with placebo Absolute results not reported The review reported no increase with tranexamic acid compared with placebo; no further data reported			
[15] RCT	187 women with mean menstrual blood loss 80 mL or more per cycle	**Adverse effects** with tranexamic acid with placebo Absolute results not reported	The RCT reported no significant differences between groups for adverse effects	⟷	Not significant

No data from the following reference on this outcome. [3]

Tranexamic acid versus NSAIDs:

We found three systematic reviews (search dates 1997, [14] 1996, [3] and not reported [16]). Two of the reviews [3] [14] identified the same RCT (49 women) comparing tranexamic acid versus mefenamic acid. Between them, the second [3] and third [16] reviews identified three further RCTs.

Menstrual blood loss

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

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Mean menstrual blood loss					
[14] Systematic review	49 women Data from 1 RCT	**Mean menstrual blood loss** with tranexamic acid with mefenamic acid Absolute results not reported	WMD –73 mL 95% CI –123 mL to –23 mL	○○○	tranexamic acid
[3] Systematic review	15 women Data from 1 RCT	**Mean menstrual blood loss** with tranexamic acid with flurbiprofen Absolute results not reported Tranexamic acid reported to improve outcome	Significance not assessed		
[3] Systematic review	19 women Data from 1 RCT	**Mean menstrual blood loss** with tranexamic acid with diclofenac	Significance not assessed		

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		Absolute results not reported Tranexamic acid reported to improve outcome			
[17] RCT **3-armed trial**	81 women In review [3] [16] The remaining arm evaluated etamsylate	**Mean menstrual blood loss** with tranexamic acid with mefenamic acid Absolute results not reported	WMD –56 mL 95% CI –90 mL to –2 mL 27% of women withdrew from the RCT before its end; the RCT also made no adjustment for the multiple treatment comparisons involved	○○○	tranexamic acid

Patient satisfaction

No data from the following reference on this outcome. [14] [3] [16]

Quality of life

No data from the following reference on this outcome. [14] [3] [16]

Anaemia

No data from the following reference on this outcome. [14] [3] [16]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse drug effects					
[14] Systematic review	49 women Data from 1 RCT	**Gastrointestinal adverse effects** with tranexamic acid with mefenamic acid The systematic review found no increase with tranexamic acid compared with other drugs; no further data reported			

No data from the following reference on this outcome. [3] [16]

Tranexamic acid versus etamsylate:

We found two systematic reviews (search dates 1996 [3] and not reported [16]), which identified the same RCT. [17]

Menstrual blood loss

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

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Mean menstrual blood loss					
[17] RCT **3-armed trial**	81 women In review [3] [16] The remaining arm evaluated mefenamic acid	**Mean menstrual blood loss** with tranexamic acid with etamsylate Absolute results not reported	WMD –97 mL 95% CI –140 mL to –54 mL 27% of women withdrew from the RCT before its end; the RCT also made no adjustment for the multiple treatment comparisons involved	○○○	tranexamic acid

Patient satisfaction

No data from the following reference on this outcome. [17]

Quality of life

No data from the following reference on this outcome. [17]

Anaemia

No data from the following reference on this outcome. [17]

Adverse effects

No data from the following reference on this outcome. [3] [16]

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 dates 1996, [3] 1997, [14] and 2007 [18]). All the reviews identified the same single RCT, which did not compare the difference in menstrual blood loss between groups. [19] However, one of the reviews performed an analysis comparing tranexamic acid versus norethisterone. [14] We found one subsequent RCT. [20]

Menstrual blood loss

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

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Menstrual blood loss					
[14] Systematic review	46 women Data from 1 RCT	**Mean menstrual blood loss** with tranexamic acid with norethisterone Absolute results not reported	WMD –111 mL 95% CI –179 mL to –44 mL	○○○	tranexamic acid
[20] RCT	100 women with dysfunctional uterine bleeding	**Change in menstrual blood loss from baseline (measured on pictorial blood loss assessment [PBAC] chart scale) , 3 months** From 356.9 to 141.6 (60.3% reduction) with tranexamic acid (500 mg four times daily for 5 days during menstruation) From 370.9 to 156.6 (57.7% reduction) with medroxyprogesterone acetate (10 mg twice daily from day 5 to day 25 of the cycle) 80 women finished the 3-month treatment period	P <0.005 for difference between pre- and post-treatment PBAC rating for each treatment The RCT also found that both treatments improved menstrual blood loss from baseline	○○○	

Patient satisfaction

No data from the following reference on this outcome. [19] [20]

Quality of life

No data from the following reference on this outcome. [19] [20]

Anaemia

No data from the following reference on this outcome. [19] [20]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse drug effects					
[20] RCT	100 women with dysfunctional uterine bleeding	**Adverse effects** with tranexamic acid (500 mg four times daily for 5 days during menstruation)			

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		with medroxyprogesterone acetate (10 mg twice daily from day 5 to day 25 of the cycle) The RCT reported that 8/49 (16%) of women in the tranexamic-acid group had adverse effects: 1 allergic reaction, 3 headaches, 3 gastrointestinal upsets, and 1 woman with giddiness 80 women finished the 3-month treatment period			

No data from the following reference on this outcome. [19]

Tranexamic acid versus intrauterine progestogens:
See option on intrauterine progestogens, p 26 .

Tranexamic acid versus gonadorelin analogues:
We found no RCTs.

Tranexamic acid versus endometrial destruction:
See option on endometrial destruction, p 46 .

Further information on studies

[3] Few RCTs in the review measured patient satisfaction.

[14] One RCT [19] identified by the 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).

Comment: 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. [21]

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

OPTION ETAMSYLATE

- For GRADE evaluation of interventions for Menorrhagia, see table, p 66 .
- Etamsylate is less effective at reducing blood loss than tranexamic acid, NSAIDs, and danazol.

Benefits and harms

Etamsylate versus placebo:

We found one systematic review (search date not reported, 4 RCTs) [16] that presented results 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] We found no subsequent RCTs comparing etamsylate versus placebo.

Etamsylate versus NSAIDs:

We found one systematic review (search date not reported), [16] which identified one RCT. [17]

Menstrual blood loss

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

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Mean menstrual blood loss					
[17] RCT **3-armed trial**	81 women In review [16] The remaining arm evaluated tranexamic acid	**Mean menstrual blood loss** with etamsylate with mefenamic acid Absolute results not reported	WMD –51 mL 95% CI –96 mL to –6 mL 27% of women withdrew from the RCT before its completion; the RCT also made no adjustment for the multiple treatment comparisons involved	○○○	mefenamic acid

Patient satisfaction

No data from the following reference on this outcome. [17]

Quality of life

No data from the following reference on this outcome. [17]

Anaemia

No data from the following reference on this outcome. [17]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse drug effects					
[17] RCT	81 women In review [16]	**Adverse effects** with etamsylate with mefenamic acid	The review found no significant difference between different drug regimens in the rate of adverse effects (nausea, headaches, and	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
3-armed trial	The remaining arm evaluated tranexamic acid	Absolute results not reported	dizziness); these adverse effects seldom caused women to withdraw from studies		

Etamsylate versus tranexamic acid:

See option on tranexamic acid, p 8 .

Etamsylate versus other drugs:

We found no RCTs.

Further information on studies

Comment: None.

OPTION DANAZOL

- For GRADE evaluation of interventions for Menorrhagia, see table, p 66 .
- Danazol reduces blood loss compared with placebo.
- 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.
- Danazol has more adverse effects compared with NSAIDs, oral progestogens, or endometrial ablation.

Benefits and harms

Danazol versus placebo:

We found two systematic reviews (search date 2007, 1 RCT, 66 women; [13] and search date 1996, 3 RCTs, 127 women [3]) comparing danazol versus placebo. The second review [3] had less-rigorous inclusion criteria, and included two RCTs excluded by the first review. [13] For further general information about adverse effects of danazol, see comment.

Menstrual blood loss

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

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Mean menstrual blood loss					
[13] Systematic review	66 women Data from 1 RCT	**Change in blood-loss scores from baseline , 3 months** with danazol with placebo Absolute results not reported	No direct statistical comparison between danazol and placebo The review reported that danazol significantly improved blood-loss scores from baseline, whereas placebo had no significant effect; however, it is unclear how this result was calculated, as blood-loss scores and significance assessments were not reported		

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[3] Systematic review	127 women 3 RCTs in this analysis	**Mean menstrual blood loss** with danazol (200 mg/day continuously for 2–3 months) with placebo Absolute results not reported	WMD –108 mL CI presented graphically	○○○	danazol

Patient satisfaction

No data from the following reference on this outcome. [3] [13]

Quality of life

No data from the following reference on this outcome. [3] [13]

Anaemia

No data from the following reference on this outcome. [3] [13]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse drug effects					
[13] Systematic review	66 women Data from 1 RCT	**Adverse effects** with danazol with placebo Absolute results not reported Adverse effects associated with danazol may include: weight gain; androgenic effects, such as acne, seborrhoea, hirsutism, and voice changes; and general complaints including irritability, musculoskeletal pains, and tiredness			

No data from the following reference on this outcome. [3]

Danazol versus NSAIDs:

See option on NSAIDs, p 3 .

Danazol versus tranexamic acid:
We found no RCTs.

Danazol versus etamsylate:
We found no RCTs.

Danazol versus combined oral contraceptives:
See option on combined oral contraceptives, p 18 .

Danazol versus oral progestogens (luteal phase):
See option on oral progestogens in luteal phase, p 23 .

Danazol versus intrauterine progestogens:
See option on intrauterine progestogens, p 26 .

Danazol versus endometrial destruction:
See option on endometrial destruction, p 46 .

Further information on studies

Comment:

Different regimens of danazol versus each other:
The systematic review [13] also identified two small RCTs comparing different danazol regimens: standard dose danazol (200 mg/day), lower dose danazol (100 mg/day), and a reducing-dose regimen. 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).

Adverse effects of danazol:
Hot flushes and breast atrophy can sometimes occur with danazol. Most of these adverse effects are reversible on stopping treatment (see option on hormonal treatments in review on endometriosis, and option on 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.

OPTION CONTRACEPTIVES (COMBINED ORAL)

- For GRADE evaluation of interventions for Menorrhagia, see table, p 66 .
- We don't know whether combined oral contraceptives are effective at reducing menorrhagia, as few trials were found.

Benefits and harms

Combined oral contraceptives versus placebo:

We found no RCTs.

Combined oral contraceptives versus NSAIDs:

We found three systematic reviews (search dates 2001, [12] 2007, [13] and 1997 [22]), all of which identified the same small RCT. For information on adverse effects, see comment.

Menstrual blood loss

Compared with NSAIDs We don't know how combined oral contraceptives and NSAIDs compare at reducing mean blood loss (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Mean menstrual blood loss					
[12] Systematic review	38 women Data from 1 RCT 4-armed trial The remaining arms evaluated naproxen and danazol	**Mean menstrual blood loss** with oral contraceptive with mefenamic acid Absolute results not reported	WMD –17.5 mL 95% CI –22.5 mL to +47.5 mL The RCT was too small to rule out a clinically important difference between groups	⟷	Not significant
[12] Systematic review	38 women Data from 1 RCT 4-armed trial The remaining arms evaluated mefenamic acid and danazol	**Mean menstrual blood loss** with oral contraceptive with naproxen Absolute results not reported	WMD +8.37 mL 95% CI –27.3 mL to +44.0 mL The RCT was too small to rule out a clinically important difference between groups	⟷	Not significant

Patient satisfaction

No data from the following reference on this outcome. [12] [13] [22]

Quality of life

No data from the following reference on this outcome. [12] [13] [22]

Anaemia

No data from the following reference on this outcome. [12] [13] [22]

Adverse effects

No data from the following reference on this outcome. [12] [13] [22]

Combined oral contraceptives versus danazol:

We found three systematic reviews (search dates 2001, [12] 2007, [13] and 1997 [22]), all of which identified the same small RCT.

