

Heavy menstrual bleeding

National Collaborating Centre for Women's
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Evidence tables

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Contents

Abbreviations

Evidence tables

Health economics studies for all sections of the guideline

Table 3.1	Menstrual bleeding patterns, prevalence of HMB, presence of uterine pathology, and risk-factors associated with HMB – comparative studies
Table 3.2	Menstrual bleeding patterns, prevalence of HMB, presence of uterine pathology, and risk-factors associated with HMB – diagnostic studies
Table 3.3	Menstrual bleeding patterns, prevalence of HMB, presence of uterine pathology, and risk-factors associated with HMB – non-comparative studies
Table 3.4	Impact on quality of life by HMB – comparative studies
Table 3.5	Impact of quality of life by HMB – non-comparative studies
Table 4.1	Estimation of menstrual blood loss and quality of life – comparative studies
Table 4.2	Estimation of menstrual blood loss – diagnostic studies
Table 4.3	Estimation of menstrual blood loss and quality of life – non-comparative studies
Table 4.4	Tests for exclusion of underlying conditions – comparative studies
Table 4.5	Tests for exclusion of underlying pathology – diagnostic studies
Table 4.6	Tests for exclusion of underlying conditions – non-comparative studies
Table 5.1	Patient education – comparative studies
Table 5.2	Patient education – non-comparative studies
Table 5.3	Patient choice – comparative studies
Table 5.4	Patient choice – non-comparative studies
Table 8.1	LNG-IUS for treatment of HMB – comparative studies
Table 8.2	LNG-IUS for treatment of HMB – non-comparative studies
Table 8.3	Combined oral contraceptives for treatment of HMB – comparative studies
Table 8.4	Oral progestogens for treatment of HMB – comparative studies
Table 8.5	Other pharmaceutical treatment for HMB – comparative studies
Table 8.6	GnRH-a for treatment of HMB – comparative studies
Table 8.7	Antifibrinolytics for treatment of HMB – comparative studies
Table 8.8	NSAIDs for treatment of HMB – comparative studies
Table 8.9	Etamsylate for treatment of HMB – comparative studies
Table 9.1	Surgery as first-line treatment for HMB – comparative studies
Table 10.1	Indications for non-hysterectomy surgery or interventional radiology – comparative studies
Table 10.2	Indications for surgery (non-hysterectomy) – non-comparative studies
Table 10.3	Endometrial ablation for treating HMB – comparative studies
Table 10.4	Endometrial ablation for treatment of HMB – additional non-comparative studies
Table 10.5	Dilatation and curettage for treatment of HMB – comparative studies
Table 11.1	UAE for treatment of uterine fibroids – comparative RCT and observational studies
Table 11.2	Radiological interventions for treatment of uterine fibroids – additional non-comparative studies
Table 11.3	Myomectomy for treatment of uterine fibroids – comparative studies
Table 11.4	Myomectomy for treatment of uterine fibroids – non-comparative studies
Table 12.1	Indications for hysterectomy – non-comparative studies
Table 12.2	Hysterectomy for treatment of HMB – comparative studies
Table 12.3	Hysterectomy for treatment of HMB – non-comparative studies
Table 13.1	Oophorectomy undertaken at the time of hysterectomy – comparative studies
Table 13.2	Oophorectomy undertaken at the time of hysterectomy – non-comparative studies
Table 14.1	Surgical competencies in HMB – comparative studies
Table 14.2	Surgical competencies in HMB – non-comparative studies

References

Abbreviations

AH	abdominal hysterectomy
AM	abdominal myomectomy
AUB	abnormal uterine bleeding
BMD	bone mineral density
BMI	body mass index
BREA	bipolar radiofrequency endometrial ablation
BSO	bilateral salpingo-oophorectomy
CI	confidence interval
COCs	combined oral contraceptives
D&C	dilatation and curettage
DMPA	depot medroxyprogesterone acetate
DUB	dysfunctional uterine bleeding
EL	evidence level (level of evidence)
ELA	endometrial laser ablation
ELITT	endometrial laser intrauterine thermo-therapy
ERT	estrogen replacement therapy
FSH	follicle-stimulating hormone
GDG	Guideline Development Group
GHQ	General Health Questionnaire
GnRH	gonadotrophin-releasing hormone
GPP	good practice point
HMB	heavy menstrual bleeding
HRQoL	health-related quality of life
HRT	hormone replacement therapy
HTA	health technology appraisal
ICER	incremental cost-effectiveness ratio
ITT	intention to treat
LAVH	laparoscopically assisted vaginal hysterectomy
LH	laparoscopic hysterectomy; luteinising hormone
LNG-IUS	levonorgestrel-releasing intrauterine system
LR	likelihood ratio
MBL	menstrual blood loss
MEA	microwave endometrial ablation
MPA	medroxyprogesterone acetate
MRI	magnetic resonance imaging
NCC-WCH	National Collaborating Centre for Women's and Children's Health
NET	norethisterone
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NPV	negative predictive value
NS	not statistically significant
NSAIDs	nonsteroidal anti-inflammatory drugs
OCP	oral contraceptive pill
OR	odds ratio
PBAC	pictorial blood loss assessment chart
PCT	primary care trust
PPIP	Patient and Public Involvement Programme
PPV	positive predictive value
QALY	quality-adjusted life year
RCT	randomised controlled trial
REA	rollerball endometrial ablation
RiCof	ristocetin cofactor
RR	relative risk

SCHS	saline contrast hysterosonography
SD	standard deviation
SE	standard error
SIGN	Scottish Intercollegiate Guidelines Network
SIS	saline infusion sonography
TAH	total abdominal hysterectomy
TBEA	thermal balloon endometrial ablation
TCRE	transcervical resection of the endometrium
<i>t.i.d.</i>	three times a day
TLH	total laparoscopic hysterectomy
TVHS	transvaginal hysterosonography
TVS	transvaginal ultrasound
TXA	tranexamic acid
UAE	uterine artery embolisation
VH	vaginal hysterectomy
VTH	vaginal total hysterectomy
vWF	von Willebrand factor
vWD	von Willebrand disease
WMD	weighted mean difference
WTP	willingness to pay

Heavy menstrual bleeding

Health economics studies for all sections of the guideline

Bibliographic information	Study details	Outcomes	Population characteristics	Analysis details	Results and comments
Cameron 1996 ⁵⁶⁰	Cost analysis Model or clinical trial: clinical trial Perspective of analysis: other	Source of utility values: N/A Primary clinical outcomes: successful surgery.		Currency: GBP Year of costing: 1994 Discount rate(s) used for costs: 6% Discount rate(s) used for benefits: N/A	Results: Costs to the NHS of TCRE and ELA were less than with hysterectomy (24% and 20% respectively). Women who underwent TCRE or ELA also incurred a lower cost. Comments and limitations: This study is not a cost-effectiveness or cost-utility analysis. It is limited by only measuring the cost of carrying out the procedure while not comparing outcomes. It does not provide an ICER.
Edwards 2006 ⁴¹⁷	Cost-utility analysis Model or clinical trial: clinical trial Perspective of analysis: healthcare provider	Source of utility values: Utility values taken from SF-36, EQ-5D and GHQ-28 scores measured as pre-treatment baseline, one month following treatment and 12 months following treatment. Primary clinical outcomes: Quality of life measures were the primary outcome measure.	157 women with uterine fibroids (myomas) recruited from six gynaecology departments in Scotland and two centres in England.	Currency: GBP Year of costing: 2004 Discount rate(s) used for costs: N/A Discount rate(s) used for benefits: N/A	Results: No statistically significant differences in quality of life as measured by the SF-36, EQ-5D and GHQ-28 were found at 12 months. The analysis was therefore based on cost-minimisation. The clinical conclusion was that 'both surgery (hysterectomy or myomectomy) and UAE provide a successful treatment for a majority of women with symptomatic fibroids'. UAE was associated with significantly lower costs at 12 months (mean of £1,685.36 compared with £2,566.87). Comments and limitations: The study is limited in that follow-up has only been to 12 months as of now. A more accurate picture of the results will be available after longer follow-up is completed. Sensitivity analysis conducted on costs showed that the conclusions from the model are robust.
Garside 2004 ⁵⁶¹	Cost-utility analysis Model or clinical trial: modelling Perspective of analysis: healthcare system	Source of utility values: Utility values for hysterectomy and ablation taken from Sculpher. ⁵⁵⁴ Some utility values are assumptions. Primary clinical outcomes: Reduced menstrual blood loss.		Currency: GBP Year of costing: 2003 Discount rate(s) used for costs: 6% Discount rate(s) used for benefits: 6%	Results: AH was more costly, but resulted in more QALYs than either MEA or TBEA. Both MEA and TBEA result in more QALYs and cost less than TCRE and Rollerball ablation. The incremental cost per QALY for AH over MEA/TBEA was estimated at just over £2,000. At a willingness to pay of £20,000 per QALY (the NHS assumed rate) AH can be considered the most cost-effective option. Comments and limitations: The study is only limited in the range of utility values that were available. This uncertainty was explored in sensitivity analysis, and was found to have an impact on the results.
Jack 2005 ⁴⁰⁰	Cost-effective analysis Model or clinical trial: Clinical trial Perspective of analysis: healthcare system	Source of utility values: HRQoL outcomes were measured using the SF-12 measure. Primary clinical outcomes: HRQoL	210 women with a complaint of excessive menstrual loss.	Currency: GBP Year of costing: 2002 Discount rate(s) used for costs: N/A Discount rate(s) used for benefits: N/A	Results: SF-12 scores for both treatment arms showed significant improvement at 12 months. There was no significant difference between arms at 12 months. A cost-minimisation analysis showed that the mean health service costs were lower in the experimental group (£444) than in the control group (£568). The study concluded that Post-menses outpatient MEA is favourable when compared with standard MEA. Comments and limitations: Because the study is set in Scotland, prices may not reflect prices in the NHS in England. The study is only reported at 1 year to date. Longer term results would be of benefit, though it seems likely that the results will not be affected.
Lumsden 2000 ⁵⁰⁰	Cost-utility analysis Model or clinical trial: clinical trial Perspective of analysis: healthcare system	Source of utility values: Utility values assessed using EQ-5D visual analogue scale. Primary clinical outcomes: QALY; length of operation, total length of stay, admission to ITU, additional surgery required, readmissions and blood transfusions		Currency: GBP Year of costing: N/A Discount rate(s) used for costs: N/A Discount rate(s) used for benefits: N/A	Results: LH took longer than AH. Length of hospital stay was lower in LH than AH. LH was more expensive due to longer operating time and the use of disposable equipment. No difference was found in patient reported outcomes including time to return to normal activities and quality of life measures or in clinical outcomes. LH is not likely to be cost-effective. Comments and limitations: Year that cost data relates to is not stated. Source of cost data was not specified. The study is limited by poor reporting of costs and by poor follow-up at 1 year. Appropriate measures were taken to address the problem of follow-up.
Raju 1994 ⁵⁰⁶	Cost-effective analysis Model or clinical trial: clinical trial Perspective of analysis: healthcare system	Source of utility values: Primary clinical outcomes: The main clinical outcome indicators were length of operation, hospital stay, recovery time and time to return to work.		Currency: GBP Year of costing: Discount rate(s) used for costs: N/A Discount rate(s) used for benefits: N/A	Results: Mean cost for LH was £1,260 compared with £1,750 for AH. No ICERs were reported. The authors conclude that LH should be preferred to AH for the patient group studied. Comments and limitations: This study lacks data on effectiveness, so it is difficult to interpret the results or calculate a cost-effectiveness ratio. Sources and justifications for costs were poorly described. Patient costs were not included, but given the faster return to work and lower pain for patients undergoing LH vs AH.
Sculpher 1998 ⁵⁵⁴	Cost-utility analysis	Source of utility values: Utility weights		Currency: GBP	Results: AH is more costly over a 2 year period, but results in more QALYs. The incremental cost

Bibliographic information	Study details	Outcomes	Population characteristics	Analysis details	Results and comments
	Model or clinical trial: modelling Perspective of analysis: healthcare system	derived using time trade-off (TTO) techniques with 60 women with menorrhagia. Primary clinical outcomes: Reduced menstrual blood loss.		Year of costing: 1994 Discount rate(s) used for costs: 6% Discount rate(s) used for benefits: 6%	per QALY of AH is £1,500. AH can be considered cost-effective compared with TCRE. Comments and limitations: This study is the source of utility weights to be used in any modelling undertaken for the HMB guideline for women following hysterectomy.
Sculpher 2004 ⁵⁶²	Cost-utility analysis Model or clinical trial: clinical trial Perspective of analysis: healthcare system	Source of utility values: Utility values for all forms of hysterectomy were obtained using the EQ-5D generic measure of health status. Primary clinical outcomes: Outcomes in the study are expressed in QALYs.		Currency: GBP Year of costing: 1999 Discount rate(s) used for costs: N/A Discount rate(s) used for benefits: N/A	Results: When LH was compared VH, mean costs were £401 higher for LH, and mean QALYs per patient were 0.0015 higher. The ICER for this is £267,333. Taking into account uncertainty, LH is never more than 50% likely to be cost-effective when compared with VH, regardless of WTP for a QALY. When compared with AH, LH mean cost was £186 higher and produced 0.007 more QALYs per patient. The ICER when comparing LH to AH is £26,571. However, when considering the uncertainty, even at a WTP of £30,000 LH is only 56% likely to be cost-effective. Comments and limitations: The study takes an NHS perspective. Numerous studies have identified a potential reduction in hospital stay and quicker recovery as a result of LH compared with AH. In that case, benefits to the patient may be greater, meaning that the ICER for LH compared with AH may be much more favourable to LH. The time frame of the study means that no discounting was undertaken.

Heavy menstrual bleeding

Table 3.1 Menstrual bleeding patterns, prevalence of HMB, presence of uterine pathology, and risk-factors associated with HMB – comparative studies

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Clevenger-Hoeft 1999 ⁸⁰	Comparison; cohort; prospective EL = 2+	180: 100 asymptomatic, 80 AUB	Women: aged > 30 years Country: USA	Presence of pathology in people with and without AUB	No follow-up	Presence of pathology; accuracy of test – specificity, sensitivity	Presence of pathology by symptom status: Asymptomatic ($n = 100$; 39.5 years) – 10% polyps, 1% myomas, 13% intramural myomas AUB patients ($n = 80$; 41.1 years) – 32.5% polyps, 21.2% myomas, 57.5% intramural myomas $P < 0.05$ for all groups comparisons Accuracy of sonohysterography for identifying pathology in 48 women with histopathology available: sensitivity = 97%, specificity = 86%, PPV = 94%, NPV = 92%	Funding source: Not stated Study summary: Study shows that women with AUB have higher prevalence of uterine pathology than those without.
Fraser 1990 ³⁶	Epidemiology; diagnostic EL = 2+	316	Population characteristics: Women; menorrhagia; no clear pathology Country: Australia	Hysteroscopy or laparoscopy to identify pathology	N/A	Presence of pathology by MBL	Presence of pathology by level of MBL (< 60 ml, 60 to 120 ml, > 120 ml, All patients): Total numbers: 47, 59, 33, 182. 43 MBL was not measured. No pathology found: 35 (75%), 26 (44%), 12 (36%), 94 (51%). 21 MBL not measured. Fibroids: 3, 12, 12, 37. 10 MBL not measured. Endometriosis: 6, 19, 7, 45. 13 did not have MBL measured. Adenomyosis: 1, 2, 5. 2 MBL not measured. Endometrial polyps: 7, 7, 8, 29. 7 MBL was not measured. Other: 2, 3, 4, 11. 2 MBL was not measured.	Funding source: Not stated Study summary: Increased levels of HMB were associated with increased levels of uterine pathology. Fibroids were associated with HMB. Endometriosis was slightly associated with increases in MBL.
Granleese 1990 ⁶⁸	Prospective case-control EL = 2+	44 Women: 22 with menorrhagia, 22 matched controls	Population characteristics: Women; (with or without menorrhagia); age range 29–46 years; All multiparous Country: UK	Association between psychosocial factors and menorrhagia	1 survey	MBL – alkaline haematin; personality scores – Eysenck personality questionnaire; sexual behaviour questionnaire; personal history questionnaire	MBL – menorrhagic group ($n = 22$) = 90 ml (SD 60), range 13–194 ml. Controls ($n = 22$) = 34 ml (SD 7), range 22.51. Menstruation symptomology scores: menorrhagic = 27.41 (9.05) vs 13.05 (7.42) control ($P < 0.001$). Personality scores (Eysenck scale): psychotism – clinical = 1.64 (1.43) vs control = 3.64 (1.65), $P < 0.001$; extraverted = 10 (6.02) vs 13.23 (3.35), $P = 0.017$; neuroticism = 13.36 vs 14.91, $P = 0.079$; lie scale = 11.54 (4.23) vs 5 (3.32), $P < 0.001$. Objective menorrhagia ($n = 10$) vs subjective menorrhagia ($n = 12$): Symptom severity score = 26.6 (8.58) vs 28.08 (9.75), (NS). Psychotism = 2 vs 1.33, NS; extraverted = 8.9 vs 10.92, NS; neuroticism = 12.9 vs 13.75, NS; lie scale = 10.5 vs 12.42, NS.	Funding source: Not stated Study summary: Women complaining of menorrhagia should be objectively tested to ensure correct treatment, as no difference in psychological impact.
Harlow 2004 ¹²⁰	Systematic review EL = 2+	25049	Population characteristics: Women; developing countries Country: Colombia, Pakistan, Syria, Iran, Lebanon, Philippines, Turkey	Epidemiological studies – menstrual disorders		Prevalence of menstrual disorders – classification varied between countries	Prevalence of self-reported excessive menstrual bleeding = 4–27% reported in 6 studies.	Funding source: Not stated
Hurskainen 2001 ⁶⁶	Cross-sectional survey EL = 2–	226: split between < 60 ml and > 60 ml MBL (lower level used to ensure group difference).	Population characteristics: Women; subjective menorrhagia; scheduled for hysterectomy; uterine pathology excluded. Country: Finland	Psychosocial impact of menorrhagia; subjective vs objective menorrhagia		Psychosocial factors; QoL – SF-36; MBL – alkaline haematin	Using univariate analysis, difference between < 60 ml and > 60 ml groups: MBL = 36.3 vs 168.8; haemoglobin = 132.2 vs 128.3 ($P < 0.001$); anxiety – 33.4 vs 31.3 ($P = 0.031$); unemployment 17% vs 4% ($P = 0.001$); perceived inconvenience bleeding = 16.3 vs 18.2 ($P = 0.01$); abdominal pain = 5.7 vs 3.9 ($P = 0.014$); ferritin = 23.4 vs 12.9 ($P < 0.001$); no statistical difference between groups for: depression, psychosomatic symptoms, social support,	Funding source: Not stated Study summary: Psychosocial factors may account for women seeking help with MBL, as many who complain of menorrhagia have normal MBL, but psychosocial symptoms.