Menstrual blood loss

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

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Menstrual blood loss					
[12] Systematic review	38 women Data from 1 RCT 4-armed trial The remaining arms evaluated naproxen and mefenamic acid	**Mean menstrual blood loss** with oral contraceptive with danazol Absolute results not reported	WMD +19.3 mL 95% CI –24.47 mL to +63.01 mL	⟷	Not significant

Patient satisfaction

No data from the following reference on this outcome. [12] [13] [22]

Quality of life

No data from the following reference on this outcome. [12] [13] [22]

Anaemia

No data from the following reference on this outcome. [12] [13] [22]

Adverse effects

No data from the following reference on this outcome. [12] [13] [22]

Combined oral contraceptives versus intrauterine progestogens:

We found two RCTs comparing combined oral contraceptives with a progestogen-releasing IUD. [23] [24]

Menstrual blood loss

Compared with intrauterine progestogens We don't know whether combined oral contraceptives are more effective at reducing menstrual blood loss in women with idiopathic menorrhagia (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Menstrual blood loss					
[23] RCT	39 women with idiopathic menorrhagia	**Percentage change in mean blood loss from baseline , 12 months** –68% with combined oral contraceptive (norethisterone acetate 1 mg) –83% with ethinylestradiol 20 micrograms with a progestogen-releasing IUD Blood loss measured by pictorial blood loss assessment (PBAC) score	P = 0.002	○○○	progestogen-releasing IUD
[24] RCT	112 women with idiopathic menorrhagia	**Reduction in mean blood loss** 34.9 mL with combined oral contraceptive (30 micrograms ethinylestradiol) 87.4 mL with 150 micrograms levonorgestrel with a progestogen-releasing IUD Blood loss assessed using alkaline haematin	P = 0.13	⟷	Not significant
[24] RCT	112 women with idiopathic menorrhagia	**Reduction in mean blood loss** 2.5 mL with combined oral contraceptive (30 micrograms ethinylestradiol) 86.6 mL with 150 micrograms levonorgestrel with a progestogen-releasing IUD	P <0.01	○○○	progestogen-releasing IUD

Quality of life

Compared with intrauterine progestogens We don't know whether combined oral contraceptives are more effective at improving quality of life in women with idiopathic menorrhagia at 12 months (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Quality of life					
[23] RCT	39 women with idiopathic menorrhagia	**Mean menorrhagia severity score , 6 months** with combined oral contraceptive (norethisterone acetate 1 mg) with ethinylestradiol 20 micrograms with a progestogen-releasing IUD Absolute results not reported	Mean difference –6.37 95% CI –12.61 to –0.14 P = 0.04	○○○	progestogen-releasing IUD
[24] RCT	112 women with idiopathic menorrhagia	**Self-rated health quality of life , 12 months** with combined oral contraceptive (30 micrograms ethinylestradiol) with 150 micrograms levonorgestrel with a progestogen-releasing IUD Absolute results not reported	P = 0.12	⟷	Not significant
[24] RCT	112 women with idiopathic menorrhagia	**Physically unhealthy days , 12 months**	P = 0.18	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		with combined oral contraceptive (30 micrograms of ethinylestradiol) with 150 micrograms levonorgestrel with a progestogen-releasing IUD Absolute results not reported			
[24] RCT	112 women with idiopathic menorrhagia	**Mentally unhealthy days , 12 months** with combined oral contraceptive (30 micrograms of ethinylestradiol) with 150 micrograms levonorgestrel with a progestogen-releasing IUD Absolute results not reported	P = 0.03	○○○	combined oral contraceptive
[24] RCT	112 women with idiopathic menorrhagia	**Activity limitations (days lost) , 12 months** with combined oral contraceptive (30 micrograms of ethinylestradiol) with 150 micrograms levonorgestrel with a progestogen-releasing IUD Absolute results not reported	P <0.01	○○○	progestogen-releasing IUD

Anaemia

Compared with intrauterine progestogens We don't know whether combined oral contraceptives are more effective at increasing haemoglobin concentration in women with idiopathic menorrhagia at 12 months (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Haemoglobin concentration					
[23] RCT	39 women with idiopathic menorrhagia	**Haemoglobin concentration , 12 months** 136 g/L with combined oral contraceptive (norethisterone acetate 1 mg) 134 g/L with ethinylestradiol 20 micrograms with a progestogen-releasing IUD	P = 0.71	⟷	Not significant

No data from the following reference on this outcome. [24]

Patient satisfaction

No data from the following reference on this outcome. [23] [24]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[23] RCT	39 women with idiopathic menorrhagia	**Adverse effects , 12 months** 5/19 (26%) with combined oral contraceptive (norethisterone acetate 1 mg) 1/20 (5%) with ethinylestradiol 20 micrograms with a progestogen-releasing IUD The RCT reported that adverse effects included intermenstrual bleeding, menstrual disorder, and headache	P value not reported		

No data from the following reference on this outcome. [24]

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

Combined oral contraceptives versus endometrial destruction:
See option on endometrial destruction, p 46 .

Further information on studies

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. [25] 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. [26] [27]

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

OPTION PROGESTOGENS (ORAL) IN LUTEAL PHASE

- For GRADE evaluation of interventions for Menorrhagia, see table, p 66 .
- Oral progestogens are less effective than tranexamic acid and danazol at reducing blood loss.
- Oral progestogens given in the luteal phase may be as effective at reducing menstrual blood loss as NSAIDs.
- We found no direct information from RCTs about whether oral progestogens are better than no active treatment.

Benefits and harms

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

Progestogens (oral) in the luteal phase versus NSAIDs:

See option on NSAIDs, p 3 .

Progestogens (oral) in the luteal phase versus tranexamic acid:

See option on tranexamic acid, p 8 .

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 2007, 3 RCTs, 68 women). [18]

Menstrual blood loss

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

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Menstrual blood loss					
[18] Systematic review	51 women 2 RCTs in this analysis	**Menstrual blood loss** with oral progestogens with danazol Absolute results not reported	WMD –56 mL 95% CI –96 mL to –15 mL	○○○	danazol
[18] Systematic review	54 women 2 RCTs in this analysis	**Proportion of women who reported a greater self-assessed menstrual blood loss after treatment** 19/28 (68%) with oral progestogens 8/26 (31%) with danazol	RR 2.2 95% CI 1.2 to 4.1 NNH 2 95% CI 1 to 9	●●○	danazol

Patient satisfaction

No data from the following reference on this outcome. [18]

Quality of life

No data from the following reference on this outcome. [18]

Anaemia

No data from the following reference on this outcome. [18]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse drug effects					
[18] Systematic review	51 women 2 RCTs in this analysis	**Adverse effects** with oral progestogens with danazol Absolute results not reported	OR 4.05 95% CI 1.60 to 10.20	●●○	oral progestogens
[18] Systematic review	51 women 2 RCTs in this analysis	**Adverse effects** with oral progestogens with danazol Absolute results not reported 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			

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

Progestogens (oral) in the luteal phase versus intrauterine progestogens:
See option on intrauterine progestogens, p 26 .

Progestogens (oral) in the luteal phase versus endometrial destruction:
See option on endometrial destruction, p 46 .

Further information on studies

Comment: None.

OPTION PROGESTOGENS (ORAL) FOR LONGER CYCLE

- For GRADE evaluation of interventions for Menorrhagia, see table, p 66 .
- Oral progestogens are less effective than tranexamic acid and danazol at reducing blood loss.
- We found no direct information from RCTs about whether oral progestogens are better than no active treatment.

Benefits and harms

Progestogens (oral) for longer cycle versus placebo:

We found no RCTs.

Progestogens (oral) for longer cycle versus progestogen-releasing IUD:

See option on intrauterine progestogens, p 26 .

Further information on studies

Comment: None.

OPTION PROGESTOGENS (INTRAUTERINE)

- For GRADE evaluation of interventions for Menorrhagia, see table, p 66 .
- We don't know whether levonorgestrel-releasing IUDs are effective at reducing menorrhagia, as few trials were found.
- The risk of serious adverse effects is lower with intrauterine progestogens compared with hysterectomy.

Benefits and harms

Intrauterine progestogens versus placebo:

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

Intrauterine progestogens versus oral progestogen (luteal phase):

We found one RCT comparing progestogen-releasing IUD with an oral luteal phase progestogen (medroxyprogesterone). [28]

Menstrual blood loss

Compared with oral progestogens Intrauterine progestogens seem more effective at decreasing menstrual blood loss at 6 months (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Menstrual blood loss					
[28] RCT	162 women	**Reduction in median menstrual blood loss , 6 months** –128.8 mL with progestogen-releasing IUD –17.8 mL with oral medroxyprogesterone	P <0.001	○○○	progestogen-releasing IUD

Patient satisfaction

No data from the following reference on this outcome. [28]

Quality of life

No data from the following reference on this outcome. [28]

Anaemia

No data from the following reference on this outcome. [28]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[28] RCT	165 women	**Headache** 13/82 (16%) with progestogen-releasing IUD 9/83 (11%) with oral medroxyprogesterone	P value not reported		
[28] RCT	165 women	**Ovarian cyst** 10/82 (13%) with progestogen-releasing IUD 2/83 (2%) with oral medroxyprogesterone	P value not reported		
[28] RCT	165 women	**Vaginitis (bacterial)** 9/82 (11%) with progestogen-releasing IUD 3/83 (4%) with oral medroxyprogesterone	P value not reported		
[28] RCT	165 women	**Urinary tract infection** 6/82 (8%) with progestogen-releasing IUD 3/83 (4%) with oral medroxyprogesterone	P value not reported		
[28] RCT	165 women	**Acne** 5/82 (6.1%) with progestogen-releasing IUD 5/83 (6.0%) with oral medroxyprogesterone	P value not reported		
[28] RCT	165 women	**Hypertension** 5/82 (6%) with progestogen-releasing IUD 1/83 (1%) with oral medroxyprogesterone	P value not reported		
[28] RCT	165 women	**Sinusitis** 5/82 (6%) with progestogen-releasing IUD 3/83 (4%) with oral medroxyprogesterone	P value not reported		

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[28] RCT	165 women	**Upper respiratory tract infections** 5/82 (6%) with progestogen-releasing IUD 1/83 (1%) with oral medroxyprogesterone	P value not reported		
[28] RCT	165 women	**Breast tenderness** 4/82 (5%) with progestogen-releasing IUD 3/83 (4%) with oral medroxyprogesterone	P value not reported		
[28] RCT	165 women	**Fatigue** 4/82 (5%) with progestogen-releasing IUD 2/83 (2%) with oral medroxyprogesterone	P value not reported		
[28] RCT	165 women	**Pelvic pain** 4/82 (5%) with progestogen-releasing IUD 2/83 (2%) with oral medroxyprogesterone	P value not reported		
[28] RCT	165 women	**Increased weight** 4/82 (5%) with progestogen-releasing IUD 5/83 (6%) with oral medroxyprogesterone	P value not reported		
[28] RCT	165 women	**Lower abdominal pain** 3/82 (4%) with progestogen-releasing IUD 5/83 (6%) with oral medroxyprogesterone	P value not reported		

Intrauterine progestogens versus oral progestogen (long cycle):

We found two systematic reviews (search dates 2007 [18] and 2005 [29]), which between them identified two RCTs comparing the progestogen-releasing IUD versus long-cycle oral progestogen (norethisterone).

Menstrual blood loss

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

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Mean menstrual blood loss					
[18] Systematic review	44 women Data from 1 RCT	**Median reduction in menstrual blood loss** 104 mL with progestogen-releasing IUD 94 mL with oral norethisterone	P = 0.56	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[29] Systematic review **4-armed trial**	30 women 4-armed RCT The remaining arms evaluated mefenamic acid and danazol	**Menstrual blood loss** with progestogen-releasing IUD (65 micrograms/day) with long-cycle oral progestogen (norethisterone) Absolute results not reported Both treatments reduced menstrual blood loss compared with baseline values	Between-group differences not assessed		
[29] Systematic review	44 women Data from 1 RCT	**Proportion of women who were amenorrhoeic , 3 months** 32% with progestogen-releasing IUD 0% with norethisterone Absolute numbers not reported	Reported as significant P value not reported	○○○	norethisterone

Patient satisfaction

Compared with oral progestogen We don't know how progestogen-releasing IUDs compare with oral progestogen at increasing patient satisfaction (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Proportion of women willing to continue with treatment					
[29] Systematic review	44 women Data from 1 RCT	**Proportion of women who were willing to continue their treatment** 77% with progestogen-releasing IUD 22% with norethisterone Absolute numbers not reported	Reported as significant P value not reported	○○○	progestogen-releasing IUD

No data from the following reference on this outcome. [18]

Quality of life

No data from the following reference on this outcome. [18] [29]

Anaemia

No data from the following reference on this outcome. [18] [29]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse drug effects					
[18]	44 women	**Adverse effects**			

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Systematic review	Data from 1 RCT	with progestogen-releasing IUD with oral norethisterone The RCT found that 56% of women taking oral progestogens did not feel "well" or "very well"; only 22% continued treatment with oral progestogens after the 3 months of the study			

No data from the following reference on this outcome. [29]

Intrauterine progestogens versus NSAIDs:

We found two systematic reviews (search dates 2007, [18] and 2005 [29]), which between them identified two RCTs comparing the progestogen-releasing IUD versus NSAIDs.

Menstrual blood loss

Compared with NSAIDs We don't know how progestogen-releasing IUDs compare with mefenamic acid at reducing menstrual blood flow (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Menstrual blood loss					
[29] Systematic review	51 women Data from 1 RCT	**Reduction in menstrual blood loss , 6 cycles** with progestogen-releasing IUD (levonorgestrel) with mefenamic acid Absolute results not reported	Reported as significant P value not reported	○○○	progestogen-releasing IUD
[29] Systematic review	30 women Data from 1 RCT 4-armed trial The remaining arms evaluated danazol and long-cycle oral progestogen (norethisterone)	**Menstrual blood loss** with progestogen-releasing IUD (65 micrograms/day) with mefenamic acid Absolute results not reported Both treatments reduced menstrual blood loss compared with baseline values	Between-group differences not assessed		

Patient satisfaction

No data from the following reference on this outcome. [18] [29]

Quality of life

No data from the following reference on this outcome. [18] [29]

Anaemia

No data from the following reference on this outcome. [18] [29]

Adverse effects

No data from the following reference on this outcome. [18] [29]

Intrauterine progestogens versus danazol:

We found two systematic reviews (search dates 2007 [18] and 2005 [29]), which between them identified one RCT.

Menstrual blood loss

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

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Menstrual blood loss					
[29] Systematic review	30 women Data from 1 RCT 4-armed trial The remaining arms evaluated mefenamic acid and oral progestogen (norethisterone)	**Menstrual blood loss** with progestogen-releasing IUD (65 micrograms/day) with danazol Absolute results not reported Both treatments reduced menstrual blood loss compared with baseline values	Between-group differences not assessed		

Quality of life

No data from the following reference on this outcome. [18] [29]

Patient satisfaction

No data from the following reference on this outcome. [18] [29]

Anaemia

No data from the following reference on this outcome. [18] [29]

Adverse effects

No data from the following reference on this outcome. [18] [29]

Intrauterine progestogens versus endometrial destruction (ablation):

We found three systematic reviews (search dates 2005, [29] 2009, [30] and 2010 [31]). The first systematic review identified 5 RCTs comparing a progestogen-releasing IUD versus transcervical endometrial resection (2 RCTs) or thermal balloon ablation (3 RCTs). [29] The second review included the same 5 RCTs but also identified a further study published in 2006 using endometrial resection as the comparator group. [30] The third systematic review identified 9 RCTs comparing a progestogen-releasing IUD versus transcervical endometrial resection (3 RCTs) or thermal balloon ablation (6 RCTs) and included all the RCTs that were included in the two earlier systematic reviews. [31] However, as all the reviews used slightly different outcomes, all are reported here.

Menstrual blood loss

Compared with endometrial ablation We don't know how intrauterine progestogens and endometrial ablation compare at reducing menstrual blood loss (as measured by pictorial blood loss assessment and blood flow) (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Pictorial blood loss assessment (PBAC)					
[29] Systematic review	210 women 3 RCTs in this analysis	**Pictorial blood loss assessment (PBAC) score <75 , 12 months** with progestogen-releasing IUD with endometrial ablation Absolute results not reported	OR 0.28 95% CI 0.14 to 0.58	●●○	endometrial ablation
[31] Systematic review	281 women 5 RCTs in this analysis	**PBAC score <75 , 12 months** with progestogen-releasing IUD with endometrial destruction Absolute results not reported	RR 1.19 95% CI 1.07 to 1.32 NNT = 7 95% CI 5 to 19	●○○	endometrial destruction
[31] Systematic review	127 women 2 RCTs in this analysis	**Mean PBAC score , 12 months** with progestogen-releasing IUD with endometrial destruction Absolute results not reported	Mean difference 44.07 95% CI 33.01 to 55.12	○○○	endometrial destruction
[30] Systematic review	Number of women not reported 5 RCTs in this analysis	**Mean PBAC score , 12 months** with progestogen-releasing IUD with endometrial ablation Absolute results not reported	WMD +7.45 95% CI –12.37 to +27.26	⟷	Not significant
Amenorrhoea					
[29] Systematic review	210 women 3 RCTs in this analysis	**Amenorrhoea , 12 months** with progestogen-releasing IUD with endometrial ablation Absolute results not reported	OR 0.75 95% CI 0.36 to 1.54	⟷	Not significant
[31] Systematic review	209 women 4 RCTs in this analysis	**Amenorrhoea , 12 months** with progestogen-releasing IUD with endometrial ablation Absolute results not reported	RR 1.27 95% CI 0.82 to 1.95	⟷	Not significant
[29] Systematic review	210 women 3 RCTs in this analysis	**Amenorrhoea , 24 months** with progestogen-releasing IUD with endometrial ablation Absolute results not reported	OR 1.3 95% CI 0.48 to 3.53	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[29] Systematic review	210 women 3 RCTs in this analysis	**Amenorrhoea , 36 months** with progestogen-releasing IUD with endometrial ablation Absolute results not reported	OR 0.6 95% CI 0.14 to 2.57	⟷	Not significant

Need for re-treatment

Compared with endometrial ablation Intrauterine progestogens and endometrial ablation seem to lead to equivalent need for further intervention because of menorrhagia (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Need for further intervention owing to menstrual blood loss					
[29] Systematic review	110 women 2 RCTs in this analysis	**Likelihood of needing further surgical treatment for their heavy bleeding** with progestogen-releasing IUD with surgery Absolute results not reported	OR 1.33 95% CI 0.47 to 3.81	⟷	Not significant
[31] Systematic review	58 women Data from 1 RCT	**Treatment failure , 1 year** 1/30 (3%) with progestogen-releasing IUD 3/28 (11%) with endometrial ablation	RR 3.21 95% CI 0.35 to 29.12 P = 0.30	⟷	Not significant
[31] Systematic review	142 women 2 RCTs in this analysis	**Treatment failure , 2 years** 19/73 (26%) with progestogen-releasing IUD 14/69 (20%) with endometrial ablation	RR 0.77 95% CI 0.42 to 1.42 P = 0.41	⟷	Not significant

No data from the following reference on this outcome. [30]

Patient satisfaction

Compared with endometrial ablation We don't know whether intrauterine progestogens are more effective at improving patient satisfaction (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Patient satisfaction					
[29] Systematic review	136 women 2 RCTs in this analysis	**Proportion of women satisfied with treatment** with progestogen-releasing IUD with endometrial ablation Absolute results not reported	OR 0.61 95% CI 0.26 to 1.46	⟷	Not significant
[31] Systematic review	56 women Data from 1 RCT	**Patient satisfaction , 6 months** 18/33 (55%) with progestogen-releasing IUD 23/30 (77%) with endometrial ablation	RR 1.41 95% CI 0.97 to 2.03 P = 0.07	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[31] Systematic review	274 women 4 RCTs in this analysis	**Patient satisfaction , 1 year** 102/138 (74%) with progestogen-releasing IUD 111/136 (82%) with endometrial ablation	RR 1.10 95% CI 0.97 to 1.24 P = 0.13	⟷	Not significant
[31] Systematic review	131 women 2 RCTs in this analysis	**Patient satisfaction , 2 years** 54/70 (77%) with progestogen-releasing IUD 48/61 (79%) with endometrial ablation	RR 1.03 95% CI 0.85 to 1.23 P = 0.79	⟷	Not significant

No data from the following reference on this outcome. [30]

Quality of life

Compared with endometrial ablation We don't know whether intrauterine progestogens are more effective at improving quality of life (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Quality of life					
[30] Systematic review	<210 women 3 RCTs in this analysis	**Overall scores or individual dimensions of the Short Form-36 (SF-36)** with progestogen-releasing IUD with endometrial ablation Absolute results not reported	Reported as not significant P value not reported	⟷	Not significant
[31] Systematic review	81 women 2 RCTs in this analysis	**SF-36 score (mental health) , 1 year** with progestogen-releasing IUD with endometrial ablation Absolute results not reported	Mean difference 6.60 95% CI 0.55 to 12.65	○○○	endometrial ablation
[31] Systematic review	81 women 2 RCTs in this analysis	**SF-36 score (vitality) , 1 year** with progestogen-releasing IUD with endometrial ablation Absolute results not reported	Mean difference +2.10 95% CI –3.89 to +8.10	⟷	Not significant
[31] Systematic review	81 women 2 RCTs in this analysis	**SF-36 score (physical role limitation) , 1 year** with progestogen-releasing IUD with endometrial ablation Absolute results not reported	Mean difference +2.33 95% CI –5.65 to +10.31	⟷	Not significant
[31] Systematic review	81 women 2 RCTs in this analysis	**SF-36 score (emotional role limitation) , 1 year** with progestogen-releasing IUD with endometrial ablation Absolute results not reported	Mean difference 10.30 95% CI 2.15 to 18.46	○○○	endometrial ablation
[31] Systematic review	81 women 2 RCTs in this analysis	**SF-36 score (social function) , 1 year** with progestogen-releasing IUD with endometrial ablation	Mean difference +4.48 95% CI –2.13 to +11.08	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		Absolute results not reported			
[31] Systematic review	79 women Data from 1 RCT	**SF-36 score (general health) , 2 years** with progestogen-releasing IUD with endometrial ablation Absolute results not reported	Mean difference –2.60 95% CI –11.18 to +5.98	⟷	Not significant

No data from the following reference on this outcome. [29]

Anaemia

Compared with endometrial ablation Intrauterine progestogens may be less effective at reducing anaemia at 1 year (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Anaemia					
[31] Systematic review	33 women Data from 1 RCT	**Haemoglobin , 1 year** with progestogen-releasing IUD with endometrial ablation Absolute results not reported	Mean difference: 2.30 95% CI 0.97 to 3.63	●●○	endometrial ablation

No data from the following reference on this outcome. [29] [30]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[29] Systematic review	141 women 2 RCTs in this analysis	**Adverse effects , 1 year** with progestogen-releasing IUD with endometrial ablation Absolute results not reported	OR 0.24 95% CI 0.11 to 0.49	●●○	progestogen-releasing IUD
[31] Systematic review	201 women 3 RCTs in this analysis	**Proportion of women with adverse effects , 1 year** 54/100 (54%) with progestogen-releasing IUD 28/101 (28%) with endometrial ablation	RR 0.51 95% CI 0.36 to 0.74 P = 0.00035	●○○	endometrial ablation

No data from the following reference on this outcome. [30]

Intrauterine progestogens versus hysterectomy:

We found three systematic reviews (search dates 2007, [18] 2009, [30] and 2010 [31]). All three reviews identified one RCT comparing a progestogen-releasing IUD versus hysterectomy.