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							negative life events, sex life, visits to doctor, absent from work, out-of-pocket expense, and hospitalisation. Using multivariate analysis – unemployment, anxiety, perceived inconvenience, abdominal pain and ferritin were significant factors in explaining variance.	
James 2004 ¹⁴⁵	Systematic review; diagnostic studies EL = 2–	107 articles identified	Population characteristics: MEDLINE. 1990 to 2003. Keyword search only.	Testing for von Willebrand disease in menorrhagia	N/A	Prevalence of vWD or platelet abnormalities; sensitivity; specificity	5 studies showed prevalence of vWD of 5.3% to 20%. Samples sizes from 19 to 150. 6 studies showed sensitivity of between 79% and 100%. 4 studies showed specificity of between 80% to 95%.	Funding source: Dade-Behring Study summary: Inadequate evidence to support routine testing for vWD in menorrhagia
Krassas 1994 ⁵²	Epidemiology EL = 2+	428: 214 with thyroid disease; 214 matched controls	Population characteristics: Women; with or without thyroid disease Country: Greece	Association between thyroid condition and menstrual disorders	No follow-up	Presence of thyroid condition – TT3 and TT4 levels; menstrual disorders; smoking status; BMI	Of the 214 patients, 168 (78.5%) had regular menstrual cycles and 46 (21.5%) irregular cycles. Out of 214 normal controls, matched for age and weight, 196 (91.6%) had normal menstruation and 18 (8.4%) irregular cycles. 2 (4.5%) and 2 (11%) of thyrotoxic and normal controls had menorrhagia. No statistical difference between groups.	Funding source: Not stated Study summary: These data demonstrate that hyperthyroidism in women is less frequently associated with menstrual abnormalities than was previously believed.
Philipp 2003 ⁵⁶³	Cohort; epidemiology EL = 2+	126: 74 menorrhagia; 52 controls	Population characteristics: patient group: women; physician-diagnosed menorrhagia; known pathology excluded; scheduled for hysterectomy during study period; those taking pharmaceutical treatments asked to stop. Mean age – 40.4 (range 17 to 55) Controls: women; same as above but no menorrhagia. Country: USA	platelet functional defects association with menorrhagia		MBL – PBAC; platelet function test	Of 59 PBACs returned by study group: 51 had score > 100; 37 had score > 185. Platelet aggregation and ATP release, comparison between study ($n = 74$) and control ($n = 52$) groups: Platelet aggregation: epinephrine 16 vs 2 ($P = 0.005$); ristocetin 20 vs 4 ($P = 0.007$); collagen 9 vs 2 ($P = 0.105$); ADP 3 vs 1 ($P = 0.5$); arachidonic acid 6 vs 1 ($P = 0.13$). ATP release: ADP 30 vs 7 ($P = 0.0009$); arachidonic acid 16 vs 1 ($P = 0.001$); collagen 18 vs 5 ($P = 0.04$); thrombin 1 vs 0 (N/A).	Funding source: Association of Teachers Preventative Medicine grant Study summary: Underlying platelet problems in majority of women with unexplained menorrhagia. Suggests need for screening for inherited blood disorders and platelet problems in women with menorrhagia.
Shankar 2004 ⁴⁸	Systematic review EL = 2–	11 studies included in review	Population characteristics: Women; menorrhagia; screened for von Willebrand disease. Search undertaken on MEDLINE only using keyword search.	vWD as risk factor in menorrhagia	N/A	Prevalence of vWD	11 studies: 988 women with menorrhagia and vWD prevalence of 131 (13%, 95% CI 11 to 15.6%). Studies reported range from 5% to 24% of vWD. 4 studies from Europe, 5 from North America, 2 from elsewhere. 6 studies based on gynaecology outpatient clinics, 1 on coagulation clinic, 1 on administrative database, 2 on population study, 1 not stated. Menorrhagia state based on history in 5 studies, PBAC in 2, alkaline haematin in 2, and not stated in 2. vWF:Ag test only one used across studies, RiCof was second most common. Cut-off for vWD varied between studies. Different study designs and inclusion criteria probably account for differences between studies.	Funding source: Not stated
Shapley 2000 ⁶⁴	case-control; before-and-after study EL = 2–	170: 85 cases; 85 controls	Population characteristics: Women; Country: UK	Mental health measure on HADS; heavy bleeding based on patient records.		Mental health status correlation with help-seeking behaviour	No correlation between mental health dimensions – anxiety, depression and neurosis – and consultation for increased menstrual bleeding, $P = 0.302$, 1, 0.2 for borderline and definite cases. OR = 0.7 (0.37–1.31), 1 (0.43–2.34), 0.67 (0.36–1.21).	Funding source: Not stated

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Shapley 2002 ⁶³	Case-control EL = 2+	943 questionnaires sent – 645 usable	Population characteristics: Women; consulting for HMB; consulting for another condition; or community controls Country: UK	Consultation for HMB cases vs consulting controls; cases vs community controls	1 questionnaire	Consultation; MBL – subjective; GHQ score; HMB interference on lifestyle	Regression analysis of those consulting vs control group also consulting for other conditions: heaviness of periods interferes with life OR = 3.26 (1.92–5.54); heavy periods OR = 2.52 (1.41–4.49). Consulting vs non-consulting controls: heaviness of period OR = 3.25 (1.72–6.14), heavy periods OR = 2.57 (1.35–4.88). GHQ scores < 4 or > 4: consulting vs consulting controls – OR = 1.26 (0.74–2.13) and consulting vs non-consulting controls OR = 1.43 (0.85–2.38).	Funding source: Not stated Study summary: Study shows that interference with QoL by HMB is main reason for consultation.
Shapley 2003 ⁶²	Cohort; case-control EL = 2–	Population 1: 186: 46 menorrhagia; 79 consulting controls; 61 non-consulting controls reporting heavy bleeding interfered with life. Population 2: 160 cases and controls. Population 3: 494 controls – not consulted about periods in last 6 months	Population characteristics: Women; Country: UK	Reason for seeking medical attention study vs controls		QoL measures	Population 1: Reason why heaviness of bleeding interfered with life (case vs consulting control <i>P</i> value, case vs non-consulting control <i>P</i> value). Performance at employed work – <i>P</i> = 0.24, 0.40; performance of house work – <i>P</i> = 0.03, 0.06; days off work – <i>P</i> = 0.56, 0.22; life causing embarrassment – = 0.02, 0.17; mood – <i>P</i> = 0.53, 0.97; sex life – <i>P</i> = 0.12, 0.03; social life – <i>P</i> = 0.01, 0.005. Population 3 (<i>n</i> = 494): reasons for not consulting in last 6 months. 281 (57%) normal periods; 29 (6%) 'Women's burden'; 167 (34%) – I am coping; 53 (11%) observing; 25 (5%) too busy; 5 (1%) scared; 15 (3%) embarrassed. Women could give more than one reason	Funding source: Not stated Study summary: Study suggests psychosocial impact of HMB is a reason why women seek help.
Vercellini 1997 ⁵³	Cohort; epidemiology EL = 2–	331 examined – 315 included. 163 with endometriosis and 152 without.	Population characteristics: Women attending or scheduled for laparoscopy – for infertility, pelvic pain, adnexal masses; fibroids; IUD; hormonal treatments or drugs that affect menstruation; NSAIDs; serious concomitant illness excluded. Country: Italy	Effect of endometriosis on menstruation	Completed questionnaire	MBL – PBAC, endometriosis	Of 315 – 163 had endometriosis, 152 did not. PBAC score by group: 110 (66.6–156.5) for endometriosis group vs 84 (56–129) in control group (<i>P</i> = 0.007 Mann–Whitney <i>u</i> test).	Funding source: Not stated Study summary: Study suggests women with endometriosis have higher MBL than those without.
Woo 2002 ⁴⁷	Cohort; prospective case-control EL = 2+	76: 38 menorrhagia; 38 matched normal MBL.	Population characteristics: Women Country: Ireland	Association of von Willebrand disease to menorrhagia menorrhagia patients vs normal patients		MBL – alkaline haematin; vWD status	Comparison of factors between those with (<i>n</i> = 26) and without (<i>n</i> = 31) menorrhagia (both groups exclude HRT users). vWD – 15.4% vs 3.2 (NS)	Funding source: Not stated Study summary: Small numbers mean that statistical significance was not achieved.
Zielhuis 1989 ⁶⁹	Cross-sectional survey EL = 2–	592 – 399 useable responses: 193 exposed to perchloroethylene; 206 unexposed.	Population characteristics: Women Country: Netherlands	Exposure or not to perchloroethylene Exposed vs unexposed		Menstrual symptoms	Menorrhagia: 22% prevalence in reference group. Odd ratio of 3.0 (95% CI 1.6–5.6) in exposed group.	Funding source: Not stated Study summary: Study shows that working with industrial chemicals is associated with HMB.

Table 3.2 Menstrual bleeding patterns, prevalence of HMB, presence of uterine pathology, and risk-factors associated with HMB – diagnostic studies

Bibliographic information	Study type and evidence level	No. of patients and prevalence	Population characteristics	Type of test and reference standard	Sensitivity, specificity, PPV and NPV	Source of funding and additional comments
Alexopoulos 1999 ⁷⁵	Case series; retrospective EL = III	2581	Women; hysteroscopies for any menstrual problem – 37.5% for menorrhagia Country: UK	Hysteroscopies	Reason for hysteroscopy: menorrhagia (37.5%), postmenopausal bleeding (33.4%), intermenstrual bleeding (26.7%), and metrorrhagia (8.8%). Findings: Submucous fibroids (11.4%), polyps (10.6%), endocervical polyps in 42 (1.6%), cervical stenosis 6 patients. Hyperplasia 22% post-menopausal vs 3.4% pre-menopausal. 19 malignant appearances found.. Submucous fibroids more common in pre- to post-menopause (11.8 vs 10.7; $P = 0.43$). Polyps more common in post- to pre-menopause (13.9 vs 8.9%; $P = 0.0001$). Hysteroscopy success rate: 96.8% undertaken, but 83 (3.2%) failed. 68.4% of patients discharged. 38.1% of pre-menopausal and 19% of post-menopausal ($P < 0.0001$) required further follow-up. 406 (16.3) needed medical treatment. 185 (17.3%) needed surgery.	Funding source: Not stated Study summary: Outpatient hysteroscopy is safe, acceptable and well-tolerated method.
Ash 1996 ⁷⁷	Diagnostic; retrospective EL = III	310	Women; diagnosed with DUB; pre-menopausal status; undergone endometrial sampling by Pipelle; Women in menopause excluded Average age 39 years (17–53) Country: Canada	Pipelle endometrial biopsy	Pipelle outcome: 266 (85.8%) normal, 8 (2.6) hyperplasia, 9 (2.9) complex hyperplasia, 4 (1.3%) hyperplasia with atypia. 23 (7.4%) biopsies were insufficient for diagnosis. Logistic regression of risk factors for hyperplasia: irregular menses: OR = 73.5 (95% CI 14.6 to 370.4), $P = 0.0001$. Hypertension: OR = 4.94 (0.95 to 25.84), $P = 0.58$. Age > 40: OR = 3.97 (1.22 to 12.95), $P = 0.022$.	Funding source: Not stated Study summary: All women with irregular menstruation should have endometrial biopsy.
Bronz 1997 ⁷³	Diagnostic; comparative; prospective EL = II	139	Women; referred due to AUB; 83 women pre-menopausal, 56 post-menopausal Country: Switzerland	Transvaginal sonography; saline infusion sonography; histology – reference	Results for pre-menopausal women: Benign polyps identified in 33 women by histology, TVS identified 21, SCHS identified 32. Submucous fibroids identified in 22 women by histology, TVS identified 21, SCHS identified 21. Endometrial hyperplasia identified in 5 women by histology, TVS identified 5, SCHS identified 2. No endometrial carcinoma reported.	Funding source: not stated Study summary: Both TVS and SCHS are highly accurate methods at diagnosing pathology
Critchley 2001 ⁶⁹	Diagnostic; randomised – block; prospective; statistical analysis blinded EL = Ib	1767 assessed, 1027 eligible, 683 recruited – 200 high risk, 326 moderate risk, 157 low risk	Women; referred due to AUB; excluded pregnant women. Women divided into groups based on risk factors for pathology – age, history, pre- or post-menopausal High risk = post-menopausal Moderate risk = pre-menopausal, < 40, no risk factors – family history Low risk = pre-menopausal, < 40 High-risk group: age = 57.6, 1% with HMB, 30% on HRT, 22% sterilised. Moderate-risk group: age = 45.2, 68% with HMB,	Hysteroscopy plus biopsy – Tao Brush or Pipelle, blind biopsy; transvaginal ultrasound; no investigation	High risk = post-menopausal Moderate risk = pre-menopausal, < 40, no risk factors – family history Low risk = pre-menopausal, < 40 Abnormalities identified by visualisation: High-risk group: Moderate-risk group: Endometrial/uterine polyp – hysteroscopy = 19, ultrasound = 7 Uterine fibroids – hysteroscopy = 31, ultrasound = 59. Cervix suspicious – hysteroscopy = 0, ultrasound = null. Cervical polyp – hysteroscopy = 7, ultrasound = null Low-risk group: Endometrial/uterine polyp – hysteroscopy = 1, ultrasound = 2 Uterine fibroids – hysteroscopy = 1, ultrasound = 6. Cervical polyp – hysteroscopy = 1, ultrasound = null Abnormalities identified by biopsy: Moderate-risk group: Endometrial cancer = 3. Hyperplasia = 3. Atrophic endometrium = 0. Inactive endometrium = 19. Cyclic endometrium = 213. Other = 59	Funding source: Health Technology Assessment, NHS Study summary: Ultrasound provides higher visualisation rates than hysteroscopy ($P = 0.002$). Tao Brush outperforms Pipelle in post-menopausal women. Polyps better identified with hysteroscopy, and fibroids by ultrasound. Hysteroscopy and biopsy more likely than ultrasound to be classified 'unpleasant'.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients and prevalence	Population characteristics	Type of test and reference standard	Sensitivity, specificity, PPV and NPV	Source of funding and additional comments
			9% on HRT, 38% sterilised. Low-risk group: age = 33.9, 57% with HMB; 0% on HRT, 28% sterilised. Country: UK		Low-risk group: Endometrial cancer = 0. Hyperplasia = 0. Atrophic endometrium = 0. Inactive endometrium = 2. Cyclic endometrium = 91. Other = 0	
Eldred 1994 ¹⁴³	Epidemiology; case-control EL = II	42	Women; presenting with subjective menorrhagia; no pathology or coagulation disease. Country: UK	Pituitary and ovarian hormone levels association with menorrhagia	20 patients had MBL > 80 ml, 22 had MBL < 80 ml. No difference between groups in hormone levels – FSH, LH-FSH and E2 No correlation between MBL and hormone levels.	Funding source: Not stated Study summary: No association between hormone levels and menstrual blood loss
Fedele 1992 ⁷⁸	Diagnostic; pre- and post treatment EL = II	43	Women; recurrent menorrhagia; enlarged uterus; no evidence of leiomyoma on examination; scheduled for hysterectomy; Country: Italy	Transvaginal ultrasound; histopathology post-hysterectomy – reference	Ultrasonography results: 22 of 43 had adenomyosis, 4 had leiomyoma > 10 cm. Pathologist: 20 had adenomyosis, confirming 16 US findings, 6 were excluded, 4 new cases. Ultrasound sensitivity = 80%, specificity = 74%, PPV 73%, PNV = 81%.	Funding source: Not stated
Higham 1999 ⁴²	Diagnostic EL = III	254: 207 subjective menorrhagia; 47 subjective controls	Women Country: UK	Clinical markers of MBL – pad use, duration of menses	MBL ranged from 8 to 616 ml (median 79 ml) in subject menorrhagia, and 2.5 to 288 ml (median 36 ml) in subjective control group. Association between pad use and MBL ($n = 412$): $r = 0.61$, $P < 0.005$ Association between duration and MBL ($n = 420$): $r = 0.35$, $P < 0.01$ Association between number of pregnancies and MBL: $P < 0.005$ Association between age and MBL: $r = 0.3$, $P < 0.01$ Association between height and MBL: $r = 0.2$, $P < 0.01$.	Funding source: Not stated Study summary: Despite some correlation between clinical measures and MBL, objective measurement of MBL is still required.
Loffer 1989 ⁸⁴	Diagnostic; comparison EL = II	187	Women; AUB – 47 post-menopausal, 192 menorrhagia, 20 menometrorrhagia, 18 metrorrhagia Country: USA	D&C; hysteroscopy	Pathology identified: Menorrhagia = 68 normal, 13 polyps, 16 fibroids, 3 hyperplasia, 0 cancer, 2 endometriosis. Sensitivity, specificity, PPV, NPV of D&C compared with histology: 65% (32/49), 100% (102/102), 100% (32/32), 17% (17/102) Sensitivity, specificity, PPV, NPV of hysteroscopy with tissue sample compared with histology: 98% (48/49), 100% (102/102), 100% (48/48), 1% (1/102) In 91 patients with negative hysteroscopy only 1 had pathology identified by biopsy.	Funding source: Not stated Study summary: Study shows value of hysteroscopy for identification of uterine pathology. Reviewer comments: Retrospective analysis without standards techniques for biopsy.
MacKenzie 1978 ⁷²	Diagnostic EL = III	1029	Women; undergoing D&C; excluded if for evacuation of retained products of conception or for hysterectomy or vaginal repair. Country: UK	D&C	Histopathology results: Proliferative phase = 310 (30.1%) Secretory phase = 274 (26.6%) Mixed = 8 (0.8%) Menstrual = 35 (3.4%) Hyperplastic = 57 (5.5%) Decidua = 12 (1.2%) Atrophic endometrium = 8 (0.8%) Endometriosis = 8 (0.8%) Endometrial polyps = 21 (2.0%) Endometrial carcinoma = 15 (1.4%) Inadequate sample = 85 (8.3%) No curettings = 153 (14.9%) No report = 43 (4.2%) Figures varying by indication for D&C. Mean stay in hospital = 1.8 days.	Funding source: Not stated Study summary: improved selection of patients for D&C could greatly reduce number of unnecessary procedures.