Patient satisfaction

Compared with hysterectomy Progestogen-releasing IUDs and hysterectomy may be equally effective at improving patient satisfaction (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Patient satisfaction					
[18] Systematic review	232 people Data from 1 RCT	**Patient satisfaction** with progestogen-releasing IUD with hysterectomy Absolute results not reported Patient satisfaction was reported as high in both groups However, at 12 months, the levonorgestrel IUD was in place in only 68% of the women, and 20% had undergone hysterectomy	OR 1.17 95% CI 0.41 to 3.34	⟷	Not significant

Quality of life

Compared with hysterectomy Progestogen-releasing IUDs and hysterectomy may be equally effective at improving quality of life at 1 year (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Quality of life					
[18] Systematic review	232 people Data from 1 RCT	**Health-related quality-of-life scores , 1 year** with progestogen-releasing IUD with hysterectomy The review reported that health-related quality-of-life had improved in both groups; no further data reported At 12 months, the levonorgestrel IUD was in place in only 68% of the women, and 20% had undergone hysterectomy			

Anaemia

Compared with hysterectomy Progestogen-releasing IUDs seem to be less effective at reducing anaemia at 1 year (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Anaemia					
[18] Systematic review	228 women Data from 1 RCT	**Haemoglobin levels , 12 months** with progestogen-releasing IUD with hysterectomy Absolute results not reported	WMD 3 units 95% CI 0.1 units to 5.9 units At 12 months, the levonorgestrel IUD was in place in only 68% of the women, and 20% had undergone hysterectomy	○○○	hysterectomy

Menstrual blood loss

No data from the following reference on this outcome. [18] [30] [31]

Need for re-treatment

No data from the following reference on this outcome. [18] [30] [31]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[18] Systematic review	Women with menorrhagia, total number of women not reported Data from 1 RCT	**Adverse effects** with progestogen-releasing IUD with hysterectomy Absolute results not reported Adverse effects with progestogen-releasing IUD included: failure of insertion, intermenstrual bleeding, hormonal symptoms, and expulsion Adverse effects with 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			
[18] Systematic review	198 women Data from 1 RCT	**Proportion of women developing ovarian cysts , 6 months** with progestogen-releasing IUD (levonorgestrel) with hysterectomy Absolute results not reported	OR 4.93 95% CI 1.96 to 12.39	●●○	hysterectomy
[18] Systematic review	180 women Data from 1 RCT	**Proportion of women developing ovarian cysts , 12 months** with progestogen-releasing IUD (levonorgestrel) with hysterectomy Absolute results not reported	OR 3.10 95% CI 1.33 to 7.24	●●○	hysterectomy

No data from the following reference on this outcome. [30] [31]

Further information on studies

[18] The review identified one RCT (56 women) that randomised women on a waiting list for hysterectomy to either a levonorgestrel IUD or their existing medical treatment (not defined). The RCT found quality-of-life scores were significantly higher in the levonorgestrel IUD group, and women in this group were significantly more likely to cancel their hysterectomy after 6 months of treatment. However, details of the existing medical treatments were not reported by the RCT.

[29] The review found that most adverse effects in women using a progestogen-releasing IUD were typical of progestogens (bloating, weight gain, and breast tenderness). **Intrauterine progestogens versus endometrial destruction (ablation)** The trials that considered long-term bleeding patterns were mainly in women <40 years of age. It is not yet known whether these results can be extrapolated to older women with menorrhagia.

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 <40 years of age. It is not yet known whether these results can be extrapolated to older women with menorrhagia.

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. [29] 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. [32] However, most women bled lightly for only 1 day a month, and about 15% were amenorrhoeic after 12 months. [33]

OPTION GONADORELIN ANALOGUES

- For GRADE evaluation of interventions for Menorrhagia, see table, p 66 .
- We don't know whether gonadorelin analogues are effective at reducing menstrual blood loss, as no trials were found.

Benefits and harms

Gonadorelin analogues:

We found no systematic review or RCTs.

Further information on studies

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. [34] Bone demineralisation occurs in most women after 6 months of treatment, but is reversible after treatment is stopped. [35] Contraception while using these drugs is not guaranteed. [36]

QUESTION What are the effects of surgical treatments for menorrhagia?

OPTION DILATATION AND CURETTAGE

- For GRADE evaluation of interventions for Menorrhagia, see table, p 66 .
- We don't know whether dilatation and curettage has any effect on menstrual blood loss.

Benefits and harms

Dilatation and curettage:

We found no systematic review or RCTs.

Further information on studies

Comment: 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. [37]

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. [38] 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

- For GRADE evaluation of interventions for Menorrhagia, see table, p 66 .
- Hysterectomy reduces blood loss, and the need for further surgery compared with medical treatment or endometrial destruction, but it can lead to complications in up to a third of women.
- Fewer women reported overall treatment dissatisfaction with hysterectomy.

Benefits and harms

Hysterectomy versus intrauterine progestogens:

See option on intrauterine progestogens, p 26 .

Hysterectomy versus endometrial destruction:

We found three systematic reviews (search dates 1996, [3] not reported, [39] and 2010 [40]). Two reviews identified the same 5 RCTs comparing hysterectomy versus endometrial destruction (transcervical endometrial resection or laser ablation). [3] [39] The third review included 7 RCTs and performed a meta-analysis with independent patient data from 6 of the RCTs (1127 women). [40]

Menstrual blood loss

Compared with endometrial destruction Hysterectomy is more effective at reducing menstrual blood loss (high-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Mean menstrual blood loss					
[3] Systematic review	440 pre-menopausal women 3 RCTs in this analysis	**Proportion of women with a reduction in menstrual blood loss , 12 months** 220/220 (100%) with hysterectomy 191/220 (87%) with endometrial destruction	NNT 8 95% CI 6 to 13 Differences in reduction in blood loss narrowed with longer follow-up; see further information on studies for full details	○○○	hysterectomy

No data from the following reference on this outcome. [40]

Need for re-treatment

Compared with endometrial destruction Hysterectomy seems more effective at reducing need for re-treatment (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Need for further surgery					
[3] Systematic review	708 pre-menopausal women Data from 1 RCT	**Proportion of women requiring repeat surgery , 12 months** 1/320 (1%) with hysterectomy 54/386 (14%) with endometrial destruction	RR 44.8 95% CI 6.2 to 321.8	●●●	hysterectomy
[3] Systematic review	708 pre-menopausal women Data from 1 RCT	**Proportion of women requiring repeat surgery , 4 years** 1/95 (1%) with hysterectomy 39/102 (38%) with endometrial destruction	RR 36.3 95% CI 5.1 to 259.2	●●●	hysterectomy

No data from the following reference on this outcome. [39] [40]

Patient satisfaction

Compared with endometrial ablation Hysterectomy seems to reduce the proportion of premenopausal women who are dissatisfied with treatment (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Patient satisfaction					
[40] Systematic review	836 pre-menopausal women 5 RCTs in this analysis	**Proportion of women expressing overall dissatisfaction with treatment** 21/382 (5%) with hysterectomy 57/454 (13%) with endometrial ablation	OR 2.46 95% CI 1.54 to 3.9 P <0.001	●●○	hysterectomy
[3] [39] Systematic review	739 pre-menopausal women 4 RCTs in this analysis	**Patients reporting moderately or very satisfied with treatment** 82% with hysterectomy 79% with endometrial ablation Absolute numbers not reported	RR 0.7 95% CI 0.4 to 1.03	⟷	Not significant

Quality of life

Compared with endometrial destruction We don't know whether hysterectomy is more effective at improving other quality-of-life scores (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Quality of life					
[40] Systematic review	213 women Data from 1 RCT	**Change in EQ-5D** with hysterectomy with endometrial ablation Absolute results not reported	P = 0.6	⟷	Not significant
[40] Systematic review	181 women Data from 1 RCT	**Change in Short Form-36 (SF-36) general health from baseline** with laparoscopic supracervical hysterectomy with endometrial resection Absolute results not reported	No direct comparison between groups P <0.01 for difference from baseline with either intervention		

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[40] Systematic review	181 women Data from 1 RCT	**Change in SF-36 social functioning from baseline** with laparoscopic supracervical hysterectomy with endometrial destruction Absolute results not reported	No direct comparison between groups P <0.01 for difference from baseline with either intervention		

No data from the following reference on this outcome. [3] [39]

Postoperative recovery

Compared with endometrial destruction Hysterectomy seems less effective at reducing time to postoperative recovery in premenopausal women (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Duration of hospital stay					
[3] Systematic review	Number of premenopausal women unclear	**Duration of hospital stay** with hysterectomy with endometrial destruction Absolute results not reported	Absolute difference –5 days Reported as significant CI and P value not reported	○○○	endometrial destruction
[40] Systematic review	1066 premenopausal women 7 RCTs in this analysis	**Duration of hospital stay in days** with hysterectomy with endometrial destruction Absolute results not reported	WMD 3 days 95% CI 2.9 days to 3.1 days P <0.0001	○○○	endometrial destruction
Return to work/normal activity					
[3] Systematic review	Premenopausal women	**Time to return to work** with hysterectomy with endometrial destruction Absolute results not reported	Absolute difference –4.5 weeks Reported as significant CI and P value not reported	○○○	endometrial destruction
[40] Systematic review	725 premenopausal women 6 RCTs in this analysis	**Return to work in days** with hysterectomy with endometrial destruction Absolute results not reported	WMD 14 days 95% CI 13 days to 16 days P <0.0001	○○○	endometrial destruction

No data from the following reference on this outcome. [39]

Intraoperative and postoperative complications

Compared with endometrial destruction Hysterectomy may be associated with a higher risk of intraoperative and postoperative complications (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Complications of surgery					
[3] Systematic review	708 premenopausal women Data from 1 RCT	**Complications of surgery** with hysterectomy with endometrial destruction Absolute results not reported	Significance not assessed		

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		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			
Pain					
[40] Systematic review	367 premenopausal women 2 RCTs in this analysis	**Surgery pain score** with hysterectomy with endometrial ablation Absolute results not reported	WMD 2.5 95% CI 2.2 to 2.9 P <0.0001	○○○	endometrial ablation

No data from the following reference on this outcome. [39]

Anaemia

No data from the following reference on this outcome. [3] [39] [40]

Adverse effects

No data from the following reference on this outcome. [3] [39] [40]

Subtotal hysterectomy versus total hysterectomy:

We found one systematic review (search date 2005, 3 RCTs, 733 women) comparing subtotal versus total abdominal hysterectomy. [41] 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.