Bibliographic information	Study type and evidence level	No. of patients and prevalence	Population characteristics	Type of test and reference standard	Sensitivity, specificity, PPV and NPV	Source of funding and additional comments
Miller 2001 ⁵⁶⁴	Epidemiological cohort EL = III	246: 123 cases – 51 Caucasian; 70 African-American, 123 controls – 45 Caucasian; 76 African-American	Women; treated for menorrhagia Country: USA	Test for von Willebrand disease	African-Americans had higher vWF:ag ($P = 0.001$), FVIII ($P = 0.008$) and vWF:Act ($P = 0.006$) than Caucasian population. vWF:RiCof, bleeding time and partial thromboplastin did not differ between racial groups. In Caucasian group 0 control and 7 cases had vWD, in African-American group 1 control and 1 case had vWD. In both racial groups those with type O blood differed from those with ABO blood type.	Funding source: not stated Study summary: Study shows higher levels of vWF factors in African-American population compared with Caucasian population. This suggest tests should take account of these differences
Motashaw 1990 ⁸¹	No comparison group EL = III	370	Women; referred for investigation due to AUB; non-pregnant; known pathology excluded. Aged 22 to 82 years. 3 28 pre-menopausal, 42 post-menopausal. Country: India	Hysteroscopy	Hysteroscopy findings: Normal cavity = 124 (33.51%) Polyps – endometrial = 66 (17.83%) Polyps – cervical = 10 (3.70%) Submucous myoma = 42 (11.35%) Endometrial hyperplasia = 85 (22.97%) Endometrial strophy = 6 (1.62%) Synechiae = 21 (5.67%) Adenocarcinoma = 5 (1.35%) Other = 11 (2.97%)	Funding source: Karl Storz GmbH and Co
Nagele 1996 ⁷¹	Diagnostic EL = III	2500	Women referred for outpatient hysteroscopy Country: UK	Hysteroscopy	Hysteroscopy successful in 96.4%. 89% completed, 7.4% incomplete, and 3.6% failed. Diagnostic outcomes: menorrhagia ($n = 1120$) 583 (52.1%) normal, 334 (29.8%) fibroids, 112 (10%) polyps, 8 (0.7%) atrophy, 29 (2.6%) irregular endometrium, 3 (0.3%) endometrial carcinoma, 51 (4.6%) miscellaneous. Total ($n = 2409$) 1172 (48.6%) normal, 585 (24.3%) fibroids, 272 (11.3%) polyps, 87 (3.6%) atrophy, 64 (2.7%) irregular endometrium, 11 (0.5%) endometrial carcinoma, 218 (9%) miscellaneous.	Funding source: Not stated Study summary: Hysteroscopy, unlike ultrasound, allows optimum assessment of patient prior to potential surgery.
Stovall 1991 ⁷⁶	Randomised; comparative; blind EL = Ia	275 – 126 Novak biopsy, 149 Pipelle biopsy	Women; referred for AUB; excluded if pregnant. Novak group: aged 44, parity 4, indication for biopsy – AUB = 83.3%, postmenopausal bleeding = 16.7% Pipelle group: aged 40, parity = 4, indication for biopsy – AUB = 89.9%, postmenopausal bleeding = 10.1% Country: USA	Novak curette; Pipelle endometrial sampling; Histology from subsequent hysterectomy	Patient pain: for Novak group mean pain score was 4.36 vs 3.21 for Pipelle group ($P < 0.05$). Failure of test: insufficient sample – Novak group = 12 (9.5%) vs 19 (12.8) for Pipelle group (NS) Sampling outcomes: Endometriosis: Novak = 23 (18.3%) vs 23 (15.4%) in Pipelle Hyperplasia: Novak = 15 (11.9%) vs 11 (7.4%) in Pipelle. Proliferative or secretory: Novak = 76 (60.3%) vs 96 (64.4%) for Pipelle Histology confirmed results in 48 of 50 (96%) of patients.	Funding source: Not stated Study summary: Study suggests that Pipelle is as effective as Novak.
Valle 1981 ⁷⁴	Diagnostic EL = II	553	Women; AUB; Age range from 20 to 75 Country: USA	Hysteroscopy; Hysteroscopic biopsy; D&C	Pre-menopausal women ($n = 419$): Number of pathologies identified via hysteroscopy; hysteroscopic biopsy; curettage histology. Endometrial polyps = 165, 150, 15 Submucous leiomyoma = 68, 8, 0 Adenomatous hyperplasia = 16, 10, 4 Intrauterine adhesions = 9, 2, 0 Intrauterine foreign body = 7, 7, 0 Uterine septum = 7, 0, 0 Caesarean section scar defect = 5, 0, 0. Post-menopausal women ($n = 134$): Number of pathologies identified via hysteroscopy; hysteroscopic biopsy; curettage histology.	Funding source: Not stated Study summary: Hysteroscopy provides a useful method for identifying intrauterine pathology not available using 'blind' D&C.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients and prevalence	Population characteristics	Type of test and reference standard	Sensitivity, specificity, PPV and NPV	Source of funding and additional comments
					Endometrial polyps = 37, 29, 5 Submucous leiomyoma = 12, 2, 0 Atrophic endometrium = 17, 15, 12 Adenomatous hyperplasia = 6, 5, 1 Aden carcinoma = 3, 3, 1	
Vercellini 1997 ⁷⁰	Diagnostic EL = II	793	Women; referred for AUB to Centre for Menorrhagia; PBAC > 100; those on hormonal treatment excluded; those who had D&C or hysteroscopy within 3 months excluded Country: Italy	Ultrasonography; hysteroscopy; hysterectomy/resection – reference	Ultrasonography: 300 normal, 417 abnormal, 53 doubtful. Hysteroscopy: 325 normal, 445 abnormal (234 submucous myomas, 155 endometrial polyps, 76 endometrial hyperplasia, 2 endometrial carcinoma).	Funding source: Not stated Study summary: Considering good specificity and NPV of transvaginal ultrasonography, it should be considered for initial investigation of pre-menopausal women.
Vercellini 1998 ⁷⁹	Diagnostic study EL = Ib	115 – 13 excluded, 102 included in analysis	Women; undergoing hysterectomy due to menorrhagia and/or dysmenorrhoea; women with known pathology excluded. Country: Italy	Transvaginal ultrasonography; myometrial needle biopsy; post-hysterectomy pathology assessment – reference	Biopsy: 29 cases of adenomyosis identified (28%) Sonography: 48 cases of adenomyosis; 24 confirmed; 5 missed	Funding source: Not stated Study summary: Both tests produced suboptimal test results, and combined did not improve results.

Table 3.3 Menstrual bleeding patterns, prevalence of HMB, presence of uterine pathology, and risk-factors associated with HMB – non-comparative studies

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Allen 1990 ⁸²	retrospective cohort EL = 3	prevalence of endometrial cancer	3241	women; referred for menorrhagia Australia	Description	2218 of 3241 had an investigative or minor procedure. No cases of endometrial cancer found, 5 of cancer of the cervix.	Funding source: Not stated Study summary: Study shows testing for cancer in menorrhagia is of limited use.
Andrade 1991 ¹⁴⁸	cohort EL = 3	haematological against total MBL	309	women; aged 15–48 years – average 29.4; parity = 2.4; suitable for entry into IUS study Brazil	haematological assay – haemoglobin, serum iron, and serum ferritin; MBL – alkaline haematin	Haematological results by MBL (MBL – haemoglobin, serum iron, serum ferritin): < 20 ml ($n = 130$) – 13.3, 78.8, 28.5; 21–40 ($n = 95$) – 13.5, 75.6, 23.4; 41–60 ($n = 50$) – 12.8, 57.3, 18.6; 61–80 ($n = 24$) – 13, 75.9, 14.5; > 80 ($n = 10$) = 12, 47.3, 10.6; All ($n = 309$) – 13.2, 72.2, 23. Normal (< 60 ml) vs heavy (> 60 ml). Age = 29.2 (SD 6.5) vs 30.6 (SD 6.4); weight = 55.9 (SD 9.7) vs 42 (SD 8.8); height = 155.3 (SD 6) vs 157 (SD 6.8); parity = 2.4 (SD 1.9) vs 3.6 (SD 2.8) $P < 0.05$.	Funding source: Not stated Study summary: Women become anaemic when MBL reaches 80 ml not 60 ml.
Ballinger 1985 ⁶¹	Cohort EL = 3	association of menstrual and mental problems	1517	women; 20–59 UK	MBL – self assessment; mental health – GHG	MBL self-assessment: light = 19%; moderate = 51.3%; heavy = 24.3%; very heavy = 5.4%. Association of GHG > 12 (moderate depression) and MBL level, chi-squared = 20.11, $P = 0.0002$	Funding source: Not stated Study summary: Demographic factors have to be taken into account when assessing impact of psychiatric morbidity in women with gynaecological problems.
Barer 1936 ⁴⁶	Cohort EL = 3	Normal MBL estimation	100	women; 15–43 years; anaemia excluded USA	MBL – alkaline haematin	For group ($n = 100$) MBL = 6.55 to 178.69 ml, mean = 50.55 (SD 25.73) (though results skewed). 50% within 23.21 to 68.43 ml range. No relationship between MBL and age. Relationship between duration and MBL: 3 days = 24.3 and 6 days = 58.66 ml. No stats given. Relationship between number of pads and MBL. No stats given	Funding source: Eli Lilly Study summary: Study shows a wide variation in 'normal' menstrual blood loss.
Belsey 1997 ³⁹	Epidemiological cohort EL = 3		6375 patient years	women WHO dataset	cycle length – days	Menstrual cycle length (mean days) within woman: 15 years – 32 days, 41 – 27 days. Bleeding patterns (as defined by WHO) – approx. Normal bleeding – 15–19 = 70%, 20–24 – 82%, 25–29 – 86%, 30–34 – 88%, 35–39 – 92%, 40–44 – 89%, 45–49 – 73%. Prolonged bleeding – 20–24 = 0.1%, 35–39 = 0.1%, 45–49 – 0.2%, all other groups = 0%	Funding source: Not stated
Campbell 1986 ¹³	Cohort EL = 3	Menstrual histories	1472 (11910 cycles) – 670 (7099 cycles) prospective and 802 (4811 cycles) retrospective	women; 11–15 years Sri Lanka; Hong Kong	menstrual cycle length; duration of menstruation	For all women: Duration of menstruation: < 3 days = 5.7%; 3–7 days = 89%; > 7 days = 5.3%. Duration of menstruation by episode from menarche (3–7 day group only): 1st = mean average 4.7 days (SD 2.2) 78% covered; 10–12th = 4.6 (SD 1.6), 92.8% covered; 19–24th = 4.5 (SD 1.5), 94.7% covered. Duration (mean days) of cycle by episode from menarche (for prospective group, $n = 670$): 1st = 50.7 days (SD 45.2); 10–12 = 32.5 (13.6); 19–24 = 30 (SD 8.5). Duration (median days) of cycle by episode from menarche: 1st = 34 days (< 20 days = 6.4%, > 40 days = 38.3%); 10–12th = 31 days (7.7%, 13.2%); 19–24th = 31 days (9%, 7.9%).	Funding source: WHO Study summary: Study focuses on adolescent women just after menarche. Study shows high variation in menstruation symptoms occurs during this time frame.
Cazzola 1994 ¹⁶	Prospective cohort EL = 3	Menstrual cycle characteristics	1798 women – 36641 cycles	women included in Catholic Marriage Advisory Council UK	Menstruation cycle length	Cycle length (all records, $n = 36641$): mean = 28.31 days, SD 5.1, range 7–286. Cycle length (non-monophasic, 15–44 years, $n = 36018$ cycles): 28.04 days, 3.5, 15–44 Cycle length (non-monophasic, 15–44 years, $n = 1789$ women): 28.46, 2.57, 21.3–38.6	Funding source: Not stated
Chiazze 1968 ²³	Epidemiological cohort EL = 3	description of menstrual cycle	2316 women – 30655 cycles	women USA and Canada	Cycle length; age	Mean cycle length ($n = 2316$) by age: 15–19 = 30.8 days (SD 3.38), 68.4% 25–31 days; 20–24 = 30.5 (3.99), 62.6%; 25–29 = 29.6 (2.68), 78.9; 30–34 = 29 (2.92), 82.8%; 35–39 = 28.5 (2.58), 86.4%; 40–44 = 28.3 (2.77), 81.8%. % cycle 25–31 days ($n = 30655$ cycles) by age: 5–19 = 56.6%; 20–24 = 61%; 25–29 = 75.4%; 30–34 = 74.6%; 35–39 = 73.2%; 40–44 = 68.1%.	Funding source: Not stated Study summary: Variability highest in younger women, and decreases with age-group.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Claessens 1981 ¹⁴⁶	Epidemiology EL = 3	Testing for coagulation disorders	83 – 59 included, 24 excluded as menorrhagia not the main presenting symptom	women; hospitalised for menorrhagia at Hospital for Sick Children (assume young adults). Study undertaken between 1971 to 1980. Canada	Prevalence of coagulation disorders	44 of 59 (74%) were found to have DUB. 11 of 59 (19%) were found to have coagulation disorder – 4 had idiopathic thrombocytopenic disorders, 3 had vWD, 2 had Glanzmann's disease, 1 had thalassemia, 1 had Fanconi's anaemia. 9 (15%) of 59, but 5 (45%) of 11 with coagulation disorders had life-threatening uterine blood loss..	Funding source: Not stated Study summary: Suggested that girls referred for HMB have in-depth history and blood test.
Cole 1971 ²⁷	Cohort EL = 3	Factors associated with MBL	348	Women; 17–45 years	MBL – spectrophotometry; haemoglobin level	MBL loss distribution ($n = 280$); < 50 ml = 206; $=50 - 99$ ml = 60; > 100 ml = 14. Heavy defined as 45 ml as represents upper 30%. ≥ 80 ml = 26 of 280. Difference in MBL in two consecutive cycles: 0–4 = 38.3%, 5–9 = 22%, 10–14 = 14.5%, 15–19 = 7.6%, 20–24 = 5.6%, 25–29 = 3.9%, 30–43 = 2.3%, 35–39 = 0.7%, 40–44 = 0.3%, 45–49 = 1.6%, 50+ = 3.3%. MBL by parity: 0 = 26.4 ml, 1 or 2 = 34.3 ml, 3+ = 40.4 ml. MBL by age: 17–19 = 27.5 ml, 20–24 = 32.3 ml, 25–29 = 36.3 ml, 30–34 = 32.7 ml, 35–39 = 37.4 ml, 40–44 = 38.3 ml MBL by height: < 160 cm = 29.6, 160 cm = 37.6 ml, 154+ = 38.4 ml.	Funding source: Not stated Study summary: MBL was associated with age, parity and birthweight of children.
Cote 2003 ⁴⁰	cross-sectional EL = 3	cost of menorrhagia; factors associated of menorrhagia	2805 women involved in NHIS household survey	women; 18–64 years old; natural menstruation in last 12 months and 3 months; never taken estrogen containing drugs, except OCP; no reproductive cancer; no recent hysterectomy. USA	Self-reported MBL; perception of general health; age	Age difference: heavy flow vs low/normal flow – 18–39 = 114 (30.6%) vs 485 (19.9%); 40–49 = 237 (63.5%) vs 1722 (70.8%); $> 49 = 22$ (5.9%) vs 225 (9.3%), $P < 0.00$ Ethnic group: white = 258 (69.2%) vs 1844 (75.8%); others = 115 (30.8%) vs 588 (24.2%), $P = 0.01$. Education level = less than high school = 68 (18.2%) vs 368 (15.1%); High school cert. = 225 (60.3%) vs 1370 (56.3%); degree = 80 (21.4%) vs 694 (28.5%), $P = 0.01$ Perception of health: excellent = 85 (22.8%) vs 881 (36.2%); very good = 121 (32.4%) vs 813 (33.4%); good = 111 (29.8%) vs 556 (22.9%); fair = 40 (10.7%) vs 149 (6.1%); poor = 16 (4.3%) vs 32 (1.3), $P < 0.00$.	Funding source: Not stated Study summary: Study provides data on association between subjective menorrhagia and socio-demographic factors.
Cramer 1990 ²⁹	Epidemiology EL = 3	Prevalence of leiomyoma	100	Uterus collected after hysterectomy USA	Prevalence of leiomyoma	In 100 uteri a total of 649 fibroids were identified. 48 uteri without fibroids on routine examination showed 67 on dissection in 25 cases. 52 uteri had 582 fibroids. 77% prevalence of fibroids in whole group 74% prevalence in pre-menopausal women. Average number of myomas in pre-menopausal women = 7.6 Average size of largest myoma in pre-menopausal women = 18.8 mm	Funding source: N/A
Cramer 1992 ³⁰	Educational tutorial EL = 3	Epidemiology of myomas			prevalence of myomas by menopausal status, age and risk factors	Prevalence of myomas by menopausal status: pre-menopausal = 74%, post-menopausal = 84% Incidence per 1000 of myomas by age: 25 to 29: 0.31 30 to 34 = 0.96 35 to 39 = 2.67 40 to 44 = 4.63 45 to 49 = 6.20 $> 50 = 4.24$ Relative risk of myomas by risk-factor: Reduced as number of pregnancies increased, age of last pregnancy increased, weight decreases, smoking increases and oral contraception use increases	Funding source: Not stated
Decloedt 1999 ⁸⁵	diagnostic; epidemiology;	hysteroscopy	673 hysteroscopies in	women; AUB – menorrhagia, post-	Pathology identification; failure	Failure rate of 6% for hysteroscopies.	Funding source: Not stated Study summary: High level of

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
	retrospective EL = 3		665 patients	menopausal bleeding, etc; average age 47 years Belgium	rate	336 (50%) women had menorrhagia – 128 (19%) < 40 and 208 (31%) > 40. Normal cavity: Menorrhagia < 40 years = 79% (96); menorrhagia > 40 years = 68% (138). Whole population = 68% (431) Fibroids and polyps: menorrhagia < 40 – submucosal fibroids = 11% (13), endometrial polyps = 7% (9). Menorrhagia > 40 – submucosal fibroids = 21% (43), endometrial polyps = 20% (10). Whole population = 12% and 17%, respectively.	pathology suggests need for hysteroscopies in AUB patients, except menorrhagia in < 30 year olds.
Emanuel 1995 ³⁷	Cohort; epidemiology EL = 3	Association of pathology to UB – including menorrhagia using hysteroscopy	1202: 502 with menorrhagia	women; referred for hysteroscopy Netherlands	pathology; disease classification	Of 502 patients referred with menorrhagia – 267 (53%) had normal/inactive pathology, 137 (27%) had submucous myoma. Other 20% not reported.	Funding source: Not stated Study summary: Study shows high levels of pathology associated with menorrhagia.
Farquhar 1999 ⁸³	Non-comparative cohort EL = 3	Risk factors associated with endometrial hyperplasia	1033	Women; pre-menopausal; heavy or irregular menstrual bleeding New Zealand	Risk factors associated with hyperplasia	Biopsy results: 914 = normal 22 = polyps 20 = simple hyperplasia 22 = complex hyperplasia 3 = atypia hyperplasia 5 = endometrial cancer 46 insufficient material Risk factor frequency: Age > 40 = 56% Age > 45 = 27.1% Weight > 90 kg = 21.1% Nulliparity = 16% Infertility = 7% Diabetes = 3.4% Previous breast cancer = 0.4% Menstrual bleeding > 7 days = 32% Menstrual bleeding > 14 days = 8% Irregular menstrual bleeding = 38.3% Polycystic Ovaries = 2.3% Family history of breast cancer = 5.3% Family history of endometrial cancer = 2.1% Use of exogenous estrogen = 18% Factors associated with abnormal pathology or hyperplasia. Risk factor OR (95% CI) for abnormal pathology: Weight > 90 kg = 5.5 (2.9 to 10.6) Family history of colon cancer = 5.0 (1.3 to 19.1) Infertility = 3.6 (1.3 to 9.9) Age > 45 = 3.1 (1.5 to 6.1) Nulliparity = 2.8 (1.1 to 7.2) Family history of endometrial cancer = NS Risk factor OR (95% CI) for complex, atypia or carcinoma: Weight > 90 kg = 7.3 (3.2 to 16.8) Family history of colon cancer = 9.1 (2.2 to 37.1) Infertility = 3.3 (0.99 to 11.1) Age > 45 = NS Nulliparity = 3.7 (1.2 to 10.9) Family history of endometrial cancer = 5.8 (1.1 to 28.6) Regularity or duration of menstruation were not significant risk factors.	Funding source: University of Auckland Study summary: The following are risk factors for endometrial hyperplasia in pre-menopausal women with abnormal menstrual bleeding: body weight ≥ 90 kg, age ≥ 45 years, infertility, family history of colonic carcinoma, and nulliparity. Current guidelines may need to be reconsidered.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Friberg 2006 ⁵⁶⁵	Epidemiological population study EL = 3	Prevalence of bleeding disorders	1410 questionnaires sent out, 1019 replies received	Secondary school pupils. Average age = 16.7 years Sweden	Reporting of menstrual bleeding problems	375 of 1019 reported menstruation as heavy. 127 of 1019 reported receiving treatment for HMB.	Funding source: Not stated Study summary: Bleeding symptoms were relatively prevalent in this population and similar to other population-based studies.
Gao 1987 ¹⁴⁹	epidemiological cohort EL = 3	Epidemiology of MBL and blood haematology – alkaline haematin methods	421	Women; 18 to 44 years; regular menstruation; normal pelvic examinations; no history of hormonal contraceptives. China	MBL levels; haematology levels	MBL(ml): range 4.1 to 273.6 ml, mean 54.2 (SD 37). 5th and 95th percentiles = 14.2 and 124.1. 2SD range = 11.3 to 169. Haemoglobin (g/dl): range = 8.3 to 16.7, mean 13.2 (SD 1.1). 5th and 95th percentiles = 11.5, 14.9. 2SD = 11. to 15.4 Ferritin (ng/ml): range 1.2 to 180. Mean = 22.8 (SD 18.3). 5th to 95th percentile = 3.6 to 55.8. 2SD = 3.49 to 83.8. Results by MBL: MBL, % haemoglobin < 12 g/dl, % ferritin < 16 ng/ml, % with both. < 20 ml (<i>n</i> = 48) 0%, 16.7%, 0% 20 to 40 (<i>n</i> = 1445) 4.1%, 27.6%, 2.1% 40 to 60 (<i>n</i> = 92) 9.8%, 33.7%, 3.3% 60 to 80 (<i>n</i> = 53) 18.9%, 54.7%, 17% 80 to 100 (<i>n</i> = 37) 13.5%, 70.3%, 13.5% > 100 (<i>n</i> = 46) 30.4%, 82.6%, 26.1%.	Funding source: United Nations Fund for Population Activities Study summary: Study shows higher average MBL than with European and US populations.
Gath 1987 ⁶⁵	cross-sectional survey EL = 3	association between gynaecological and mental factors	521 women	Women; aged 35–59. UK	Psychiatric state – present state; GHG; Eysenck personality inventory.	Pad use > 6 (<i>n</i> = 86) was NS for all except neuroticism (<i>P</i> < 0.05). Pad use > 8 (<i>n</i> = 38) was NS for all measures. Subjective assessment: very heavy periods (<i>n</i> = 16) – <i>P</i> < 0.001 on present case (case vs non-case); <i>P</i> < 0.05 on present state (total core). <i>P</i> < 0.05 on GHG (higher scores). NS for other scores. Interference with life from heavy periods (<i>n</i> = 59): NS on all scores except neuroticism (<i>P</i> < 0.05).	Funding source: Oxford regional health authority Study summary: Some association between heavy period and psychiatric symptoms, but less than for dysmenorrhoea and premenstrual symptoms.
Gordley 2000 ⁵⁶	Cross-sectional survey EL = 3		335 approached, 202 eligible, 170 replied.	women; menstruating; serving in US Army; excluded if – pregnant, pregnant in < 6 months, using hormonal contraceptives, HIV/AIDs, diabetes, cancer of reproductive organs, systemic lupus, Cushing syndrome, TB. multiple sclerosis, hysterectomy, BSO. USA	Stress – JCQ and MEQ questionnaires	Multiple logistic regression (allowing for common confounders) of risk factors for hypomenorrhoea: life event, OR = 2.99 (1.2–7.42); race, OR = 4.99 (2.07)–12.05); military, OR = 4.12 (0.89–19.16). Non-significant for fuel-handling, passive smoking, exercise, BMI, education level, age, and job strain. Life events – any major life change, good or bad.	Funding source: Department of Defence grant Study summary: Study suggests life events linked to menstrual problems.
Greenberg 1983 ⁶⁷	Cohort EL = 3	association between mental health and menorrhagia	50	women; referred to clinic for menorrhagia UK	MBL; psychological assessment – GHG	62% of people referred had GHG > 12 (moderate depression GHG +). Haemoglobin levels were 13.19 in GHG+ (depressed) and 12.2 in GHG – (not depressed) (<i>P</i> < 0.05). Ferritin levels were 18.4 vs 14, respectively.	Funding source: Not stated Study summary: Study suggests that women complaining of menorrhagia but who have depressive symptoms have lower MBL than those that do not.

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Hallberg 1966 ²⁵	Cross-sectional survey EL = 3	Menstrual patterns	748 approached – data available on 476. Women either refused or were excluded.	women; age stratified 15–50; menstruating Sweden	MBL – alkaline haematin; blood tests	<p>MBL (ml) by age: (mean, SD, 90th percentile) 15 = 33.8, 2.4, 65.1; 23 = 38.9, 3.7, 77.8; 30 = 49.7, 86.3; 40 = 44.5, 5.7, 87.1; 45 = 42.7, 4.5, 88.1; 50 = 62.4, 13.2, 133.1; All = 43.4, 2.3; 83.9.</p> <p>MBL (ml) by age of 'series B' – subjective assessment of 'normal', haemoglobin > 12 g/100 ml, plasma iron > 80 µg/100 ml, MCHC > 30%: (mean, SD) 15 = 32.9, 2.6; 23 = 38.8, 4.8; 30 = 29.7, 3.9; 40 = 29.8, 3.0; 45 = 31.7, 3.7; 50 = 52, 7.5; All = 33.2, 1.6.</p> <p>All subjects: Haemoglobin concentration decrease ($P < 0.01$) at > 80 ml MBL. MHC decrease ($P < 0.01$) at > 80 ml. Iron concentration decrease ($P < 0.01$) at > 80 ml.</p> <p>Series B – 95th percentile = 76.4 ml</p>	<p>Funding source: Swedish Medical Council</p> <p>Study summary: MBL > 80 ml is seen as abnormal based on average MBL and change in blood counts.</p>
Hammouda 1967 ⁸⁶	Epidemiology; retrospective; case series EL = 3	Epidemiology of women referred with DUB	660 of 9642 women seen were for DUB (10.4%)	Women; admitted to hospital with diagnosis of DUB Saudi Arabia	Age stratified prevalence; pathology identified	<p>Age structure: Of 660 women: 370 were aged 40 to 45, 205 were aged 45 to 50, and 85 were over 50 years old.</p> <p>Endometrial findings: Normal = 504 Endometrial hyperplasia = 124 (18.8%) Atrophic = 32</p> <p>Pathology findings: Myomas = 103 Adenomyosis = 24 Endometriosis = 20 Polyps = 32 Cysts of ovary = 6 Ovarian thecoma = 1 Carcinoma = 9</p>	<p>Funding source: Not stated</p> <p>Study summary: Study shows that label of DUB is often over-used, and pathological cause of DUB can be found with proper investigation.</p>
Harlow 1997 ⁵⁷	Cohort EL = 3	Examination of menstrual cycles	248	women; Aged 12–14 USA	cycle length – days	<p>Median cycle length (days): African-American ($n = 111$) = 29.8 (21–85); European-American ($n = 119$) = 30.4 (22–53), $P = 0.49$.</p> <p>Regression analysis: risk factors associated with a cycle length > 45 days = European-American OR = 1.86, 10th percentile of BMI (low weight), OR = 1.48; Diet to lose weight, OR = 0.53; time since menarche < 12 months, OR = 1.44.</p>	<p>Funding source: National Institute of Child Health and Development</p> <p>Study summary: Weight and high exercise are associated with increases cycle length.</p>
Harlow 1991 ²⁴	Epidemiological Cohort EL = 3	Menstrual cycle patterns	158 women – 1180 cycles	Women; 17–19 years; 1st year of college; part of women's health project cohort. USA	MBL cycle length (days)	<p>Cycle length based on cycles ($n = 1180$) = 28.9 days, variance = 20.4. Cycle length based on women ($n = 158$) = 29 days, variance = 15.8.</p> <p>Transition in cycle length within each category in any one month:</p> <p>< 17 days ($n = 14$) – < 25 years old = 0.5%, 26–34 years old = 0.25%, > 35 years old = 0.25%.</p> <p>17–25 days ($n = 207$) – < 25 years old = 0.2%, 26–34 years old = 0.65%, > 35 years old = 0.15%.</p> <p>26–34 days ($n = 708$) – < 25 years old = 0.19%, 26–34 years old = 0.65%, > 35 years old = 0.16%.</p> <p>35–43 days ($n = 103$) – < 25 years old = 0.13%, 26–34 years old = 0.65%, > 35 years old = 0.19%.</p> <p>44–59 days ($n = 33$) – < 25 years old = 0.11%, 26–34 years old = 0.66%, > 35 years old = 0.23%.</p> <p>> 59 days ($n = 17$) – < 25 years old = 0.29%, 25–34 years old = 0.4%, > 35 years old = 0.31%.</p>	<p>Funding source: Not stated</p> <p>Study summary: Study shows a degree of variation in cycle length between cycles in same women.</p>
Harlow 1994 ¹²	Cohort EL = 3	Factors associated with duration of	179 – 1078 cycles	women; aged 17–19; not married; not pregnant; using	length of MBL (days)	Range of duration of MBL = 1 to 19 days. Median = 5. 97% between 3 and 8 days.	<p>Funding source: Not stated</p> <p>Study summary: Exercise</p>

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
		menstrual bleeding		hormonal contraceptives; not have children USA			associated with longer cycle length.
Hartz 1979 ⁶⁰	Cohort EL = 3	Obesity as risk factor in menstrual problems	26638	women; members of TOPS charity; ahead 20–40 years USA	Cycle length; MBL – self-assessed; weight	Weight was associated with longer cycle length (normal 14–33): > 36 days were +16.94 lbs ($P < 0.001$); < 21 days were +5.91 ($P < 0.05$). Weight associated with amount of flow (subjective): heavy flow 8.8 lbs heavier than normal ($P < 0.01$).	Funding source: TOPS, inc (weight charity) and Obesity and Metabolic Research Program.
Hefnawi 1979 ⁴⁵	Physiological study EL = 3	factors associated with MBL	812 – 774 participated	Women; aged 14 – 49; regular menstrual bleeding Egypt	MBL correlates	Mean MBL = 25.6, median MBL = 20.2 MBL and age: $r = +0.06$ (NS). MBL and parity $r = +0.21$. MBL and systolic blood pressure $r = +0.18$. MBL and diastolic blood pressure, $r = +0.12$.	Funding source: Not stated
Janssen 1998 ²⁶	Epidemiological; Cohort EL = 3	measurement of MBL	313	Women; aged 18–50; no amenorrhea. Netherlands	MBL – alkaline haematin; haemoglobin; anaemia; ferritin; subjective assessment of heavy bleeding	Haemoglobin significantly decreased ($P < 0.05$) at 60 ml MBL. Anaemia increased rapidly at 60 ml and then again at 120 ml. Ferritin decreased at 20 ml. Low ferritin at 40 ml. anaemia levels with MBL: 1–20 = 1.5%, 21–40 = 5.9%, 41–60 = 5.3%, 61–80 = 10.3%, 81–100 = 18.8%, 101–120 = 16.7%, 121–160 = 37.5%, 161–240 = 50%, > 240 = 93.8	Funding source: Not stated Study summary: Risk of developing anaemia increases substantially at 120 ml, not 80 ml. Suggests that 80 ml definition of menorrhagia needs to be revised upwards.
Janssen 1997 ⁴³	cohort, prospective EL = 3	Risk factors for menorrhagia	347 – after exclusion criteria 182 remained. Study population enrolled in separate clinical study.	women; 18–50 years; uterine pathology excluded; irregular bleeding excluded; hormonal treatment within 2 months excluded. Netherlands	MBL	Median MBL = 32.7 ml (range 0.3–230.5). Incidence of menorrhagia = 13.5%. Multiple regression and logistic regression analysis of risk factors for MBL: age ($r^2 = 0.28$) was only variable to explain some variance. Parity, BMI and smoking were non-significant in analysis. Univariate analysis shows trends for increase MBL with parity and BMI, but allowing for age show no that there is no effect.	Funding source: Organon and Sanofi Winthrop Study summary: Study shows that age is only risk-factor associated with increased MBL.
Jeyaseelan 1992 ²⁰	Non-comparative cohort EL = 3		1740	women; part of WHO cohort India	cycle length – days	Cycle length (days) by women age (mean, SD, range): < 19 years = 31.7, 3.4, 23–41; 20–24 = 31.4, 3.4, 24–45; 25–29 = 31.2, 3.4, 20–46; 30–34 = 30.8, 2.8, 25–41; 35–39 = 31.1, 3, 24–41; > 40 = 30.6, 3.1, 25–43; All = 31.2, 3.2, 20–46.	Funding source: Not stated Study summary: Cycle length decreases with age up until pre-menopausal period when it increases.
Kadir 1998 ⁴⁹	Cohort; epidemiology EL = 3	testing for inherited blood disorders	208 assessed. 58 with PBAC < 100 excluded. 150 included	Women; PBAC score > 100; regular bleeding; known blood or endocrine disorders excluded; use of hormonal treatment within 2 months excluded; identified pathology excluded. UK	MBL – PBAC; inherited blood disorder presence.	Of 150 – 123 had no inherited disorder, 20 had vWD, 6 had FXI deficiency. Menorrhagia since menarche in 11, 13 ($P = 0.001$), and 4 ($P < 0.001$) respectively.	Funding source: Not stated Study summary: Routine testing for inherited bleeding disorders suggested in women presenting with menorrhagia.
Kato 1999 ¹⁸	cohort EL = 3	Factors associated with menstrual cycle	4900	Women; age 34–45 USA	Menstrual cycle length – self reported	Cycle length: < 26 days = 18.8%; between 27–29 days – 50.2%; > 30 days = 18.8%; Irregular = 12.2%	Funding source: National Cancer Institute and National Institute of Environmental Health Sciences. Study concentrates on factors associated with cycle length, not MBL, so not relevant.