Menstrual blood loss

Subtotal compared with total hysterectomy Subtotal hysterectomy seems to be less effective at reducing menstrual blood loss in women with benign gynaecological disease including menorrhagia (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Cyclical vaginal bleeding					
[41] Systematic review	733 women with benign gynaecological conditions, mostly fibroids or heavy menstrual bleeding 3 RCTs in this analysis	**Ongoing cyclical vaginal bleeding** with subtotal hysterectomy with total hysterectomy	OR 11.3 95% CI 4.1 to 31.2	●●●	total hysterectomy

Intraoperative and postoperative complications

Subtotal compared with total hysterectomy Subtotal and total hysterectomy seem to be associated with similar rates of complications (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Intraoperative and postoperative complications					
[41] Systematic review	411 women with benign gynaecological conditions, mostly fibroids or heavy menstrual bleeding 2 RCTs in this analysis	**Blood loss** with subtotal hysterectomy with total hysterectomy Absolute results not reported	WMD 85 mL 95% CI 27 mL to 142 mL	○○○	subtotal hysterectomy
[41] Systematic review	411 women with benign gynaecological conditions, mostly fibroids or heavy menstrual bleeding 2 RCTs in this analysis	**Need for blood transfusion** with subtotal hysterectomy with total hysterectomy Absolute results not reported	OR 1.06 95% CI 0.45 to 2.5	⟷	Not significant
[41] Systematic review	411 women with benign gynaecological conditions, mostly fibroids or heavy menstrual bleeding 2 RCTs in this analysis	**Adverse effects** with subtotal hysterectomy with total hysterectomy Absolute results not reported The review found similar rates of urinary symptoms, bowel symptoms, or sexual dysfunction in both groups; no further data reported			

Patient satisfaction

No data from the following reference on this outcome. [41]

Quality of life

No data from the following reference on this outcome. [41]

Anaemia

No data from the following reference on this outcome. [41]

Postoperative recovery

No data from the following reference on this outcome. [41]

Adverse effects

No data from the following reference on this outcome. [41]

Abdominal hysterectomy versus vaginal or laparoscopic hysterectomy:

We found one systematic review (search date 2004, 27 RCTs, 3643 women) comparing abdominal, vaginal, and laparoscopic approaches. [42] 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. For further information on adverse effects from observational studies, see comment.

Postoperative recovery

Abdominal compared with vaginal and laparoscopic hysterectomy Complications of surgery are greater with abdominal or laparoscopic hysterectomy. Postoperative recovery is faster with vaginal or laparoscopic hysterectomy in women with benign gynaecological disease including menorrhagia (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Time taken to return to normal activities					
[42] Systematic review	176 women 3 RCTs in this analysis	**Return to normal activities** with abdominal hysterectomy with vaginal hysterectomy Absolute results not reported	WMD 9.5 days 95% CI 6.4 days to 12.6 days	○○○	vaginal hysterectomy
[42] Systematic review	250 women 6 RCTs in this analysis	**Return to normal activities** with abdominal hysterectomy with laparoscopic hysterectomy Absolute results not reported	WMD 13.6 days 95% CI 11.8 days to 15.4 days	○○○	laparoscopic hysterectomy
Duration of hospital stay					
[42] Systematic review	295 women 4 RCTs in this analysis	**Duration of hospital stay** with abdominal hysterectomy with vaginal hysterectomy Absolute results not reported	WMD 1.0 day 95% CI 0.7 days to 1.2 days	○○○	vaginal hysterectomy
[42] Systematic review	1007 women 10 RCTs in this analysis	**Duration of hospital stay** with abdominal hysterectomy with laparoscopic hysterectomy Absolute results not reported	WMD 2 days 95% CI 1.9 days to 2.2 days	○○○	laparoscopic hysterectomy

Menstrual blood loss

No data from the following reference on this outcome. [42]

Patient satisfaction

No data from the following reference on this outcome. [42]

Quality of life

No data from the following reference on this outcome. [42]

Anaemia

No data from the following reference on this outcome. [42]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Intraoperative and postoperative complications					
[42] Systematic review	295 women 4 RCTs in this analysis	**Unspecified infections or febrile episodes** 30/147 (20%) with abdominal hysterectomy 15/148 (10%) with vaginal hysterectomy	OR 0.42 95% CI 0.21 to 0.83	●●○	vaginal hysterectomy
[42] Systematic review	2138 women 15 RCTs in this analysis	**Unspecified infections or febrile episodes** 124/925 (13%) with abdominal hysterectomy 125/1213 (10%) with laparoscopic hysterectomy	OR 0.65 95% CI 0.49 to 0.87	●○○	laparoscopic hysterectomy

Vaginal hysterectomy versus laparoscopic hysterectomy:

We found one systematic review (search date 2004, 27 RCTs, 3643 women) comparing abdominal, vaginal, and laparoscopic approaches. [42] 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 no evidence of benefit for laparoscopic compared with vaginal hysterectomy.

Further information on studies

[3] [39] [40] 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. Two RCTs included in the reviews found no significant difference between treatments in satisfaction rates after 3 and 4 years. The three reviews found that, compared with hysterectomy, endometrial destruction significantly reduced the duration of surgery by about 30 minutes.

[41] The review found that subtotal abdominal hysterectomy significantly reduced operating time compared with total abdominal hysterectomy (2 RCTs, 411 women; WMD 11.4 minutes, 95% CI 6.6 minutes to 16.3 minutes).

Comment: We found one additional UK study of 37,928 women with benign disease, which compared abdominal (24,772 women), vaginal (11,122 women), and laparoscopic (1154 women) hysterectomies performed during 1994 and 1995. [43] The study reported that overall mortality was 0.38 per 1000 (95% CI 0.25 per 1000 to 0.64 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.

One large population-based analysis stratified by age found that mortality after hysterectomy for non-malignant conditions is about 1/2000 in women aged <50 years. [44]

OPTION ENDOMETRIAL DESTRUCTION (RESECTION OR ABLATION)

- For GRADE evaluation of interventions for Menorrhagia, see table, p 66 .
- 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 to another.

Benefits and harms

Endometrial destruction (resection or ablation) versus intrauterine progestogens:

See option on intrauterine progestogens, p 26 .

Endometrial destruction (resection or ablation) versus oral drugs:

We found one systematic review (search date 2010, 1 RCT, 187 women) comparing endometrial resection (93 women) versus oral drugs. [31] See comment for further information from observational studies on intraoperative complications associated with endometrial destruction.

Menstrual blood loss

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).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Mean menstrual blood loss					
[31] Systematic review	187 women Data from 1 RCT	**Proportion of women with reduction in menstrual blood loss , 4 months** 77/93 (83%) with endometrial resection 29/93 (31%) with oral drugs Oral drugs assessed were: tranexamic acid (22 women), danazol (15 women), combined oral contraceptives (24 women), oral progestogens (31 women), and HRT plus an NSAID (2 women)	RR 2.66 95% CI 1.94 to 3.64	●●○	endometrial resection
[31] Systematic review	187 women Data from 1 RCT	**Proportion of women with reduction in menstrual blood loss , 5 years** with endometrial resection with oral drugs Absolute results not reported By 5 years, 77% of the women randomised to medical treatment had received surgery	Reported as non-significant P value not reported	⟷	Not significant

Need for re-treatment

No data from the following reference on this outcome. [31]

Patient satisfaction

No data from the following reference on this outcome. [31]

Quality of life

No data from the following reference on this outcome. [31]

Anaemia

No data from the following reference on this outcome. [31]

Postoperative recovery

No data from the following reference on this outcome. [31]

Intraoperative and postoperative complications

No data from the following reference on this outcome. [31]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[31] Systematic review	187 women Data from 1 RCT	**Proportion of women with adverse effects , 4 months** 12/93 (13%) with endometrial resection 46/93 (49%) with oral drugs Oral drugs assessed were: tranexamic acid (22 women), danazol (15 women), combined oral contraceptives (24 women), oral progestogens (31 women), and HRT plus an NSAID (2 women)	RR 0.26 95% CI 0.15 to 0.46	●○○	endometrial resection

Endometrial destruction (resection or ablation) versus hysterectomy:
See option on hysterectomy, p 39 .

First-generation versus second-generation techniques:
We found two systematic reviews (search dates 2009). [45] [40] The first review [45] included 21 RCTs (3395 premenopausal women). The second review [40] included 14 RCTs, all of which were included in the first larger review.

Both reviews compared first-generation techniques (including hysteroscopic methods such as laser ablation, rollerball ablation, transcervical endometrial resection, and vaporising electrode ablation) versus 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). Therefore, only results from the larger review are reported here.

Menstrual blood loss

Compared with second-generation techniques First-generation and second-generation endometrial ablation techniques are equally effective at reducing blood loss in premenopausal women (high-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Amenorrhoea					
[45] Systematic review	49 premenopausal women Data from 1 RCT	**Amenorrhoea , 6 months** 13/19 (68%) with first generation 26/30 (87%) with second generation	OR 3.00 95% CI 0.72 to 12.53 P = 0.13	⟷	Not significant
[45] Systematic review	2085 premenopausal women 11 RCTs in this analysis	**Amenorrhoea , 1 year** 322/857 (38%) with first generation 459/1228 (37%) with second generation	OR 0.92 95% CI 0.62 to 1.37 P = 0.70	⟷	Not significant
[45] Systematic review	701 premenopausal women 3 RCTs in this analysis	**Amenorrhoea , 2 years** 110/308 (35.7%) with first generation 143/393 (36.4%) with second generation	OR 0.94 95% CI 0.58 to 1.51 P = 0.79	⟷	Not significant
[45] Systematic review	672 premenopausal women 4 RCTs in this analysis	**Amenorrhoea , 2 to 5 years** 147/304 (43%) with first generation 194/368 (53%) with second generation	OR 1.30 95% CI 0.61 to 2.79 P = 0.49	⟷	Not significant

Need for re-treatment

Compared with second-generation techniques First-generation and second-generation endometrial ablation techniques are equally effective at reducing the need for further surgery at 1 to 5 years (high-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Need for further surgery					
[45] Systematic review	1028 premenopausal women 7 RCTs in this analysis	**Need for further surgery , 1 year** 31/459 (7%) with first generation 24/569 (4%) with second generation	OR 0.74 95% CI 0.42 to 1.31 P = 0.31	⟷	Not significant
[45] Systematic review	988 premenopausal women 5 RCTs in this analysis	**Need for further surgery , 2 years** 40/432 (9%) with first generation 44/556 (8%) with second generation	OR 0.80 95% CI 0.48 to 1.34 P = 0.41	⟷	Not significant
[45] Systematic review	647 premenopausal women 3 RCTs in this analysis	**Need for further surgery , 2 to 5 years** 70/280 (25%) with first generation 76/367 (21%) with second generation	OR 0.94 95% CI 0.64 to 1.39 P = 0.77	⟷	Not significant

Patient satisfaction

Compared with second-generation techniques First-generation and second-generation endometrial ablation techniques seem equally effective at increasing patient satisfaction (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Patient satisfaction					
[45] Systematic review	50 premenopausal women Data from 1 RCT	**Patient satisfaction , 6 months** 19/20 (95%) with first generation 30/30 (100%) with second generation	OR 4.69 95% CI 0.18 to 121.10 P = 0.35	⟷	Not significant
[45] Systematic review	1690 premenopausal women 11 RCTs in this analysis	**Patient satisfaction , 1 year** 610/700 (88%) with first generation 904/990 (91%) with second generation	OR 1.20 95% CI 0.85 to 1.70 P = 0.30	⟷	Not significant
[45] Systematic review	802 premenopausal women 5 RCTs in this analysis	**Patient satisfaction , 2 years** 279/365 (76%) with first generation 372/437 (85%) with second generation	OR 1.60 95% CI 1.00 to 2.56 P = 0.05	⟷	Not significant
[45] Systematic review	672 premenopausal women 4 RCTs in this analysis	**Patient satisfaction , 2 to 5 years** 246/304 (88%) with first generation 341/368 (93%) with second generation	OR 1.43 95% CI 0.59 to 3.46	⟷	Not significant

Intraoperative and postoperative complications

Compared with second-generation techniques First-generation and second-generation endometrial destruction techniques seem equally effective at reducing rates of serious postoperative complications (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Complications of surgery					
[45] Systematic review	681 premenopausal women 4 RCTs in this analysis	**Fluid overload** 10/327 (3%) with first generation 0/354 (0%) with second generation	OR 0.17 95% CI 0.04 to 0.77 P = 0.22	⟷	Not significant
[45] Systematic review	1885 premenopausal women 8 RCTs in this analysis	**Perforation** 10/771 (1.3%) with first generation 3/1114 (0.2%) with second generation	OR 0.32 95% CI 0.10 to 1.00 P = 0.05	⟷	Not significant
[45] Systematic review	1676 premenopausal women 8 RCTs in this analysis	**Cervical lacerations** 15/671 (2%) with first generation 2/1005 (0.2%) with second generation	OR 0.22 95% CI 0.08 to 0.60 P = 0.0031	●●○	second generation