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Kjerulff 1996 ³²	Retrospective case series EL = 3	Epidemiology of uterine fibroids	1245 women – 409 (301 had fibroids) black, 838 white (281 had fibroids)	Women; undergone hysterectomy for benign condition; aged > 18 years; uterine fibroids USA	Epidemiology of uterine fibroids;	Black women were diagnosed with fibroids at earlier age than white women ($P < 0.001$) Average age was 41.6 for white women and 37.5 for black women ($P < 0.001$) Black women had hysterectomy at younger age than white women ($P < 0.001$) Average age for white women = 44.6 and for black women was 41.7 ($P < 0.001$) Black women waited longer before having hysterectomy (3.9 years vs 2.8, $P = 0.002$) Uterine weight was greater in black women compared with white women (420.8 g vs 319.1 g, $P < 0.001$) Black women had more fibroids than white women ($P, 0.001$) Black women more likely to have subserosal or submucosal fibroids than white women ($P < 0.05$) No difference between groups in size of largest fibroid. No difference between groups in terms of symptoms, except anaemia and severe pelvic pain that were more common in black women. No difference within groups in terms of BMI, years since last birth, or age of hysterectomy and uterine weight. In multiple regression analysis, race and menopausal were associated with uterine weight ($P < 0.001$), while BMI, year since last birth and age of hysterectomy were not.	
Kritz-Silverstein 1999 ⁴⁴	Cross-sectional survey EL = 3	Effect of obesity, smoking alcohol consumption and exercise on menstruation	2912	women; serving in US Navy USA	Regression analysis of factors	Logistic regression of risk-factors for heavy periods showed that smoking, OR = 1.17 ($P < 0.001$), and high alcohol consumption, OR 1.4 ($P < 0.05$), were significant factors. Age, race, pay grade, BMI, exercise were non-significant. No assessment of existing pathology or parity.	Funding source: US Army Medical Research and Material Command
Looker 1997 ¹⁴⁷	Epidemiology EL = 3	Blood test – haemoglobin levels, serum iron levels; questionnaire – socio-economic-cultural variables	24894	Men and women; Part of National Health and Nutrition Survey; > 1 year of age USA	Prevalence of iron deficiency by risk factors	Prevalence of iron deficiency and iron deficiency anaemia by age and sex: Females: 12–15 ($n = 786$) – 9%, 2% 16–19 ($n = 700$) – 11%, 3% 20–49 ($n = 4495$) – 11%, 5% 50–69 ($n = 2034$) – 5%, 2% > 70 ($n = 1630$) – 7%, 2% Males : 12–15 ($n = 691$) – 1%, < 1% 16–19 ($n = 658$) – < 1%, < 1% 20–49 ($n = 4048$) – < 1%, 1% 50–69 ($n = 1929$) – 2%, 1% > 70 ($n = 1437$) – 4%, 2% Univariate analysis showed racial minorities, poor, lower educated, and higher parity. Multivariate analysis showed racial group and parity were significant risk factors, but poverty and education did not.	Funding source: Not stated Study summary: Study shows a high prevalence of iron deficiency amongst women in USA.
Lurie 2005 ³¹	Epidemiology EL = 3	Ultrasound	799	women; underwent ultrasound – for pain, bleeding or suspected myoma Israel	Age related rates of fibroids	Rates and Relative Risks of fibroids by age: < 20 = 0%, null 21–30 = 4.5%, 1 (reference) 31–40 = 11.7%, 2.8 41–50 = 33%, 10.4 51–60 = 33.7%, 10.6 61–70 = 8.3%, 1.9 71–90 = 11.5%, 2.7 All = 20.1%, 2.7	Funding source: Not stated

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Mahmood 1991 ⁵⁶	Prospective; cohort study; epidemiology EL = 3	Prevalence of endometriosis	1542 patients – 134 women with DUB	Women; scheduled for laparoscopic or hysterectomy due to gynaecological problems – infertility, abdominal pain, sterilisation. UK	Percentage of women with endometriosis	Of 1542 women included in study, 933 had normal pelvis, 382 had pelvic adhesions, 227 (15%) had endometriosis. Of 134 women with DUB (included in above figures), 73 had normal pelvis, 28 had pelvic adhesions, 33 (25%) had endometriosis. Severity of endometriosis based on AFS score: For 227 women with condition – mild in 162, moderate in 51 and severe in 14 (6%). For women with DUB – mild in 25 (76%), moderate in 7 (21%), and severe in 1 (3%).	Funding source: Not stated Study summary: Study shows that prevalence of endometriosis is higher in DUB patients than in other gynaecological populations.
Matsumoto 1962 ¹⁵	epidemiological cohort EL = 3	description of menstruation	study 1 – 13380 cycles; study 2 – 701 women, 18213 cycles	women Japan	menstrual cycle description	Cycle length based on questionnaire ($n = 13380$) = 31 days, 10–90 percentile = 35–39, range = 7 to 198. Cycle length based on records ($n = 18213$) = 30.37 days (SD 6.54), 10–90 percentile = 25–36. Age difference in cycle length – 13–17 mean average = 34.67 (10–90 percentile = 28–44), 18–19 = 33.16 days (27–42); 20–24 = 32 (26–38); 25–29 = 31.28 (26–37); 30–34 = 30.07 (25–36); 35–39 = 29.4 (25–35); 40–52 = 28.37 (25–32). Duration of menstruation ($n = 5307$ women) – mean average = 5.03 days (SD 1.41). Duration of menstruation by age: 13–17 = 4.71 days (SD 1.22); 18–19 = 4.88 (0.98); 20–24 = 4.83 (1.14); 25–29 = 4.67 (1.31); 30–34 = 4.57 (1.22); 35–39 = 4.19 (SD 1.37); > 40 = 4.12 (1.07). Amount of menstruation ($n = 2012$ women) based on 4 point scale (1 low – 4 very heavy) by age: 14 = index 2 (normal) – 30.2% vs index 4 (very heavy) = 6.2%; 15 = 25.5% vs 15.9%; 16 = 11.2% vs 18.9%; 17 = 11.3% vs 18%; 18–19 = 14.2% vs 19.2%; 20–24 = 21% vs 30%; 25–29 = 24.6% vs 11%; 30–34 = 20.8% vs 10%; 35–39 = 31.7% vs 7.3%; > 40 = 42.6% vs 7.4%. Variation in cycle length (within -women) over 2 cycles: only 10% same. < 24 days = 1131 and 1136 – 173 same, 25–39 = 894 > 40 = 64. 25–39 = 15036, 15105 – < 24 = 894 (most from 25–29 group. 25–39 = 13395, > 40 = 747. > 40 = 1120, 1046. < 24 = 69, 25–39 – 816, > 40 = 235	Funding source: Not stated Study summary: Study demonstrates the variation in 'normal' menstruation that occurs.
Monari 1998 ¹⁷	Prospective, cohort study EL = 3	Menstrual cycle length	1781 – 31290 cycles	women; > 6 cycles recorded; no illness; < 100 day cycle UK	Menstruation cycle length (days)	Cycle length (days) by age (mean, SD, range): 16–20 – 28.97, 3.48, 29; 21–25 – 29.3, 4.15, 59; 26–30 – 28.83, 3.94, 73; 31–35 – 28.39, 3.92, 51; 36–40 – 27.77, 3.56, 42; 41–45 – 26.95, 4.46, 66; 46–50 – 27.55, 7.64, 82; 51–55 – 29.83, 9.29, 55; All – 28.27, 4.33, 82.	Funding source: Not stated Study summary: Study shows re-education in cycle length with age up until pre-menopausal phase, when it increases.
Munster 1992 ²²	Epidemiological survey EL = 3	Menstrual cycle length	3743 questionnaires sent – 2865 responded – 620 had menstrual calendar, 289 had calendar but not kept it, 617 had made no calendar.	Women; 15–44 years Denmark	Menstrual cycle length – menstrual calendars or retrospective recall.	Regular vs Irregular menstruation by age: All – 86% vs 12.7% (1.3 missing); 15–19 – 77.4% vs 20.8; 30–34 – 88.7 vs 10.5; 40–44 – 87.1 vs 10.8. Menstrual cycle length by age for those with regular menstruation (irregular – no pattern or regularity over 1 year): (< 25 days; 26–31; 32+) 15–19 years old = 8.5%, 74.4%, 17.1%; 20–24 = 11.2%, 78.6%, 10.3%; 25–29 = 11.2%, 79.1%, 9.8%; 30–34 = 9.6%; 83.2%, 7.3%; 35–39 = 12.7%; 80.7%; 6.6%; 40–44 = 18.7%, 79.2%, 2.1%. Maximum cycle variation (median days): (< 3, 3–8, 9–14, > 15): 15–19 = 5.9, 26.6, 33.5, 34; 20–24 = 7.8, 56.9, 18.6, 16.7; 25–29 = 12.9, 51.4, 23.6, 12.1; 30–34 = 18.1, 54.8, 18.1, 9; 35–39 = 14.1, 61.2, 15.4, 9.3; 40–44 = 15.9, 54.4, 19.1, 10.6 Average and percentiles: Age 15–14 = 28.8 days (2.9), 5th-95th percentile = 23–34; Age 25–34 = 28.4 (2.6), 24–33; Age 35–44 = 27.5 (2.4), 23–31.	Funding source: Multiple non-commercial funding Study summary: Study shows that menstruation becomes less variable with age, up until pre-menopausal phase.
Odujinrin 1991 ²¹	cohort EL = 3	Menstrual cycle	950	Women. Aged 10 to 18 years. Nigeria	Regularity of period; menstruation cycle length and flow; other symptoms; factors	Of 889 – 318 (35.8%) irregular; 481 (54.1%) regular, 90 (10.1%) unsure. Mean number of irregular months = 3.7. 134 had cycle < 21 days, 129 had cycle > 29days, 70.4% between 22–29. 47 flow < 3 days,	Funding source: Not stated Study summary: Study focuses on period immediately after

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
					associated with irregularity	3–5 days in 699 (78.6%), and > 5 days in 143 (16.1%). 144 (16.2%) thought flow was heavy.	menarche rather than across the menstrual life-time.
Philipp 2005 ⁵⁶⁶	Epidemiological study EL = 3	Testing for inherited bleeding disorders	115	women; diagnosis of menorrhagia; aged 13 to 55; primary care setting; excluded if known pathology; hormonal treatments within 2 months excluded USA	Prevalence of inherited bleeding disorders	Haemostatic abnormalities: Platelet aggregation – for all ($n = 115$), < 19 ($n = 25$), 10–44 ($n = 65$), > 45 ($n = 25$): 44%, 44%, 48%, 32% ($P = 0.48$). von Willebrand factor: 7%, 4%, 8%, 8%, $P = 0.78$. Coagulation factor: 5%, 8%, 6%, 0%, $P = 0.34$. Any abnormality: 47%, 48%, 52%, 32%, $P = 0.32$.	Funding source: Association of Teachers Preventive Medicine/Centres for Disease Control and Prevention Grant Study summary: Study suggests bleeding disorders common in women with menorrhagia Reviewer comment: Study had no comparison group, and small sample size.
Quinn 1920 ⁹³	Epidemiology EL = 3	Risk factors for endometrial cancer	106	Women; endometrial cancer; pre-menopausal Australia	Risk factors for endometrial cancer	Of 106 women: 11 were under 40 years of age, and 95 were 40 or over years of age. In women under 40: weighing 80 kg or more ($P < 0.01$), being nulliparous ($P < 0.001$), and heavy or irregular bleeding ($P < 0.02$) were significant risk factors.	Funding source: Not stated
Rodeghiero 1987 ⁵⁰	epidemiology; cohort EL = 3	Test for von Willebrand factors and family history of bleeding orders	1218	children; both sexes; aged 11 to 14; one province Italy	Prevalence of vWD	Of 1218 children, between 7 (0.57%) and 14 (1.15%) could be classified as having vWD. This was based of being below 90th% confidence interval of whole group. 8 of 14 were female 9 of 14 were in type O blood group.	Funding source: Health Department of Veneto Region Study summary: Prevalence of vWD in population may be higher than previously thought. Reviewer comment: Study on general population provides a baseline figure for prevalence of vWD. Study appears well conducted.
Rybo 1966 ⁵⁸	cohort EL = 3	Description of menstrual cycle length	344 community survey	Women; 23–45 years Sweden	MBL vs parity; MBL vs age	Nulliparous ($n = 102$) MBL = 38 (3.7) vs 45.5 (3.4) for parous women ($n = 242$), NS. By number of births: 0 = 38 ml (3.7), 1 = 41.7 ml (5.1), 2 = 50.6 ml (7.4), 3 = 47.3 (5.8), > 3 = 40 ml (6.6). Birthweight of children: 2000–2499 = 38.3 ml (20.5), 2500–2999 = 46.9 (10.8), 3000–3499 = 30.3 (4.4), 3500–3999 = 60.2 (15.1), 4000–4499 = 33.3 (7.9); 4500–4999 = 45.4 (13.7).	Funding source: Not stated Study summary: Study found no significant association between parity and MBL when age taken into account.
Sensky 1979 ⁵⁴	case series; retrospective EL = 3	Association of endometriosis and menorrhagia	215	women UK	reported menorrhagia	History of menorrhagia = 76% in women with endometriosis	Funding source: Not stated Study summary: Study shows high prevalence of menorrhagia with endometriosis, but does not show prevalence of endometriosis with menorrhagia.
Shapley 2004 ⁴¹	Cross-sectional survey + prospective cohort EL = 3	prevalence of menstrual disorders	2435 questionnaires sent – 1861 replies – 1513 replied to baseline, 6 month and 12 month follow-up	women UK	menorrhagia; periods heavier than usual. At baseline, 6 months, 12 months.	Baseline: Prevalence of menorrhagia (heavy periods for last 6 months) by age: 18–24 = 46.8% of 218; 25–34 = 43.1% of 390; 35–55 = 59.9% of 479; 45–54 = 53% of 338; All = 51.6% of 1425. Increase with age ($P = 0.002$) Heavier periods than usual by age: 18–24 = 16.1%; 25–34 = 17.7%; 35–44 = 29.2%; 45–54 = 23.1%; All = 22.6%. 12 month follow-up: Cumulative incidence (excluding those with menorrhagia at baseline) of menorrhagia (heavy periods for last 6 months) by age: 18–24 = 24.7% of 73; 25–34 = 22.4% of 156; 35–	Funding source: NHS executive West Midlands Study summary: Study shows high prevalence and incidence of HMB in general population in UK.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
						<p>55 = 25.3% of 158; 45–54 = 27.8% of 144; All = 25% of 531.</p> <p>No statistically significant trend with age.</p> <p>Heavier periods than usual by age: 18–24 = 15.8%; 25–34 = 16%; 35–44 = 24.4%; 45–54 = 22.6%; All = 20.5%.</p>	
Snowden 1983 ¹²³	cohort EL = 3	Assessment of menstruation cycles	5292	women; menstruating Worldwide	MBL – subjective self-assessment; duration of menses – days; length of cycle – days	<p>MBL estimation: 'light' = 870 (16.5%); moderate = 3375 (64%); heavy = 1008 (19.5%)</p> <p>Amount of MBL by duration of menses: 'light' ($n = 870$) – 1–2 days = 17%, 3–4 days = 61%, 5–6 days = 17%, 7+ days = 5%; 'moderate' ($n = 3375$) – 1–2 days = 3%, 3–4 days = 51%, 5–6 days = 37%, 7+ days = 10%. 'Heavy' ($n = 1008$) – 1–2 days = 1%, 3–4 days = 27%, 5–6 days = 42%, 7+ days = 30%.</p> <p>Preference and behaviour related to menses by MBL (% wanting factors by MBL class – light, moderate, heavy): no amenorrhoea – 68%, 75%, 61%; less blood loss – 13%, 15%, 54%; more blood loss – 34%, 6%, 8%; work less during menses – 13%, 17%, 23%; rest taken – 22%, 27%, 34%; mood change prior to menses – 34%, 33%, 44%; mood change during menses – 42%, 43%, 57%; discomfort prior to menses – 53%, 55%, 61%; discomfort during menses – 48%, 52%, 66%</p>	<p>Funding source: WHO</p> <p>Study summary: Large WHO study shows variation in menstrual patterns from worldwide populations.</p>
Schmeler ⁹¹	Case series EL = 3	Factors associated with endometrial cancer	188	Women; aged less than 50; diagnosed with endometrial cancer USA		73 of 188 women had history of irregular menstruation.	Funding source: Not stated
Sulaiman 2004 ³⁴	non-comparative retrospective case series EL = 3	Association of fibroids and MBL	50	women; MRI identified fibroids; under-going UAE UK	MBL – alkaline haematin; fibroid size and location – MRI	<p>MBL by number of fibroids: 1 or 2 = 195 (± 40.1) ml vs 3+ = 236 (± 56.6) ml (NS).</p> <p>Site of fibroid and MBL: submucosal ($n = 12$) = 323.5 (± 55.82) ml; intramural ($n = 42$) = 206.02 (± 43.03); subserosal ($n = 5$) = 495 (± 98.9) ml. (NS)</p> <p>Largest fibroid and MBL: submucosal ($r = -0.567$, $P < 0.01$); intramural ($r = -0.396$, $P < 0.01$); subserosal ($r = -0.837$, $P < 0.001$).</p>	<p>Funding source: Not stated</p> <p>Study summary: MBL correlated neither with size nor location of fibroids.</p>
Thomas 1990 ¹⁹	Cohort EL = 3	Menstrual patterns	768	women; 13–14 years old Nigeria	Length of MBL cycle	menstrual cycle length (days): 14–16 = 1%; 17–19 = 0%; 20–22 = 2.6%; 23–25 = 9.9%; 26–28 = 64.3%; 29–31 = 16.6%; 32–34 = 1.8%; 35–37 = 1.5%; 38–40 = 1%; > 40 = 1%.	<p>Funding source: Not stated</p> <p>Study summary: Study shows cycle length in adolescent population in Nigeria.</p>
Treloar 1967 ¹⁴	cohort EL = 3	description of menstrual cycle length	2700 women – 25825 person years	Women USA	Menstrual history	<p>Abnormal menstrual cycle length ($n = 275945$) = 0.97%.</p> <p>Median average cycle length by age: 20 ($n = 4928$) = 27.8 (10–90 percentiles = 23.5 to 34.6); 25 ($n = 10548$) = 27.8 (24.1 to 33.6); 30 ($n = 9255$) = 27.2 (23.8 to 32.5); 35 ($n = 9278$) = 26.7 (23.3 to 31.2); 40 ($n = 8303$) = 26.2 (22.7 to 30.1).</p> <p>Mean average cycle length by age: 20 ($n = 452$) = 36.09 days; 25 ($n = 1005$) = 29.84; 30 ($n = 916$) = 29.3; 35 ($n = 850$) = 28.22; 40 ($n = 730$) = 27.26.</p> <p>Mean duration of menstruation by age: 20 ($n = 452$) = 3.94 days; 25 = ($n = 1005$) = 3.45; 30 ($n = 916$) = 3.16; 35 ($n = 860$) = 2.67; 40 ($n = 730$) = 2.83.</p>	<p>Funding source: Not stated</p> <p>Study summary: Study shows variation in menstrual cycle, with variation in menstrual symptoms decreasing and stabilising with increased age.</p>
Treloar 1999 ¹²⁴	Cohort EL = 3	prevalence of HMB	3096	women; twins; age 46.3; Australia	Prevalence of heavy menstrual bleeding	1266 (41.3%) of women reported menstrual problems during lifetime. 650 (or 80.2% of those that responded) reported heavy menses from 3096 (21%). 164 (31.3%) of 524 women reported HMB was reason for having hysterectomy.	Funding source: University of Queensland grant
Utman 2002 ³⁸	Cohort EL = 3	Pathology associated with menorrhagia	250	women; 12–19 years; excessive menstrual bleeding (> 5 pads a day) Pakistan		Aetiology: DUB = 226 (90.4%); Coagulation disorder = 20 (8%); fibroids = 2 (0.8%); Non-specific endometritis = 2 (0.8%).	<p>Funding source: Not stated</p> <p>Study summary: Study shows that pathology is low amongst adolescents with HMB.</p>