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[45] Systematic review	1188 pre-menopausal women 5 RCTs in this analysis	**Endometriosis** 6/444 (1%) with first-generation endometrial destruction techniques 15/744 (2%) with second-generation endometrial destruction techniques	OR 1.26 95% CI 0.44 to 3.60 P = 0.66	⟷	Not significant
[45] Systematic review	1834 pre-menopausal women 8 RCTs in this analysis	**Urinary tract infections** 12/702 (1.7%) with first-generation endometrial destruction techniques 19/1132 (1.7%) with second-generation endometrial destruction techniques	OR 0.88 95% CI 0.43 to 1.83 P = 0.88	⟷	Not significant
[45] Systematic review	1133 pre-menopausal women 5 RCTs in this analysis	**Haematometra** 11/460 (2%) with first-generation endometrial destruction techniques 5/673 (1%) with second-generation endometrial destruction techniques	OR 0.31 95% CI 0.11 to 0.85 P = 0.23	⟷	Not significant
[45] Systematic review	239 pre-menopausal women Data from 1 RCT	**Hydrosalphinx** 1/114 (0.8%) with first-generation endometrial destruction techniques 0/125 (0%) with second-generation endometrial destruction techniques	OR 0.30 95% CI 0.01 to 7.74 P = 0.46	⟷	Not significant
[45] Systematic review	982 pre-menopausal women 5 RCTs in this analysis	**Haemorrhage** 12/400 (3%) with first-generation endometrial destruction techniques 7/582 (1%) with second-generation endometrial destruction techniques	OR 0.69 95% CI 0.25 to 1.92 P = 0.48	⟷	Not significant
[45] Systematic review	267 pre-menopausal women Data from 1 RCT	**Myometritis** 1/123 (0.8%) with first-generation endometrial destruction techniques 0/144 (0%) with second-generation endometrial destruction techniques	OR 0.28 95% CI 1.01 to 7.00 P = 0.44	⟷	Not significant
[45] Systematic review	265 pre-menopausal women Data from 1 RCT	**Pelvic inflammatory disease** 1/90 (1.1%) with first-generation endometrial destruction techniques 2/175 (1.1%) with second-generation endometrial destruction techniques	OR 1.03 95% CI 0.09 to 11.50 P = 0.98	⟷	Not significant
[45] Systematic review	265 pre-menopausal women Data from 1 RCT	**Pelvic abscess** 1/90 (1%) with first-generation endometrial destruction techniques 0/175 (0%) with second-generation endometrial destruction techniques	OR 0.17 95% CI 0.01 to 4.22 P = 0.28	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[45] Systematic review	322 pre-menopausal women Data from 1 RCT	**Cervical stenosis** 0/107 (0%) with first-generation endometrial destruction techniques 1/215 (0.4%) with second-generation endometrial destruction techniques	OR 1.50 95% CI 0.06 to 37.22 P = 0.80	⟷	Not significant
[45] Systematic review	601 pre-menopausal women 2 RCTs in this analysis	**Uterine cramping** 64/193 (33%) with first-generation endometrial destruction techniques 157/408 (38%) with second-generation endometrial destruction techniques	OR 1.75 95% CI 1.08 to 2.83 P = 0.023	●○○	first-generation endometrial destruction techniques
[45] Systematic review	683 pre-menopausal women 3 RCTs in this analysis	**Severe pelvic pain** 5/238 (2.1%) with first-generation endometrial destruction techniques 9/445 (2.0%) with second-generation endometrial destruction techniques	OR 0.86 95% CI 0.18 to 4.41 P = 0.18	⟷	Not significant
[45] Systematic review	269 pre-menopausal women Data from 1 RCT	**External burns** 0/85 (0%) with first-generation endometrial destruction techniques 2/184 (1%) with second-generation endometrial destruction techniques	OR 2.34 95% CI 0.11 to 49.32 P = 0.58	⟷	Not significant

Quality of life

No data from the following reference on this outcome. [45]

Anaemia

No data from the following reference on this outcome. [45]

Postoperative recovery

No data from the following reference on this outcome. [45]

Adverse effects

No data from the following reference on this outcome. [45]

First-generation techniques versus each other:

We found one systematic review (search date 2009, 3 RCTs [45]) and one subsequent RCT. [46] One RCT included in the review (120 women with heavy dysfunctional bleeding) has published a 10-year follow-up assessing need for re-treatment (hysterectomy). [47] See further information on studies for data on operative difficulty.

Menstrual blood loss

Different first-generation techniques compared with each other Laser ablation, transcervical endometrial resection, rollerball, and vaporising electrode ablation seem equally effective at reducing blood loss (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Amenorrhoea					
[45] Systematic review	306 women Data from 1 RCT	**Amenorrhoea , 1 year** 37/160 (23%) with laser ablation 32/146 (22%) with transcervical endometrial resection	OR 1.07 95% CI 0.63 to 1.83 P = 0.80	⟷	Not significant
[45] Systematic review	91 women Data from 1 RCT	**Amenorrhoea , 1 year** 17/47 (36%) with vaporising electrode ablation 21/44 (47%) with transcervical endometrial resection	OR 0.62 95% CI 0.27 to 1.44 P = 0.27	⟷	Not significant
[45] Systematic review	348 pre-menopausal women 2 RCTs in this analysis	**Amenorrhoea , 6 months** 38/176 (21.6%) with laser ablation 38/172 (22.1%) with transcervical endometrial resection	OR 0.97 95% CI 0.58 to 1.61 P = 0.90	⟷	Not significant
[46] RCT	50 women	**Amenorrhoea , 2 years** 36% with 5-mm rollerball with unmodulated cutting current 7% with 5-mm rollerball with modulated coagulating current Absolute numbers not reported	P = 0.54	⟷	Not significant

Need for re-treatment

Different first-generation techniques compared with each other We don't know how rollerball ablation and transcervical endometrial resection compare at reducing rates of hysterectomy at up to 10 years (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Need for re-treatment					
[45] Systematic review	120 women with heavy dysfunctional bleeding	**Rates of hysterectomy , 5+ years** 23/61 (38%) with rollerball ablation 16/59 (27%) with transcervical endometrial resection 22% of the women who were randomised had proceeded to hysterectomy in the 10 years after the initial ablation	OR 1.63 95% CI 0.75 to 3.52 P = 0.22	⟷	Not significant
[45] Systematic review	388 pre-menopausal women 2 RCTs in this analysis	**Need for re-treatment , 1 year** 32/197 (16%) with laser ablation 37/191 (19%) with transcervical endometrial resection	OR 0.81 95% CI 0.48 to 1.36 P = 0.43	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[45] Systematic review	120 pre-menopausal women Data from 1 RCT	**Need for re-treatment , 2 years** 15/61 (25%) with rollerball 14/59 (24%) with transcervical endometrial resection	OR 1.05 95% CI 0.45 to 2.42 P = 0.91	⟷	Not significant
[46] RCT	50 women	**Re-intervention , 2 years** 36% with 5-mm rollerball with unmodulated cutting current 32% with 5-mm rollerball with modulated coagulating current Absolute numbers not reported	P = 0.75	⟷	Not significant

Patient satisfaction

Different first-generation techniques compared with each other Laser ablation, transcervical endometrial resection, and vaporising electrode ablation seem equally effective at increasing patient satisfaction (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Patient satisfaction					
[45] Systematic review	321 women Data from 1 RCT	**Patient satisfaction , 12 months** 148/166 (89%) with laser ablation 140/155 (90%) with transcervical endometrial resection	OR 0.88 95% CI 0.43 to 1.81 P = 0.73	⟷	Not significant
[45] Systematic review	91 women Data from 1 RCT	**Patient satisfaction , 12 months** 45/47 (96%) with vaporising electrode ablation 41/44 (93%) with transcervical endometrial resection	OR 1.65 95% CI 0.26 to 10.35 P = 0.60	⟷	Not significant
[46] RCT	50 women	**Satisfied or very satisfied , 2 years** 64% with 5-mm rollerball with unmodulated cutting current 68% with 5-mm rollerball with modulated coagulating current Absolute numbers not reported	P = 0.46	⟷	Not significant

Intraoperative and postoperative complications

Different first-generation techniques compared with each other Rollerball, transcervical endometrial resection, and laser ablation seem equally effective at reducing the rate of intraoperative and postoperative complications (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Intraoperative and postoperative complications					
[45] Systematic review	120 pre-menopausal women Data from 1 RCT	**Fluid deficit** 1/61 (1.6%) with rollerball 1/59 (1.7%) with transcervical endometrial resection	OR 0.32 95% CI 0.01 to 7.94 P = 0.48	⟷	Not significant
[45] Systematic review	366 pre-menopausal women Data from 1 RCT	**Fluid overload** 15/185 (8%) with laser ablation 3/181 (2%) with transcervical endometrial resection	OR 5.24 95% CI 1.5 to 18.4 P = 0.009	●●●	transcervical endometrial resection

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[45] Systematic review	120 pre-menopausal women Data from 1 RCT	**Perforation** 0/61 (0%) with rollerball 1/59 (2%) with transcervical endometrial resection	OR 0.32 95% CI 0.01 to 7.95 P = 0.48	⟷	Not significant

No data from the following reference on this outcome. [46]

Quality of life

No data from the following reference on this outcome. [45] [46]

Anaemia

No data from the following reference on this outcome. [45] [46]

Postoperative recovery

No data from the following reference on this outcome. [45] [46]

Adverse effects

No data from the following reference on this outcome. [46] [45]

Second-generation techniques versus each other:

We found one systematic review (search date 2007 [48]) comparing thermal balloon ablation with other second-generation techniques. We found two subsequent RCTs comparing thermal balloon and bipolar radiofrequency ablation [49] [50] and one RCT comparing thermal balloon ablation with and without post-procedural curettage. [51] We also found a 5-year follow-up of one RCT already included in the systematic review. [48]

Menstrual blood loss

Different second-generation techniques compared with each other Bipolar radiofrequency ablation seems more effective at reducing blood loss by 12 months post procedure than thermal balloon ablation. However, post-procedure curettage does not seem to improve the efficacy of thermal balloon ablation (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Menstrual blood loss					
[48] Systematic review	126 pre-menopausal women Data from 1 RCT	**Amenorrhoea , 1 year** 3/43 (8%) with thermal balloon ablation 36/83 (43%) with bipolar radiofrequency ablation	Reported as significant P value not reported	○○○	bipolar radiofrequency ablation

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[50] RCT	160 pre-menopausal women	**Amenorrhoea , 1 year** 17/71 (24%) with hydrothermablation 35/75 (47%) with bipolar radiofrequency ablation	RR 2.0 95% CI 1.2 to 3.1	●●○	bipolar radiofrequency ablation
[49] RCT	81 premenopausal women	**Amenorrhoea , 1 year** 6/26 (23%) with thermal balloon ablation 14/25 (56%) with bipolar radiofrequency ablation	RR 2.4 95% CI 1.1 to 5.3	●●○	bipolar radiofrequency ablation
[51] RCT	250 pre-menopausal women	**Amenorrhoea , 1 year** 46/124 (37%) with thermal balloon ablation 42/126 (33%) with thermal balloon ablation plus post-procedural curettage	P = 0.53	⟷	Not significant

Need for re-treatment

Different second-generation techniques compared with each other We don't know whether thermal balloon ablation is more effective than bipolar frequency ablation at reducing the need for further ablation or hysterectomy (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Re-intervention rate					
[50] RCT	160 pre-menopausal women	**Re-intervention rate , 1 year** 20/71 (28%) with hydrothermablation 6/75 (8%) with bipolar radiofrequency ablation	RR 0.29 95% CI 0.12 to 0.67	●●○	bipolar radiofrequency ablation
[49] RCT	81 premenopausal women	**Re-intervention , 1 year** 2/26 (8%) with thermal balloon ablation 0/25 (0%) with bipolar radiofrequency ablation	P value not reported		
Rates of hysterectomy					
[50] RCT	160 pre-menopausal women	**Hysterectomy rates , 1 year** 8/71 (11%) with hydrothermablation 4/75 (5%) with bipolar radiofrequency ablation	RR 0.49 95% CI 0.15 to 1.5	⟷	Not significant
[49] RCT	81 premenopausal women	**Hysterectomy rates , 1 year** 1/26 (3.8%) with thermal balloon ablation 1/25 (4.0%) with bipolar radiofrequency ablation	P value not reported		

No data from the following reference on this outcome. [48] [51]

Patient satisfaction

Different second-generation techniques compared with each other Bipolar radiofrequency ablation seems more effective than thermal balloon ablation at increasing the rate of patient satisfaction (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Patient satisfaction					
[50] RCT	160 premenopausal women	**Patient satisfaction , 1 year** 48/71 (68%) with hydrothermablation 65/75 (87%) with bipolar radiofrequency ablation	RR 1.3 95% CI 1.03 to 1.6	●○○	bipolar radiofrequency ablation
[48] Systematic review	126 premenopausal women Data from 1 RCT	**Patient satisfaction with treatment , 1 year** 79% with thermal balloon ablation 90% with bipolar radiofrequency ablation Absolute numbers not reported	Reported as significant P value not reported	○○○	bipolar radiofrequency ablation

No data from the following reference on this outcome. [49] [51]

Quality of life

Different second-generation techniques compared with each other We don't know which second-generation technique is more effective at improving quality-of-life scores (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Quality of life					
[49] RCT	81 premenopausal women	**Mean improvement in EQ-5D multi-attribute utility tool , 1 year** 39.5 with thermal balloon ablation 48.3 with bipolar radiofrequency ablation	Difference: +8.9 95% CI –6.5 to +24.2 P = 0.3	⟷	Not significant

No data from the following reference on this outcome. [48] [50] [51]

Intraoperative and postoperative complications

Different second-generation techniques compared with each other We don't know which second-generation technique is more effective at reducing intraoperative and postoperative complications (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Intraoperative and postoperative complications					
[48] Systematic review	126 premenopausal women Data from 1 RCT	**Complication rate** 0 with thermal balloon ablation 0 with bipolar radiofrequency ablation	The review found no complications for either group		
[50] RCT	160 premenopausal women	**Uterine perforation** 0/71 (0%) with hydrothermablation 1/75 (1%) with bipolar radiofrequency ablation	P value not reported		

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[49] RCT	81 premenopausal women	**Endometritis** 5/39 (13%) with thermal balloon ablation 2/42 (5%) with bipolar radiofrequency ablation	RR 2.7 95% CI 0.6 to 13.1 P = 0.2	⟷	Not significant

No data from the following reference on this outcome. [51]

Anaemia

No data from the following reference on this outcome. [48] [49] [50] [51]

Postoperative recovery

No data from the following reference on this outcome. [48] [49] [50] [51]

Adverse effects

No data from the following reference on this outcome. [48] [49] [50] [51]

Further information on studies

[48] **Second-generation techniques versus each other:** One of the RCTs comparing thermal balloon ablation with a bipolar radiofrequency technique found that the bipolar procedure was significantly quicker to perform than the thermal ablation (12 minutes [5–40 minutes] with bipolar radiofrequency *v* 28 minutes [14–55 minutes] with thermal ablation; P <0.001). The time taken for the procedures was not reported in the other studies. The study reporting 5-year follow-up of a trial included in the review [48] reported 48% amenorrhoea in the bipolar ablation group and 32% in the balloon arm (RR 1.6, 95% CI 0.93 to 2.6). There were 8 women in the bipolar ablation group (9.8%) and 5 in the balloon group (12.9%) who had undergone a hysterectomy.

[45] **First-generation techniques versus each other:** 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 were significantly higher in the laser ablation group (OR 6.0, 95% CI 1.7 to 20.9).The single RCT comparing cutting and coagulating waveforms with rollerball ablation showed that both were equally effective. [46] **First-generation techniques versus second-generation techniques:** The review found that second-generation techniques significantly reduced operating times compared with first-generation techniques (9 RCTs, 988 women with first-generation techniques, 774 women with second-generation techniques; WMD –14.86 minutes, 95% CI –19.68 minutes to –10.05 minutes). It found that operative difficulties were significantly higher in the second-generation technique group compared with the first-generation group (2 RCTs; 13/166 [8%] with second-generation *v* 3/167 [2%] with first-generation; 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 (OR 6.4, 95% CI 3.0 to 13.70), although there was significant heterogeneity in the trials when reporting this outcome.

Comment: 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%. [52] Intraoperative emergency procedures were performed in 1% of people, and two procedure-related deaths occurred.

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

OPTION GONADORELIN ANALOGUES (PREOPERATIVE)

- For GRADE evaluation of interventions for Menorrhagia, see table, p 66 .
- Preoperative gonadorelin analogues reduce long-term postoperative moderate or heavy blood loss, and increase amenorrhoea compared with placebo.

Benefits and harms

Gonadorelin analogues (GnRHa) versus placebo or no treatment:

We found one systematic review (search date 2001, 11 RCTs, 998 women). [53] The review identified 8 RCTs (618 women) that compared preoperative gonadorelin analogues (GnRHa) versus placebo or no treatment. See further information on studies for details on duration and difficulty of subsequent surgery.

Menstrual blood loss

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

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Amenorrhoea					
[53] Systematic review	Women with menorrhagia 2 RCTs in this analysis	**Postoperative amenorrhoea , 24 months** with gonadorelin analogues with placebo/no treatment Absolute results not reported	RR 1.62 95% CI 1.04 to 2.52 None of the RCTs included in the review used objective measures of postoperative menstrual blood loss. Rates of withdrawal or loss to follow-up were low in all RCTs	●○○	gonadorelin analogues
Continued heavy bleeding					
[53] Systematic review	Women with menorrhagia 4 RCTs in this analysis	**Risk of continued moderate or heavy periods , 6 to 12 months** with gonadorelin analogues with placebo/no treatment Absolute results not reported	RR 0.74 95% CI 0.59 to 0.92 None of the RCTs included in the review used objective measures of postoperative menstrual blood loss. Rates of withdrawal or loss to follow-up were low in all RCTs	●○○	gonadorelin analogues

Patient satisfaction

No data from the following reference on this outcome. [53]

Quality of life

No data from the following reference on this outcome. [53]

Anaemia

No data from the following reference on this outcome. [53]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse drug effects					
[53] Systematic review	618 women 2 RCTs in this analysis	**Intraoperative uterine perforations in people receiving endometrial thinning** 2/266 (0.8%) with gonadorelin analogues (goserelin) 1/275 (0.4%) with treatment or placebo	RR 2.01 95% CI 0.19 to 22.67	⟷	Not significant

GnRHa versus danazol:

We found one systematic review (search date 2001, 11 RCTs, 998 women). [53] The review identified three RCTs (340 women) that compared GnRHa (goserelin or decapeptyl) versus danazol. See further information on studies for details on duration and difficulty of subsequent surgery.

Menstrual blood loss

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

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Postoperative amenorrhoea					
[53] Systematic review	340 women 3 RCTs in this analysis	**Postoperative amenorrhoea , 12 months** with gonadorelin analogues (goserelin or decapeptyl) with danazol Absolute results not reported	RR 1.18 95% CI 0.18 to 1.57	⟷	Not significant

Patient satisfaction

No data from the following reference on this outcome. [53]

Quality of life

No data from the following reference on this outcome. [53]

Anaemia

No data from the following reference on this outcome. [53]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse drug effects					
[53] Systematic review	705 women 3 RCTs in this analysis	**Withdrawal because of adverse effects** 1/566 (1%) with gonadorelin analogues (goserelin or decapeptyl) 11/139 (8%) with danazol	RR 44.80 95% CI 5.83 to 344.00	●●●	gonadorelin analogues
[53] Systematic review	340 women 3 RCTs in this analysis	**Adverse effects** with gonadorelin analogues (goserelin or decapeptyl) with danazol The review found that goserelin significantly increased hot flushes, depression, vaginal dryness, and reduced libido compared with danazol. Oily skin, hirsutism, and weight gain were significantly more common with danazol			

GnRHa versus other medical treatments:

We found one systematic review (search date 2001). [53] The review identified two RCTs (140 women) that compared 4 interventions: preoperative GnRHa, danazol, progestogens, and no treatment. The trials were too small to allow firm conclusions to be drawn.

Further information on studies

[53] **GnRHa versus placebo:** The review found no significant difference in patient satisfaction or in the likelihood of having further surgery. The 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).

[53] **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).

Comment:

OPTION **DANAZOL**

- For GRADE evaluation of interventions for Menorrhagia, see table, p 66 .
- We don't know whether danazol is beneficial when used preoperatively.

Benefits and harms

Danazol versus placebo:

We found one systematic review (search date 2001). [53] The review identified two small RCTs, and we found one subsequent RCT, [54] comparing preoperative danazol versus preoperative placebo. See further information on studies for details on duration of subsequent surgery.

Menstrual blood loss

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

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Postoperative amenorrhoea					
[53] Systematic review	50 women Data from 1 RCT	**Postoperative amenorrhoea , 12 months** with danazol with placebo Absolute results not reported	RR 1.31 95% CI 0.82 to 2.08	⟷	Not significant
[53] Systematic review	20 women Data from 1 RCT	**Postoperative amenorrhoea , 24 months** with danazol with placebo Absolute results not reported	RR 3.00 95% CI 0.79 to 11.44	⟷	Not significant
[54] RCT	132 women	**Postoperative amenorrhoea rate , 1 year** 49% with danazol 52% with placebo Absolute numbers not reported 129 women analysed	Reported as not significant P value not reported	⟷	Not significant

Patient satisfaction

No data from the following reference on this outcome. [53] [54]

Quality of life

No data from the following reference on this outcome. [53] [54]

Anaemia

No data from the following reference on this outcome. [53] [54]

Adverse effects

No data from the following reference on this outcome. [53] [54]

Danazol versus gonadorelin analogues:

See option on gonadorelin analogues, p 58 .

Danazol versus other medical treatments:

We found one systematic review (search date 2001), [53] which identified two RCTs (140 women) comparing 4 interventions: preoperative danazol, gonadorelin analogues, progestogens, and no treatment. The trials were too small to allow firm conclusions to be drawn.

Further information on studies

[54] The RCT found that danazol significantly reduced operating time compared with placebo (25.7 minutes with danazol *v* 33.6 minutes with placebo; P <0.001).

Comment: None.

OPTION PROGESTOGENS (ORAL)

- For GRADE evaluation of interventions for Menorrhagia, see table, p 66 .
- We don't know whether oral progestogens are beneficial when used preoperatively.

Benefits and harms

Oral progestogens versus no treatment:

We found one systematic review (search date 2001, 3 RCTs, 110 women). [53]

Menstrual blood loss

Compared with no preoperative treatment Oral progestogens may be no more effective at producing postoperative amenorrhoea (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Postoperative amenorrhoea					
[53] Systematic review	70 women 2 RCTs in this analysis	**Postoperative amenorrhoea , 2 years** with oral progestogens with no treatment Absolute results not reported	RR 0.75 95% CI 0.36 to 1.54	⟷	Not significant

Patient satisfaction

No data from the following reference on this outcome. [53]

Quality of life

No data from the following reference on this outcome. [53]

Anaemia

No data from the following reference on this outcome. [53]

Adverse effects

No data from the following reference on this outcome. [53]

Oral progestogens versus other medical treatments:

We found one systematic review (search date 2001, 3 RCTs, 110 women). [53] Two RCTs included in the review (140 women) compared 4 interventions: oral progestogens, gonadorelin analogues, danazol, and no treatment. The trials were too small to allow firm conclusions to be drawn.