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Vercellini 1993 ³⁵	epidemiological cohort EL = 3	hysteroscopy	61	women; AUB; moderate to severe anaemia Italy	Cause of AUB	Of 61 cases: submucous myomas = 23; intramural/subserous myomas = 8; endometrial polyps = 8; submucous adenomyomas = 2; DUB (anovulation) = 15; unexplained menorrhagia = 5.	Funding source: Not stated
Warner 2004 ¹¹²	Cross-sectional survey EL = 3	Correlation of MBL to clinical features	226 who collected sanitary towels of 865 eligible in cohort of 952	women; 25–49 years; referred for menstrual problems UK	MBL – alkaline haematin; demographics; menstrual blood clots; iron status; number of pads used; pathway to clinic	Univariate analysis: MBL associated with ($P < 0.05$) subjective heaviness of bleeding; referral for bleeding; patient believes referral is for bleeding; clot size; clot number; ferritin level; haemoglobin level; number of pads used; rate of change of pads; pads changes during night; blood on clothing or sheets; duration of period; number of leakage onto underclothes. MBL not associated with age, deprivation, parity or volume of loss a reason for seeking help. Regression model: clot size, ferritin level, and frequency of pad change ($P = 0.001, 0.002, 0.006$) provide best predictive model for MBL > 80 ml.	Funding source: Chief Scientist's Office Study summary: Study shows correlation between suggestive assessment of MBL and objective MBL. Study highlights factors associated with MBL levels.
Wegienka 2003 ³³	Survey EL = 3	Fibroid association with menstrual bleeding	2384 approached – 910 suitable and responded.	women; 35–49 years; part of NIEHS fibroid study USA	menstrual flooding; length of menses; number of pads used	Sonogram information on 878 of 910; 564 with fibroids and 314 without. Mean tampon/pad use by status: no fibroid = 6.1 (SD 3.8); fibroid < 5 cm = 7 (4.2); fibroid > 5 cm = 10.7 (7.3). Relative risks of HMB: no fibroid = 1; diffuse only = 1.5 (1.1–2); largest fibroid < 2 cm = 0.9 (0.6–1.3); Largest fibroid 2–5 cm = 1.5 (1.2–2); Largest fibroid > 5 cm = 2.4 (1.8–3.1). Relative risk of HMB amongst women with leiomyomata: has single or diffuse only = 1; multiple leiomyomata = 1.1; no submucosal fibroids = 1; has at least one submucosal fibroid = 0.9.	Funding source: National Institute of Environmental Health Sciences
Dilley 2001 ⁵¹	comparative cohort study EL = 3	Prevalence of von Willebrand disease	244 – 121 menorrhagia, 123 controls	women; reproductive age; either treated for menorrhagia or not; average age – menorrhagia = 35.5, controls = 34.3 Country: USA	von Willebrand factor, Factor VIII, ristocetin cofactor, platelet function	Prevalence of vWD: menorrhagia = 11%, controls = 3.2% vWD in women with menorrhagia compared with those without, OR 6.6% vs 0.8% = 8.6 (1.3–194.6); factor deficiencies 1.6% vs 0 = NA; platelet abnormality 2.5% vs 2.4% = 1.0	Funding source: Not stated Study summary: Suggests routine testing for vWD may be appropriate.

Table 3.4 Impact on quality of life by HMB – comparative studies

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Abbott 2003 ¹⁰¹	Cohort EL = 2+	139 – 55 Cavaterm, 34 ELA, 13 ELITT, 37 NovaSure	Population characteristics: Women; menorrhagia; PBAC > 150; No intrauterine pathology; normal biopsy; Uterine length < 12 cm; pre-menopausal gonadotrophon level; Normal smear test; no plans for future childbearing. Country: UK and Australia	ELA, Cavaterm, ELITT, Novasure	12 months	QoL: EQ-5D, SF-12	Endometrial ablation vs general population at baseline: EQ-5D index: ablation = 0.72 (SD 0.28) vs general population = 0.89 (SD 0.17), $P < 0.0001$ EQ-5D VAS: 75.79 (SD 17.21) vs 85.19 (SD 15.51), $P < 0.0001$ SF-12 PCS: 46.31 (SD 8.80) vs 52.8, $P < 0.0001$ SF-12 MCS: 43.28 (SD 4.55) vs 51.9, $P < 0.0001$ Endometrial ablation baseline vs 12 month: EQ-5D index: ablation = 0.72 (SD 0.28) vs general population = 0.83 (SD 0.25), $P = 0.005$ EQ-5D VAS: 75.79 (SD 17.21) vs 82.49 (SD 15.28), $P < 0.0001$ SF-12 PCS: 46.31 (SD 8.80) vs 51.24 (SD 7.54), $P < 0.0001$ SF-12 MCS: 43.28 (SD 4.55) vs 49.31 (SD 10.07), $P < 0.0001$ Endometrial ablation 12 months results vs general population: EQ-5D index: ablation = 0.83 (SD 0.25) vs general population = 0.89 (SD 0.17), $P = 0.03$ EQ-5D VAS: 82.49 (SD 15.28) vs 85.19 (SD 15.51), NS SF-12 PCS: 51.24 (SD 7.54) vs 52.8, NS SF-12 MCS: 49.31 (SD 10.07) vs 51.9, NS	Funding source: Unclear. Grants for research on ELITT and NovaSure. Study summary: Quality of life in women who have undergone ablation is improved to normal level, equivalent to the general population.
Clark 2002 ⁹⁶	Systematic review EL = 2++	19 studies	Population characteristics: A systematic review of published research. Papers were identified through MEDLINE (1966–April 2000), EMBASE (1980–April 2000), Science Citation Index (1981–April 2000), Social Science Citation Index (1981–April 2000), CINAHL (1982–1999) and PsychLIT (1966–1999), and by manual searching of bibliographies of known primary and review articles.	QoL measures for menorrhagia		Quality assessment of measures	A total of 19 articles, 8 on instrument development and 11 on application, were included in the review. The generic Short Form 36 Health Survey Questionnaire (SF-36) was used in 12/19 (63%) studies. Only two studies developed new specific QoL instruments for menorrhagia but they complied with 7/17 (41%) and 10/17 (59%) of the quality criteria. Quality assessment showed that only 7/19 (37%) studies complied with more than half the criteria for face validity whereas 17/19 (90%) studies complied with more than half of the criteria for measurement properties ($P = 0.0001$).	Funding source: Not stated Study summary: Among existing QoL instruments, there is good compliance with the quality criteria for measurement properties but not with those for clinical face validity. There is a need to develop methodologically sound disease specific QoL instruments in menorrhagia focussing both on face validity and measurement properties.
Cooper 1997 ¹¹⁸	RCT EL = 1+	197	Population characteristics: Women; seeking treatment for HMB from specialist Country: UK	Medical management; hysteroscopic management	3 cycles	Quality of life – SF-36	Baseline QoL: Medical group ($n = 93$) (0 = worst, 100 = best) Physical function = 78.88 Social function = 69.06 Role – physical = 54.26 Role – emotional = 57.80 Mental health = 58.32 Energy = 41.24 Pain = 53.8	Funding source: Scottish Office – Department Health Study summary: Study shows that benefits from surgery in terms of QoL have greater than with medical treatment

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							<p>General health = 68.02</p> <p>Change in scores after treatment:</p> <p>Physical function = 4.84</p> <p>Social function = 7.57</p> <p>Role – physical = 15.32</p> <p>Role – emotional = 8.96</p> <p>Mental health = 4.78</p> <p>Energy = 7.07</p> <p>Pain = 8.84</p> <p>General health = -0.25</p> <p>Surgical group ($n = 93$) (0 = worst, 100 = best)</p> <p>Physical function = 81.94</p> <p>Social function = 69.06</p> <p>Role – physical = 56.72</p> <p>Role – emotional = 53.41</p> <p>Mental health = 59.14</p> <p>Energy = 41.51</p> <p>Pain = 57.95</p> <p>General health = 65.10</p> <p>Change in surgical scores after treatment:</p> <p>Physical function = 10.16</p> <p>Social function = 17.44</p> <p>Role – physical = 32.26</p> <p>Role – emotional = 31.54</p> <p>Mental health = 15.01</p> <p>Energy = 20.53</p> <p>Pain = 21.62</p> <p>General health = 10.49</p> <p>All $P < 0.05$ compared with changes from medical treatments</p>	
Cooper 1999 ¹⁰²	randomised – balanced blocks; allocation concealment – sequential envelopes; blinding not mentioned EL = 1++	263 randomised – 129 (116 completed follow-up) to MEA, 134 (124 completed follow-up) to TCRE	Population characteristics: Women; HMB – subjective; uterine size no larger than 10 weeks pregnant; pre-menopausal. Average age: MEA = 41.1, TCRE = 41.0 Country: UK	Microwave endometrial ablation (MEA); Transcervical resection of the endometrium (TCRE); pre-treatment of goserelin 3.6 mg Surgery vs baseline; surgery vs surgery	12 months	Patient satisfaction; patient acceptability; QoL – SF-36	<p>Patient satisfaction with treatment: MEA = 89 (77%), TCRE = 93 (75%), $P = 0.88$</p> <p>Cure or acceptable improvement in symptoms: MEA = 91 (78%), TCRE = 94 (76%), $P = 0.76$</p> <p>Treatment acceptable: MEA = 109 (94%), TCRE = 112 (90%), $P = 0.34$</p> <p>QoL score (SF-36) and standard deviation for MEA and TCRE, and change from baseline to 12 months:</p> <p>Physical functioning: 84.6 (SD 19.2), 82.2 (SD 23.3), $P = 0.40$, 0.7 (SD 18.9), 2.4 (SD 16.8), $P = 0.45$</p> <p>Social functioning: 60.1 (23.0), 60.1 (22.9), $P = 0.99$, 20.6 (26.5), 16.2 (24.4), $P = 0.18$</p> <p>Role – physical: 56.5 (42.2), 62.9 (41.7), $P = 0.24$, 23.9 (49.4), 11.3 (41.7), $P = 0.03$</p> <p>Role – emotional: 61.8 (42.5), 62.6 (43.2), $P = 0.88$, 17.0, 13.7, $P = 0.59$</p> <p>Mental health: 63.6 (18.8), 63.8 (21.7), $P = 0.92$, 6.3, 6.0, $P = 0.89$</p> <p>Energy/fatigue: 44.3(22.6), 43.3 (24.3), $P = 0.75$, 12.8</p>	Funding source: Microsulis plc

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							(21.7), 12.1 (23.0), $P = 0.80$ Pain: 55.4 (28.2), 63.7 (26.1), $P = 0.02$, 14.8 (31.0), 7.2 (31.1), $P = 0.06$ General Health: 69.7 (21.7), 73.0 (19.4), $P = 0.22$, 2.4 (20.3), -2.9 (20.0), $P = 0.04$.	
Coulter 1995 ¹¹⁶	cohort; prospective EL = 2-	518 recruited: Paper on 209 who visited gynaecologist – 150 NHS, 59 private	Population characteristics: women; referred for menorrhagia; aged 30–49 Country: UK	NHS vs private healthcare	1 survey	satisfaction questionnaire; QoL – Sf-36	Impact of menorrhagia: severity of symptoms: NHS ($n = 150$) – 2 (1.3%) mild, 65 (43.3%) moderate, 83 (55.3%) severe. Private ($n = 59$) – 1 (1.7%) mild, 28 (47.5%) moderate; 30 (50.8%) severe. Social impact of periods: NHS – 12 (8%) mild; 93 (62%) moderate; 45 (30%) severe. Private – 8 (13.6%) mild, 37 (62.7%) moderate; 14 (23.7%) severe. Treatment preference: NHS – prefer surgery – 76 (50.7%), drug therapy – 16 (10.7%), minimal treatment – 2 (1.3%), no preference – 56 (37.3%). Private – surgery – 32 (54.2%), drug – 6 (10.2%), minimal treatment – 4 (6.8%), no preference – 17 (28.8%). Got preferred treatment: NHS – yes 71 (77.2%), no – 21 (22.8%). Private – yes – 38 (90.5%), no – 4 (9.5%). Satisfaction with treatment: NHS – satisfied – 91 (66.4%), OK – 28 (20.4%), Dissatisfied – 18 (13.2%). Private – satisfied – 42 (76.3%), OK – 7 (12.7%), dissatisfied – 6 (10.9%).	Funding source: Department of Health, UK
Hawe 2003 ¹⁰³	blinded; randomised – block; allocation concealment – sealed, sequential envelopes EL = 1+	72: Cavaterm = 37 (3 lost to follow-up by 12 months), Endometrial laser ablation = 35 (2 lost to follow-up by 12 months)	Population characteristics: Women; MBL > 100 on PBAC; pre- menopausal gonatrophin levels; uterine length < 12 cm; no intrauterine pathology; normal endometrial biopsy; normal cervical cytology; completed family and using reliable contraception; no previous caesarean section or clotting problems; no contraindications to surgery – hyperplasia, pelvic infection. Average age: Cavaterm = 41.4 vs laser = 41.1 Parity: Cavaterm = 2.3 vs laser = 2.6 MBL (PBAC): Cavaterm = 354.5 vs laser = 424.3 Country: UK	Cavaterm – thermal balloon ablation; endometrial laser ablation; Pre- treatment of goserelin 3.6 mg (used to maintain blinding) Surgery vs surgery	6 and 12 months	Amenorrhoea rates; patient satisfaction; patient acceptability; QoL – EQ-5D and SF-12	Amenorrhoea rates at 12 months: Cavaterm ($n = 34$) = 10 (29%) vs laser = 13 (39%) MBL (PBAC) at baseline and 6 months: Cavaterm = 354.5 (SD 130.5) to 28.8 (SD 59.6); Laser = 424.3 (SD 297.1) to 27.7 (SD 57.6) Patient satisfaction at 12 months (Satisfied or greater): Cavaterm = 93.4% vs Laser = 95.9%. QoL (SF-12) at baseline, 6- and 12 months: Cavaterm: Physical component = 46.0, 52.1, 49.9; mental component = 45.4, 52.2, 51.0. Significant difference except for baseline vs 12 months for physical component Laser: physical component = 45.1, 50.4, 50.1; medical component = 43.0, 48.8, 48.9. Significant differences from baseline on all measures. QoL (EQ-5D) at baseline, 6 and 12 months: Cavaterm = 0.78, 0.81, 0.81 Laser = 0.65, 0.80, 0.82. Cavaterm changes not significant, Laser changes significant. QoL (EQ-5D – VAS) at baseline, 6 and 12 months. Cavaterm = 77.3, 82.1, 84.9	Funding source: Not stated – Wallsten Medical supplied Cavaterm equipment Study summary: Cavaterm is equivalent to laser ablation.

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							Laser = 69.4, 80.9, 74.8 Cavaterm and Laser only significant change at one time period.	
Hurskainen 2001 ⁶⁶	Cross-sectional survey EL = 2-	226: split between < 60 ml and > 60 ml MBL (lower level used to ensure group difference).	Population characteristics: women; subjective menorrhagia; scheduled for hysterectomy; uterine pathology excluded. Country: Finland	Psychosocial impact of menorrhagia; subjective vs objective menorrhagia		psychosocial factors; QoL – SF-36; MBL – alkaline haematin	Using univariate analysis, difference between < 60 ml and > 60 ml groups: MBL = 36.3 vs 168.8; haemoglobin = 132.2 vs 128.3 ($P < 0.001$); anxiety – 33.4 vs 31.3 ($P = 0.031$); unemployment 17% vs 4% ($P = 0.001$); perceived inconvenience bleeding = 16.3 vs 18.2 ($P = 0.01$); abdominal pain = 5.7 vs 3.9 ($P = 0.014$); Ferritin = 23.4 vs 12.9 ($P < 0.001$); no statistical difference between groups for: depression, psychosomatic symptoms, social support, negative life-events, sex life, visits to doctor, absent from work, out-of-pocket expense, and hospitalisation. Using multivariate analysis – unemployment, anxiety, perceived inconvenience, abdominal pain and ferritin were significant factors in explaining variance.	Funding source: Not stated Study summary: Psychosocial factors may account for women seeking help with MBL, as many who complain of menorrhagia have normal MBL, but psychosocial symptoms.
Hurskainen 2004 ¹⁰⁴	randomised; allocation concealed; controlled EL = 1++	236: 119 LNG-IUS (57 had IUS; 10 nothing; 50 had hysterectomy by 5 years); 117 hysterectomy (109 had hysterectomy by 5 years). 5 LNG-IUS, 7 hysterectomy lost to follow-up.	Population characteristics: women; menorrhagia; no pathology Country: Finland	LNG-IUS; hysterectomy treatment vs baseline; treatment vs treatment	5 years	QoL – EQ-5D, SF-36	QoL at 5 years: change in EQ-5D was 0.08 for IUS vs 0.1 for hysterectomy from baseline of 0.76 (0.7, 0.8) and 0.78 (0.7, 0.8). No difference between groups ($P = 0.6$). SF-36: change in general health = 3.6 vs 4.4 from baseline of 64 vs 65; physical functioning = -1.4 vs -2 from baseline of 83 vs 84; social functioning = 8.7 vs 9.0 from baseline of 72 vs 76. No difference between groups ($P = 0.8, 0.9, 0.9$). At 5 years: 50 LNG-IUS users had hysterectomy. Another 10 women were without LNG-IUS <i>in situ</i> . 7 Hysterectomy group had cancelled operation or had IUD fitted. Baseline figures: EQ-5D (LNG-IUS, Hysterectomy) – 0.76, 0.78; SF-36 general health – 64, 65; physical functioning – 83, 84; emotional well-being – 67, 70; social functioning – 72, 76; energy – 55, 57; pain 63, 62; role functioning – emotional – 65, 66; emotional – 61, 66. No data for entire population average.	Funding source: Government grant Study summary: Study shows that at 5 years LNG-IUS offered effective alternative to hysterectomy.
Hurskainen 2001 ¹⁰⁵	randomised; allocation concealed EL = 1++	236: 117 LNG-IUS (24 had hysterectomy); 119 hysterectomy (107 underwent operation). 3 LNG-IUS and 5 hysterectomy patients were lost to follow-up.	Population characteristics: women; menorrhagia; no pathology – fibroids, cancer etc.; no previous failure with LNG-IUS; no acne Country: Finland	LNG-IUS; hysterectomy treatment vs baseline; treatment vs treatment	12 months	QoL – EQ-5D, SF-36	Baseline QoL: EQ-5D – IUS = 0.76 (0.7 to 0.80), Hysterectomy = 0.78 (0.70 to 0.80) SF-36 scores: General health – IUS = 64 (60.6 to 67.4), Hysterectomy = 65 (61.0 to 69.0) Physical functioning – IUS = 83 (79.4 to 86.6), Hysterectomy = 84 (80.8 to 87.2) Emotional functioning – IUS = 67 (63.2 to 70.8), Hysterectomy = 70 (66.6 to 73.4) Social functioning – IUS = 72 (67.6 to 76.4), Hysterectomy = 76 (72.2 to 79.8)	Funding source: Government funded. IUD provided free by Leiras. Study summary: Study shows LNG-IUS was effective alternative to hysterectomy at 12 months.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							<p>Energy – IUS = 55 (50.6 to 59.4), Hysterectomy = 57 (53.0 to 61.0)</p> <p>Pain – IUS = 63 (58.4 to 67.4), Hysterectomy = 62 (57.6 to 66.4)</p> <p>Role functioning – physical – IUS = 65 (57.5 to 72.3), Hysterectomy = 66 (58.9 to 73.1)</p> <p>Role functioning – emotional – IUS = 61 (53.5 to 68.5), Hysterectomy = 66 (58.7 to 73.3)</p> <p>General Health questionnaire – IUS = 73 (69.4 to 76.6), Hysterectomy = 75 (71.8 to 78.2)</p> <p>Anxiety – IUS = 32 930.8 to 33.2), Hysterectomy = 31 (30.0 to 32.0)</p> <p>Depression – IUS = 5.2 (4.2 to 6.2), Hysterectomy = 4.2 (3.4 to 5.0)</p> <p>Sexual satisfaction – IUS = 23.6 (22.4 to 24.8), Hysterectomy = 23.7 (22.9 to 24.5)</p> <p>Sexual problems – IUS = 4.4 (4.0 to 4.8), Hysterectomy = 4.5 (4.1 to 4.9)</p> <p>Partner satisfaction – IUS = 11.2 (10.6 to 11.8), Hysterectomy = 11.6 (11.2 to 12.0)</p> <p>QoL at 12 months (intention-to-treat): all measured improved for both groups. EQ-5D by 0.1 in both groups ($P = 0.0001$) from baseline of 0.76 (0.7, 0.8) for LNG-IUS and 0.78 (0.7, 0.8) for hysterectomy. SF-36 General health – 5.5 for IUS and 6.2 for hysterectomy from baseline of 64 vs 65; physical functioning 4.8 vs 7.1 from baseline of 83 vs 84; social functioning 11.8 vs 12.4 from baseline of 72 vs 76. No difference between groups, except pain 11.8 vs 21.2 ($P = 0.01$).</p> <p>At 12 months – 24 LNG-IUS group had undergone hysterectomy. Another 10 women had had LNG-IUS removed. 5 hysterectomy group cancelled operation.</p>	
Learman 2004 ¹¹⁹	randomised – block; non-blinded; concealment EL = 1+	63 in total, 31 (2 lost to follow-up) to hysterectomy and 32 (2 lost to follow-up) to medical treatment	Population characteristics: Women; failed medical treatment – medroxyprogesterone; 30 to 50 years of age; minimum of 2 months AUB; no hyperplasia on biopsy; excluded if – wanted future fertility desired, pregnant, or coagulopathy; long-acting treatments within 6 months; COC or IUD within 3 months; pelvic pathology for which surgery was indicated. Average age: hysterectomy = 42, medicine = 40 Health insurance = 65%, 81% < high school education = 39%,	medical treatment; hysterectomy treatments vs baseline	2 years	Menstrual bleeding; Pelvic discomfort; urinary symptoms; menopausal symptoms	<p>Baseline symptomology figures:</p> <p>Hysterectomy group = pelvic pain 74%, pelvic or bladder pressure 55%, low back pain 68%, hot flushes 19%, urinary symptoms – urgency 26%, frequent urination 26%, stress incontinence 29%</p> <p>Continued vaginal bleeding at 6 months was 87% for medicine and 11% for hysterectomy ($P < 0.001$).</p> <p>Continued vaginal bleeding at 24 months was 37% for medicine and 7% for hysterectomy ($P < 0.001$).</p> <p>Continued bleeding in hysterectomy group due to cross-over between treatments.</p> <p>Medicine group = pelvic pain 88%, pelvic or bladder pressure 84%, low back pain 72%, Hot flushes 41%, Urinary symptoms – urgency 44%, frequent urination 41%, stress incontinence 25%</p>	<p>Funding source: Agency of HealthCare Research and Quality grant</p> <p>Study summary: Hysterectomy was more effective treatment than additional medical treatment in this selected patient group.</p>

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			<p>38%</p> <p><\$25,000 income = 42%, 53%</p> <p>Uterine fibroids = 65%, 63%</p> <p>Previous treatment:</p> <p>hysterectomy = COC 39%, prostaglandin inhibitors 13%, GnRH-a 10%, D&C 19%, myomectomy 6%, endometrial ablation 3%</p> <p>Medicine = COC 50%, prostaglandin inhibitors 19%, GnRH-a 6%, D&C 38%, myomectomy 0%, endometrial ablation 0%</p> <p>Country: USA</p>				<p>Change in symptom frequency from baseline at 6 months (intention-to-treat)</p> <p>Pelvic pain: hysterectomy = -2.3, medicine = -0.7, $P < 0.01$</p> <p>Urinary urgency: hysterectomy = -0.7, medicine = 0.0, $P = 0.03$</p> <p>Urinary incomplete emptying: hysterectomy = -0.6, medicine = +0.1, $P = 0.03$</p> <p>Breast pain: hysterectomy = -1.3, medicine = -0.5, $P = 0.02$</p> <p>No difference for other pelvic, urinary or menopausal symptoms.</p> <p>Change in symptom frequency for baseline at 2 years (intention-to-treat)</p> <p>Urinary incomplete emptying: hysterectomy = -0.8, medicine = -0.3, $P = 0.04$</p> <p>Hot flushes: hysterectomy = -0.6, medicine = 0.5, $P < 0.01$</p> <p>No difference for other pelvic, urinary or menopausal symptoms.</p> <p>Change in symptoms for groups as treated:</p> <p>Hysterectomy only groups produced significant reduction in symptoms, except for stress incontinence ($P = 0.34$) and urge incontinence ($P = 0.74$)</p> <p>Medicine then hysterectomy group produced same results, except hot flushes not significant ($P = 0.13$)</p> <p>Medicine only group produced significant reductions in symptoms for pelvic pain, pelvic pressure, and stress incontinence ($P < 0.05$), all other changes were non-significant.</p>	
Shapley 2002 ⁶³	Case-control EL = 2+	943 questionnaires sent – 645 usable	<p>Population characteristics: women; consulting for HMB; consulting for another condition; or community controls</p> <p>Country: UK</p>	<p>Consultation for HMB</p> <p>cases vs consulting controls; cases vs community controls</p>	1 questionnaire	<p>consultation; MBL – subjective; GHQ score; HMB interference on lifestyle</p>	<p>Regression analysis of those consulting vs control group also consulting for other conditions: heaviness of periods interferes with life OR = 3.26 (1.92–5.54); heavy periods OR = 2.52 (1.41–4.49). Consulting vs non-consulting controls: heaviness of period OR = 3.25 (1.72–6.14), heavy periods OR = 2.57 (1.35–4.88).</p> <p>GHQ scores < 4 or > 4: consulting vs consulting controls – OR = 1.26 (0.74–2.13) and consulting vs non-consulting controls OR = 1.43 (0.85–2.38).</p>	<p>Funding source: Not stated</p> <p>Study summary: Study shows that interference with QoL by HMB is main reason for consultation.</p>
Shapley 2003 ⁶²	Cohort; case-control EL = 2–	Population 1: 186: 46 menorrhagia; 79 consulting controls; 61 non-consulting controls reporting heavy bleeding	<p>Population characteristics: women; Country: UK</p>	<p>Reason for seeking medical attention</p> <p>study vs controls</p>		QoL measures	<p>Population 1: Reason why heaviness of bleeding interfered with life (case vs consulting control P value, case vs non-consulting control P value). Performance at employed work – $P = 0.24$, 0.40; performance of house work – $P = 0.03$, 0.06; days off work – $P = 0.56$, 0.22; life causing embarrassment – $P = 0.02$, 0.17; mood – $P = 0.53$, 0.97; sex life – $P = 0.12$, 0.03; social</p>	<p>Funding source: Not stated</p> <p>Study summary: Study suggests psychosocial impact of HMB is a reason why women seek help.</p>

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			interfered with life. Population 2: 160 cases and controls. Population 3: 494 controls – not consulted about periods in last 6 months				life – $P = 0.01, 0.005$. Population 3 ($n = 494$): reasons for not consulting in last 6 months. 281 (57%) normal periods; 29 (6%) 'women's burden'; 167 (34%) – I am coping; 53 (11%) Observing; 25 (5%) too busy; 5 (1%) scared; 15 (3%) embarrassed. Women could give more than one reason	

Table 3.5 Impact of quality of life by HMB – non-comparative studies

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Ballinger 1985 ⁶¹	Cohort EL = 3	association of menstrual and mental problems	1517	women; 20–59 Country: UK	MBL – self assessment; mental health – GHG	MBL self-assessment: light = 19%; moderate = 51.3%; heavy = 24.3%; very heavy = 5.4%. Association of GHG > 12 (moderate depression) and MBL level, chi-squared = 20.11, $P = 0.0002$	Funding source: Not stated Study summary: Demographic factors have to be taken into account when assessing impact of psychiatric morbidity in women with gynaecological problems.
Bytes 1997 ¹⁰⁸	Qualitative; focus groups EL = 3	Women's experience of menstrual disorders	200	Women; 30–50 years; complaining of heavy, frequent or painful periods. Country: Australia		The main patient experience themes to emerge were: mood changes, impact on family, jobs and lifestyle; self-conscious; dread of menstruation, and feelings of guilt. Help-seeking themes: difficulty finding doctor that they're comfortable with; difficulties asking question – no knowledge; not being told enough by health professionals; problem dismissed – menstrual cycles differ. Factors that helped women deal with problem: to feel doctor listened and understood; information provision; normalisation – self-help groups; medications – don't like taking tablets; alternative therapies – relaxation.	Funding source: Not stated Study summary: Interaction between health professional and patient important in the management of menstrual disorders.
Chapple 1999 ¹⁰⁹	Qualitative EL = 3		30	women; subjective menorrhagia Country: UK	Patient experience of menorrhagia	Women explained experience of menorrhagia. 1. Period of uncertainty – deciding if MBL was abnormal. 2. Watchful waiting – seeing if symptoms go on their own. 3. Seek help only when life is disrupted. 4. Experience of healthcare – often found difficult to get treatment or referral for condition.	Funding source: Not stated Study summary: Nurses may be able to provide information and education to women about menorrhagia.
Cote 2002 ¹¹³	Cross-sectional survey EL = 3		2805 from National Health Interview Survey	women; regular cycle Country: USA	work status; lost earnings	Odd ratios for risk factors of being in labour force: menstrual flow – low/normal = reference, heavy = 0.72 (0.56–0.92). Heavy bleeding leads to on average 3.6 weeks work lost or \$1,692 earnings.	Funding source: Not stated Study summary: Study highlights the potential economic impact of HMB.
Cote 2003 ⁴⁰	cross-sectional EL = 3	cost of menorrhagia; factors associated of menorrhagia	2805 women involved in NHIS household survey	women; 18–64 years old; natural menstruation in last 12 months and 3 months; never taken estrogen containing drugs, except OCP; no reproductive cancer; no recent hysterectomy. Country: USA	Self-reported MBL; perception of general health; age	Age difference: heavy flow vs low/normal flow – 18–39 = 114 (30.6%) vs 485 (19.9%); 40–49 = 237 (63.5%) vs 1722 (70.8%); > 49 = 22 (5.9%) vs 225 (9.3%), $P < 0.00$ Ethnic group: white = 258 (69.2%) vs 1844 (75.8%); others = 115 (30.8%) vs 588 (24.2%), $P = 0.01$. Education level = less than high school = 68 (18.2%) vs 368 (15.1%); High school cert. = 225 (60.3%) vs 1370 (56.3%); degree = 80 (21.4%) vs 694 (28.5%), $P = 0.01$ Perception of health: excellent = 85 (22.8%) vs 881 (36.2%); very good = 121 (32.4%) vs 813 (33.4%); good = 111 (29.8%) vs 556 (22.9%); fair = 40 (10.7%) vs 149 (6.1%); poor = 16 (4.3%) vs 32 (1.3%), $P < 0.001$.	Funding source: Not stated Study summary: Study provides data on association between subjective menorrhagia and socio-demographic factors.
Coulter 1994 ¹¹⁵	Cohort EL = 3	QoL impact of HMB	518 recruited – 425 eligible and returned questionnaire. 348 returned baseline and follow-up questionnaire.	Women; subjective HMB; 30–49 years old Country: UK	QoL	Baseline characteristics: duration of periods > 6 days ($n = 269$) – 77.3%; > 9 pads used on heaviest day ($n = 204$) – 58.6%; flooding ($n = 247$) – 71%; Clots ($n = 236$) – 67.8%; Clothes bloodstained ($n = 205$) – 58.9%; Painful periods ($n = 181$) – 52%. Social impacts: cause of anxiety or depression ($n = 175$) – 50.3%; cause of moodiness or irritability ($n = 238$) – 68.4%; Interfere with job ($n = 48$) – 13.8%; Interfere with domestic life ($n = 86$) – 24.7%; Interfere with relationship ($n = 115$) – 33%; Spoil sex life ($n = 152$) – 43.7%; Interfere with social life ($n = 101$) – 29%; Interfere with hobbies ($n = 119$) – 34.2%; Interfere with holidays ($n = 125$) – 35.9%; interfere with life in general ($n = 151$) – 43.4%.	Funding source: Department of Health, UK
Gath 1982 ¹⁰⁶	Cohort; prospective EL = 3	hysterectomy	174 invited: 18 refused, 156 entered study.	women; menorrhagia – benign origin; scheduled for hysterectomy	psychiatric state – present state examination (PSE); Eysenck Personality	Baseline PSE: 1–4 = 66 (42.3%), 5a = 37 (23.7%), 5b = 22 (14.1%), 6–8 = 31 (19.9%). (5 or > = case). Patients had higher PSE scores than general population ($P < 0.001$).	Funding source: Not stated Study summary: Hysterectomy reduces level of psychiatric

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
				Country: UK	inventory; Profile of Mood States.	<p>Patients vs general population:</p> <p>Worry = 45% vs 89% ($P < 0.001$), Somatic features of depression = 9% vs 85% ($P < 0.001$), tension = 33% vs 77% ($P < 0.001$), irritability = 17% vs 62% ($P < 0.001$), situational anxiety = 28% vs 55% ($P < 0.001$), lack of energy = 8% vs 53% ($P < 0.001$), simple depression = 16% vs 47% ($P < 0.001$), social unease = 23% vs 43% ($P < 0.001$), anxiety = 6% vs 40% ($P < 0.001$), loss of concentration = 12% vs 31% ($P < 0.001$).</p> <p>Patients after vs patients before surgery (P values for after surgery figures vs general population figures:</p> <p>Worry = 61% vs 89% ($P < 0.01$), Somatic features of depression = 37% vs 85% ($P < 0.001$), tension = 64% vs 77% ($P < 0.001$); irritability = 22% vs 62% (NS), situational anxiety = 48% vs 55% ($P < 0.001$), lack of energy = 27% vs 53% ($P < 0.001$), simple depression = 24% vs 47% (NS), social unease = 28% vs 43% (NS), anxiety = 22% vs 40% ($P < 0.001$), loss of concentration = 22% vs 31% ($P < 0.05$).</p>	morbidity. Hysterectomy did not cause psychiatric morbidity. Psychiatric morbidity higher in patient group than general population.
Marshall 1998 ¹¹⁰	Qualitative; semi-structured interviews EL = 3	Women's experience of HMB	43	women; 21–53 years; referred for HMB Country: UK	Women's experience of HMB	<p>Main themes:</p> <p>Menstruation: patients main concerns were – amount, duration, frequency, presence of blood clots, unpredictability, change from 'normal'</p> <p>Symptoms: main symptoms were – anaemia, tiredness, fainting and dizziness.</p> <p>Anxiety associated with symptoms – concerns about underlying pathology</p> <p>Impact of menstrual problems – daily living effected</p> <p>What is 'normal' – no perception of 'normal' just not heavy.</p> <p>Health professionals: information provision important; communication important; treatment prior to referral.</p> <p>Women concerned about seeking help, so go to doctor with other problems – such as sore throats.</p> <p>No agreement on if gender of doctor is important (JAC – perhaps trust more important)</p> <p>High degree of anxiety about medical encounters – worried about treatments and what might be found</p>	<p>Funding source: Wirral Health Authority</p> <p>Study summary: Study highlights patient concerns with MBL and treatment. This themes should be the focus of patient education.</p>
Mikhail 1985 ¹¹⁴	Survey EL = 3	Women's health experiences and concerns	200	Women; 40–60 years of age Country: Egypt	QoL	<p>Menstrual and gynaecological problems: Concerned about – menstrual disturbances = 50%, experienced = 28.5%, premenstrual symptoms = 11.5%, 1.5%; vaginitis/cervicitis = 20%, 12%; Family planning problems = 17.5%, 17.5%; uterine prolapse = 16.5%, 6.5%.</p> <p>Would seek medical help – heavy menstrual bleeding = 100%. Same as blood in stool or urine.</p>	<p>Funding source: Not stated</p> <p>Study summary: Study shows that HMB seen as serious symptom in this population.</p>
O'Flynn 2000 ¹²⁵	qualitative; cross-sectional survey EL = 3	Patient definition and experience of menorrhagia	21	women; aged 29–57 years; primary-care only; subjective menorrhagia Country: UK	patient experience	<p>Women presented a number of themes:</p> <p>Describe heavy periods in quantitative and qualitative terms – length of cycle or colour of blood.</p> <p>Describe HMB as change from usual patterns.</p> <p>HMB often about mental health than purely MBL.</p> <p>HMB commonly associated with passing large clots of blood.</p> <p>Patients believe their personal definition of HMB are valid.</p> <p>Variety of explanations for HMB – these mainly linked to biomedical descriptions.</p> <p>Definitions and explanations for HMB influenced help seeking.</p> <p>Reassurance of no underlying pathology. a reason for seeking help.</p> <p>Women want to be taken seriously in consultation – often felt they were being ignored.</p>	Funding source: Scientific Foundation Board – RCGP
Smith 2004 ¹⁰⁷	cohort EL = 3	UAE	80	Women; undergone UAE Baseline: Age: 45.6	QoL	<p>QoL for UAE ($n = 64$) – baseline (SD), post-UAE (SD), change (SD), P value:</p> <p>Symptom severity (0 to 100): 61.61 (20.95), 26.42 (23.38), 35.19 (23.58), $P < 0.0001$.</p> <p>Concern (0 to 100): 38.83 (30.31), 82.27 (22.48), –43.44 (31.48), $P < 0.0001$.</p> <p>Activities (0 to 100): 44.81 (29.48), 84.71 (24.29), –39.89 (30.46), $P < 0.0001$.</p>	<p>Funding source: Not stated</p> <p>Study summary: Women who undergo UAE have a significant decrease in symptom severity</p>