Further information on studies

Comment:

GLOSSARY

Laser ablation A hysteroscopic procedure in which endometrium is destroyed under direct vision by a laser beam.

Transcervical endometrial resection A hysteroscopic procedure in which endometrium is removed under direct vision by using an electrosurgical loop.

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

Contraceptives (combined oral) New evidence added. [23] [24] Categorisation unchanged (Unknown effectiveness), as there remains insufficient good-quality evidence to assess the effects of combined oral contraceptives in women with menorrhagia.

Endometrial destruction New evidence added. [40] [48] [49] [50] [51] Two systematic reviews updated. [31] [45] Categorisation unchanged (Likely to be beneficial).

Hysterectomy New evidence added. [40] Categorisation unchanged (Beneficial).

Progestogens (intrauterine) New evidence added [28] [30] and one review updated. [31] Categorisation unchanged (Unknown effectiveness), as there remains insufficient good-quality evidence to assess the effects of intrauterine progestogens in women with menorrhagia.

Tranexamic acid New evidence added. [15] Categorisation unchanged (Beneficial).

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Competing interests: KD is the co-author of two systematic reviews referenced in this review. She has also been reimbursed by Berlex, Canada, for speaking on menorrhagia. SC declares that she has no competing interests.

Disclaimer

GRADE **Evaluation of interventions for Menorrhagia.**

Important outcomes	Anaemia, Intraoperative and postoperative complications, Menstrual blood loss, Need for re-treatment, Patient satisfaction, Postoperative recovery, Quality of life								
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]	Menstrual blood loss	NSAIDs versus placebo	4	0	0	–1	0	Moderate	Directness point deducted for differences in regimens between trials
2 (61) [12]	Menstrual blood loss	NSAIDs versus each other	4	–1	0	–1	0	Low	Quality point deducted for sparse data. Directness point deducted for small number of comparisons
3 (79) [12] [13]	Menstrual blood loss	NSAIDs versus danazol	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
2 (48) [12]	Menstrual blood loss	NSAIDs versus oral progestogens (luteal phase)	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
3 (at least 340) [3] [14] [15]	Menstrual blood loss	Tranexamic acid versus placebo	4	–1	0	0	0	Moderate	Quality point deducted for incomplete presentation of results
1 (187) [15]	Quality of life	Tranexamic acid versus placebo	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
4 (164) [14] [3] [17]	Menstrual blood loss	Tranexamic acid versus NSAIDs	4	–3	0	0	0	Very low	Quality points deducted for sparse data, poor follow-up, and other methodological flaws
1 (81) [17]	Menstrual blood loss	Tranexamic acid versus etamsylate	4	–3	0	0	0	Very low	Quality points deducted for sparse data, poor follow-up, and other methodological flaws
2 (146) [19] [20]	Menstrual blood loss	Tranexamic acid versus oral progestogens (luteal phase)	4	–2	0	0	0	Low	Quality points deducted for sparse data and methodological flaws
1 (81) [17]	Menstrual blood loss	Etamsylate versus 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]	Menstrual blood loss	Danazol versus 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) [12] [13] [22]	Menstrual blood loss	Combined oral contraceptives versus NSAIDs	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (38) [12] [13] [22]	Menstrual blood loss	Combined oral contraceptives versus danazol	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
2 (151) [23] [24]	Menstrual blood loss	Combined oral contraceptives versus intrauterine progestogens	4	–1	–1	–1	0	Very low	Quality point deducted for sparse data. Consistency point deducted for conflicting results. Directness point deducted for different doses of contraceptive
2 (151) [23] [24]	Quality of life	Combined oral contraceptives versus intrauterine progestogens	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
1 (39) [23]	Anaemia	Combined oral contraceptives versus intrauterine progestogens	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
2 (51) [18]	Menstrual blood loss	Progestogens (oral) in the luteal phase versus danazol	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
1 (162) [28]	Menstrual blood loss	Intrauterine progestogens versus oral progestogen (luteal phase)	4	–1	0	0	0	Moderate	Quality point deducted for sparse data

Important outcomes	Anaemia, Intraoperative and postoperative complications, Menstrual blood loss, Need for re-treatment, Patient satisfaction, Postoperative recovery, Quality of life								
Studies (Participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
2 (<74) [18] [29]	Menstrual blood loss	Intrauterine progestogens versus oral progestogen (long cycle)	4	–3	0	–1	0	Very low	Quality points deducted for sparse data, incomplete reporting of results, and baseline differences in severity of menorrhagia. Directness point deducted for analysis of indirect comparisons
1 (44) [29]	Patient satisfaction	Intrauterine progestogens versus oral progestogen (long cycle)	4	–2	0	–1	0	Very low	Quality points deducted for sparse data and incomplete reporting of results. Directness point deducted for unclear clinical importance of outcome measure
2 (<81) [18] [29]	Menstrual blood loss	Intrauterine progestogens versus NSAIDs	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
1 (30) [29]	Menstrual blood loss	Intrauterine progestogens versus danazol	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
at least 5 (at least 317) [29] [30] [31]	Menstrual blood loss	Intrauterine progestogens versus endometrial destruction (ablation)	4	–1	–1	–1	0	Very low	Quality point deducted for incomplete reporting of results. Consistency point deducted for conflicting results. Directness point deducted for study involving mainly women <40 years
3 at least (310 at most) [29] [31]	Need for re-treatment	Intrauterine progestogens versus endometrial destruction (ablation)	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
4 at most (at least 274) [29] [31]	Patient satisfaction	Intrauterine progestogens versus endometrial destruction (ablation)	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
3 (210 at most) [30] [31]	Quality of life	Intrauterine progestogens versus endometrial destruction (ablation)	4	–1	–1	0	0	Low	Quality point deducted for incomplete reporting of results. Consistency point deducted for conflicting results
1 (33) [31]	Anaemia	Intrauterine progestogens versus endometrial destruction (ablation)	4	–2	0	0	0	Low	Quality points deducted for for sparse data and incomplete reporting of results
1 (232) [18] [30] [31]	Patient satisfaction	Intrauterine progestogens versus hysterectomy	4	–1	0	–1	0	Low	Quality point deducted for incomplete reporting. Directness point deducted for high switch rates to surgery
1 (232) [18] [30] [31]	Quality of life	Intrauterine progestogens versus hysterectomy	4	–1	0	–1	0	Low	Quality point deducted for incomplete reporting. Directness point deducted for high switch rates to surgery
1 (228) [18] [30] [31]	Anaemia	Intrauterine progestogens versus 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?									
3 (440) [3] [39]	Menstrual blood loss	Hysterectomy versus endometrial destruction	4	0	0	0	0	High	
1 (708) [3]	Need for re-treatment	Hysterectomy versus endometrial destruction	4	–1	0	0	0	Moderate	Quality point deducted for wide confidence intervals in largest RCT contributing results regarding this outcome

Important outcomes	Anaemia, Intraoperative and postoperative complications, Menstrual blood loss, Need for re-treatment, Patient satisfaction, Postoperative recovery, Quality of life								
Studies (Participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
at least 5 (at least 836) [40]	Patient satisfaction	Hysterectomy versus endometrial destruction	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
2 (394) [40]	Quality of life	Hysterectomy versus endometrial destruction	4	–1	0	–1	0	Low	Quality point deducted for incomplete reporting. Directness point deducted for no direct comparison between groups
at least 7 (at least 1066) [3] [40]	Postoperative recovery	Hysterectomy versus endometrial destruction	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
at least 2 (at least 708) [3] [40]	Intraoperative and postoperative complications	Hysterectomy versus endometrial destruction	4	–1	–1	0	0	Low	Quality point deducted for incomplete reporting of results. Directness point deducted for contradictory results
3 (733) [41]	Menstrual blood loss	Subtotal hysterectomy versus total hysterectomy	4	0	0	–1	0	Moderate	Directness point deducted for analysis not limited to women with menorrhagia
2 (411) [41]	Intraoperative and postoperative complications	Subtotal hysterectomy versus total hysterectomy	4	0	0	–1	0	Moderate	Directness point deducted for analysis not limited to women with menorrhagia
23 (1728) [42]	Postoperative recovery	Abdominal hysterectomy versus vaginal or laparoscopic hysterectomy	4	0	0	–1	0	Moderate	Directness point deducted for analysis not limited to women with menorrhagia
1 (187) [31]	Menstrual blood loss	Endometrial destruction (resection or ablation) versus oral drugs	4	–1	0	–1	0	Low	Quality point deducted for sparse data. Directness point deducted for range of drugs in comparison
4 (2085) [45]	Menstrual blood loss	First-generation versus second-generation techniques	4	0	0	0	0	High	
7 (1028) [45]	Need for re-treatment	First-generation versus second-generation techniques	4	0	0	0	0	High	
11 (1690) [45]	Patient satisfaction	First-generation versus second-generation techniques	4	0	0	0	0	High	
8 (1885) [45]	Intraoperative and postoperative complications	First-generation versus second-generation techniques	4	0	–1	0	0	Moderate	Consistency point deducted for conflicting results
4 (391) [45] [46]	Menstrual blood loss	First-generation techniques versus each other	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
3 (438) [45] [46]	Need for re-treatment	First-generation techniques versus each other	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
3 (462) [45] [46]	Patient satisfaction	First-generation techniques versus each other	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting
2 (486) [45]	Intraoperative and postoperative complications	First-generation techniques versus each other	4	0	–1	0	0	Moderate	Consistency point deducted for conflicting results
4 (517) [48] [49] [50] [51]	Menstrual blood loss	Second-generation techniques versus each other	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
2 (241) [49] [50]	Need for re-treatment	Second-generation techniques versus each other	4	–1	–1	0	0	Low	Quality point deducted for incomplete reporting of results. Consistency point deducted for conflicting results

Important outcomes	Anaemia, Intraoperative and postoperative complications, Menstrual blood loss, Need for re-treatment, Patient satisfaction, Postoperative recovery, Quality of life								
Studies (Participants)	**Outcome**	**Comparison**	**Type of evidence**	**Quality**	**Consistency**	**Directness**	**Effect size**	**GRADE**	**Comment**
2 (286) [48] [50]	Patient satisfaction	Second-generation techniques versus each other	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
1 (81) [49]	Quality of life	Second-generation techniques versus each other	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
3 (367) [48] [49] [50]	Intraoperative and postoperative complications	Second-generation techniques versus each other	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
What are the effects of endometrial thinning before endometrial destruction in treating menorrhagia?									
8 (618) [53]	Menstrual blood loss	Gonadorelin analogues (GnRHa) versus placebo or no treatment	4	–1	0	0	0	Moderate	Quality point deducted for no objective measure of menorrhagia
3 (340) [53]	Menstrual blood loss	GnRHa versus danazol	4	0	0	0	0	High	
3 (202) [53] [54]	Menstrual blood loss	Danazol versus placebo	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
2 (70) [53]	Menstrual blood loss	Oral progestogens versus no treatment	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting

We initially allocate 4 points to evidence from RCTs, and 2 points to evidence from observational studies. To attain the final GRADE score for a given comparison, points are deducted or added from this initial score based on preset criteria relating to the categories of quality, directness, consistency, and effect size. Quality: based on issues affecting methodological rigour (e.g., incomplete reporting of results, quasi-randomisation, sparse data [<200 people in the analysis]). Consistency: based on similarity of results across studies. Directness: based on generalisability of population or outcomes. Effect size: based on magnitude of effect as measured by statistics such as relative risk, odds ratio, or hazard ratio.