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
				Mean BMI: 27.4 Mean uterine size (weeks): 14.7 Symptoms: menorrhagia: 84% Pain: 38.2% Mass symptoms: 48.1% Previous treatments: COC; Pupron; myomectomy; Endometrial ablation Uterine volume(cm ³): 678.4 Country: USA		Energy/mood (0 to 100): 48.90 (31.68), 79.85 (25.67), -30.96 (29.66), $P < 0.0001$. Control: 48.75 (31.10), 82.27 (25.85), -33.51 (30.52), $P < 0.0001$. Self-conscious: 47.14 (31.57), 73.31 (28.91), -26.17 (29.24), $P < 0.001$. Sexual function: 48.17 (32.87), 78.28 (26.80), -30.11 (33.15), $P < 0.0001$. HRQL total: 44.92 (25.24), 80.58 (23.66), -35.66 (27.10), $P < 0.0001$.	and increase in HRQOL, associated with high levels of satisfaction with the procedure, even when subsequent therapies are pursued.
Spies 1999 ¹¹⁷	Cohort EL = 3	UAE	50 – 17 completed 12 month follow-up	women; fibroids; scheduled for UAE Country: USA	QOL – fibroid specific questionnaire	QoL: (0–100, 0 – worst, 100 – best) General Health baseline ($n = 50$) = 71.6 (± 24.73), 3 months ($n = 37$) = 84.46 (15.98), 6 months ($n = 31$) = 79.83. Comparative health: baseline = 42.5, 3 months = 80.41, 6 months = 77.42. Physical function: baseline = 77, 3 months = 93.29, 6 months = 90.59. Mental Health: baseline = 66.33, 3 months = 80.22, 6 months = 78.97. Self-image: baseline = 53.89, 3 months = 78.01, 6 months = 75. Energy: baseline = 37.44, 3 months = 64.84, 6 months = 60.97. Pain (higher = worse, lower = better): baseline = 31.08, 3 months = 13.96, 6 months = 19.09. Scores for symptoms: HMB: baseline = 36.61, 3 months = 90.81 ($P < 0.001$), 6 months = 85.03 ($P < 0.001$).	Funding source: Cardiovascular And Interventional Radiology Research and Education Foundation. Study summary: UAE improves QoL of patients with fibroids.
Warner 2004 ¹¹¹	Cohort EL = 3	Relationship of MBL or symptoms	952	Women; referred for HMB Country: UK	MBL – alkaline haematin; menstrual symptoms – pain, mood, etc.	Reported problems of HMB ($n = 865$): period pain = 33%, mood change = 32.8%, blood loss greater than previously = 29.1%, duration of periods too long = 25.3%, Blood loss = 24.6%, interruption of daily life = 24.2%, feel unwell/tired due to period = 23.4%, Other changes = 22.6%, blood leakage uncontrollable = 20.1%. Relationship between MBL and symptoms based on 4 groupings (< 50 ml, 50–79 ml, 80–119 ml, > 120 ml): negative relationships – pain and MBL, $P = 0.015$, pain around period, $P = 0.003$, mood change around period, $P = 0.002$, unpredictable onset of periods, $P = 0.012$, any cyclic changes, $P = 0.007$. Positive relationships: accidents are severe problem, $P < 0.001$; impact of daily life causes help seeking, $P = 0.046$; extra laundry as a severe problem, $P = 0.029$. No relationship: feeling unwell/tired, volume of bleeding, worried that something is wrong. No correlation between MBL and factors between 50–79 ml and 80–199 ml groups.	Funding source: Chief Scientist's Office grant Study summary: Little difference between two groups around 80 ml. 80 ml definition is of limited clinical usefulness.
Ruta 1995 ⁹⁹	Survey development EL = 3	SF-36 vs menorrhagia severity score				Correlation between menorrhagia severity score and SF-36 scales: Physical function = 0.33, social function = 0.53, role limitation physical = 0.48, role limitation emotional = 0.31, mental health = 0.38, energy and fatigue = 0.46, pain = 0.51, general health = 0.38. 15 item questionnaire for assessing severity of menstrual bleeding on quality of life. Internal reliability ($P < 0.001$); validity – significant correlation on all SF-36 scales.	Study summary: Questionnaire may be using in selecting treatment for menorrhagia.

Heavy menstrual bleeding

Table 4.1 Estimation of menstrual blood loss and quality of life – comparative studies

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Hurskainen 2001 ⁶⁶	Cross-sectional survey EL = 2–	226: split between < 60 ml and > 60 ml MBL (lower level used to ensure group difference).	Population characteristics: women; subjective menorrhagia; scheduled for hysterectomy; uterine pathology excluded. Country: Finland	Psychosocial impact of menorrhagia; subjective vs objective menorrhagia		psychosocial factors; QoL – SF-36; MBL – alkaline haematin	Using univariate analysis, difference between < 60 ml and > 60 ml groups: MBL = 36.3 vs 168.8; haemoglobin = 132.2 vs 128.3 ($P < 0.001$); anxiety – 33.4 vs 31.3 ($P = 0.031$); unemployment 17% vs 4% ($P = 0.001$); perceived inconvenience bleeding = 16.3 vs 18.2 ($P = 0.01$); abdominal pain = 5.7 vs 3.9 ($P = 0.014$); Ferritin = 23.4 vs 12.9 ($P < 0.001$); no statistical difference between groups for: depression, psychosomatic symptoms, social support, negative life events, sex life, visits to doctor, absent from work, out-of-pocket expense, and hospitalisation. Using multivariate analysis – unemployment, anxiety, perceived inconvenience, abdominal pain and ferritin were significant factors in explaining variance.	Funding source: Not stated Study summary: Psychosocial factors may account for women seeking help with MBL, as many who complain of menorrhagia have normal MBL, but psychosocial symptoms.
Rees 1991 ¹³⁴	cohort EL = 2–	17	Population characteristics: Women; subjective menorrhagia Country: UK	Informed of normal MBL	3 years	Treatment use	All 17 women had MBL < 80 ml over 2 cycles. 3 year follow-up showed: 14 accepted advice, 2 using mefenamic acid; 1 hysterectomy.	Funding source: Not stated Study summary: Study shows that reassurance of normal MBL is an effective intervention for women with normal MBL but concerns about HMB.

Table 4.2 Estimation of menstrual blood loss – diagnostic studies

Bibliographic information	Study type and evidence level	No. of patients and prevalence	Population characteristics	Type of test and reference standard	Sensitivity, specificity, PPV and NPV	Source of funding and additional comments
Barr 1999 ¹³⁹	Diagnostic EL = III	307	women Country: Nigeria	PBAC; alkaline haematin	Comparison of PBAC to alkaline haematin: sensitivity = 58%; specificity = 75% at chart cut-off of 50	Funding source: Not stated Study summary: PBAC recommended as a useful screening device.
Cheyne 1970 ¹²⁷	diagnostic EL = III	7 samples	No patients – laboratory experiment Country: UK	Chemical recovery of iron. Atomic recovery of iron	Atomic ($n = 4$) recovered 97.5 to 105% of iron. Chemical ($n = 3$) recovered 98.1 to 100.9% of iron.	Funding source: Not stated Reviewer comments: Very small study which makes any statistical interpretation difficult.
Chimbira 1980 ¹⁴⁰	Diagnostic EL = II	92	Women; menorrhagia – subjective Country: UK	assessment of MBL	Objective vs subjective MBL assessment: 23 of 68 (34%) of cycles termed light were > 80 ml; 28 of 59 periods (47%) termed heavy were < 80 ml; 32 of 57 termed medium were > 80 ml. Quantity of sanitary towels/tampons used: < 10 pads = 11 ml; 31–40 pads = 141 ml; > 40 = 113 ml; 41–50 = 58 ml (but small numbers at higher levels). Duration of menstruation: median = 2 to 9 days (45 to 83 ml). Small numbers mean no statistical analysis.	Funding source: Sterling Winthrop Laboratories. Study summary: That menorrhagia was associated with a large uterus or endometrial surface area could not be confirmed.
Deeny 1994 ¹³⁸	Diagnostic EL = III	53	women; 30–52 years; DUB; referred for ablation Country: UK	alkaline haematin test; PBAC	Median MBL = 73 ml, median PBAC = 156. Regression analysis: PBAC to ml ($P = 0.001$). At PBAC > 100 – sensitivity = 88%, specificity = 52%, false positive = 59%. ROC curve shows PBAC only has intermediate discriminatory power.	Funding source: Not stated Study summary: PBAC is useful, but alkaline haematin is 'gold' standard.
Fraser 1984 ¹⁴¹	Diagnostic EL = III	69	women; menorrhagia – subjective Country: Australia	factors influencing MBL	Perception of menstrual loss ($n = 60$) patients able to differentiate 'lightest' from 'heaviest' periods during study ($P < 0.001$). 45% correctly assessed order of MBL for all four periods. Daily MBL vs patient assessment: 'spotting' = 2.5 ml; light = 5.7 ml; moderate = 16.1 ml; very heavy = 22 ml. Spotting to light, $P < 0.001$; light to moderate, $P < 0.001$; moderate to heavy, $P < 0.02$. Age difference in MBL perception: < 27 years – light = 5.1 ml, moderate = 13.8 ml and heavy = 11.6 ml. > 36 years – light = 10.1 ml, moderate = 20.1 ml and heavy = 20.1 ml. Difference between groups were: NS, < 0.5, < 0.001. Duration and MBL: lightest = 4.7 days, heaviest = 5.8 days	Funding source: Not stated Study summary: Studies provides some indication of correlation between patient assessment of MBL and objective measures, but that alkaline haematin remains only reliable method.
Fraser 2001 ¹⁶⁷	Diagnostic test EL = II	56 – 3 failed to complete 2 cycles	women; menstruating; not using hormonal treatment Country: Australia	alkaline haematin test for blood content; total fluid test, including clots	Correlation between blood and non-blood volumes, $r = 0.74$. Correlation between total fluid and blood and non-blood $r = 0.93$, 0.93 respectively. Regression analysis for total fluid against blood loss, $r = 0.93$, $P < 0.001$. For women with menorrhagia total fluid to blood loss correlation, $r = 0.95$, $P < 0.001$. Estimated blood loss (ml) = $[(\text{total fluid (ml)})^{1.07243}]/2.9319$ Pads only: Estimated blood loss (ml) = $[(\text{total fluid (ml)})^{1.0955}]/2.878$ Has a 90% predictive value. Using cut-off points it can be used to classify – normal, heavy and excessive bleeding. Tampons only: Estimated blood loss (ml) = $\{[(\text{total fluid (ml)})^{1.0955}]/2.878\} \times 0.796$	Funding source: Not stated Study summary: Carefully measured total fluid could be inexpensive method of estimating MBL.
Gannon 1996 ¹³⁵	diagnostic EL = II	372	women; menorrhagia; scheduled for ablation; fibroids > 5 cm excluded.	spectrophotometric analysis	Mean average MBL ($n = 373$) 63 ml (2–808 ml). MBL < 80 ml in 231 (62%), and > 80 ml in 146 (39%). 146 repeat measures $r = 0.713$, $P < 0.001$. Learning of normal MBL 40 (11%) of women declined surgery. Of 25 who replied to survey – 92% with measurement of normal MBL, 72% felt MBL was less of a	Funding source: Yorkshire Regional Health Authority Study summary: Objective measurement of MBL can be

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients and prevalence	Population characteristics	Type of test and reference standard	Sensitivity, specificity, PPV and NPV	Source of funding and additional comments
			Mean average age = 40 years (24 to 54) Country: UK		problem than before.	undertaken in routine setting. Study also presents data on intervention outcome suggesting that those treatment who had objective menorrhagia were more satisfied than those that did not have menorrhagia.
Heath 1999 ¹⁴²	Diagnostic EL = III	32 recruited. 29 completed	women; 18–29 years Country: New Zealand	Weighed menstrual loss; menstrual loss record diary; menstrual loss recall	Weighed menstrual loss and menstrual record, $r = 0.47$ ($P = 0.012$). 19 of 29 in same category, 2 of 29 were 4 categories out. Weighed menstrual loss and menstrual recall, $r = 0.61$ ($P = 0.001$). 17 of 29 in same category, and 2 were two categories out.	Funding source: Health Research Council
Higham 1990 ¹³⁶	diagnostic EL = II	18 women: 55 cycles. 1 gynaecologist: 122 cycles at clinic.	Women – involved in separate drug trial. Mean average age = 39 years. Country: UK	alkaline haematin; pictorial blood loss assessment chart – PBAC	Patient PBAC vs alkaline haematin ($n = 55$) $r = 0.847$. Sensitivity = 86%, specificity = 89%. Gynaecologist PBAC vs alkaline haematin ($n = 122$) $r = 0.872$. Sensitivity = 86%, specificity = 81%. Sanitary towel/tampon vs alkaline haematin ($n = 122$) $r = 0.74$.	Funding source: Winthrop laboratories Study summary: PBAC could have routine use. Variation increases at higher MBL, perhaps due to visual change being limited at higher values.
Higham 1999 ¹⁴²	Diagnostic EL = III	254: 207 subjective menorrhagia; 47 subjective controls	women Country: UK	Clinical markers of MBL – pad use, duration of menses	MBL ranged from 8 to 616 ml (median 79 ml) in subject menorrhagia, and 2.5 to 288 ml (median 36 ml) in subjective control group. Association between pad use and MBL ($n = 412$): $r = 0.61$, $P < 0.005$. Association between duration and MBL ($n = 420$): $r = 0.35$, $P < 0.01$. Association between number of pregnancies and MBL: $P < 0.005$. Association between age and MBL: $r = 0.3$, $P < 0.01$. Association between height and MBL: $r = 0.2$, $P < 0.01$.	Funding source: Not stated Study summary: Despite some correlation between clinical measures and MBL, objective measurement of MBL is still required.
Janssen 1995 ¹³¹	diagnostic EL = II	288 (489 menstrual cycles)	Women; menstruating; not pregnant. Mean age = 33.4 years; mean parity = 1.3 (40.3% nulliparous) Country: Netherlands	alkaline haematin; pictorial blood loss chart	66 (56%) of women complaining of menorrhagia had ml > 80 ml. 52 (44%) of women complaining of menorrhagia had MBL < 80 ml. 23 (13.5%) of women who did not complain of menorrhagia had MBL > 80 ml. 147 (86.5%) who did not complain of menorrhagia had MBL < 80 ml. Correlation between alkaline haematin and PBAC – $r = 0.56$. PBAC sensitivity and specificity against alkaline haematin gold standard maximised at score 130: sensitivity = 91% and specificity = 81.9%; PPV = 69.2% and NPV = 95.3%. PPV and NPV maximised when score = 185 – 85.9%, 84.8%; sensitivity = 61.8%, specificity = 95.5%. Alkaline haematin test showed no significant difference between first and second cycles – 44.1 vs 43.9, $P > 0.25$. 171 (85.1%) consistency in assessment based cut-off of 185 between women measured over 2 cycles using PBAC. 30 (14.9%) inconsistent In sub-group of 56 women – 91% who complained of menorrhagia reported clots, while 55% of non-complainers reported clots. 97% of those with menorrhagia noted clots vs 52% of women with MBL < 80 ml.	Funding source: Commercially funded – Sanofi Winthrop, Organon International, Kimberly Clark Study summary: Show PBAC is a valid measure of MBL, especially if clots taken into account.
Mansfield 2004 ⁹⁸	Diagnostic questionnaire EL = III	31	women; menstruating; 35–55 years old Country: USA	Mansfield-Voda-Jorgensen (MVJ) bleeding questionnaire vs weighing of menstrual pads	Correlation between MVJ and weighed menstrual blood loss = 0.683. 26 of 31 patients had significant correlation (0.48–0.894). 5 did not either misread instructions or used few pads.	Funding source: Not stated Study summary: Questionnaire offers inexpensive method of estimating MBL.
Pendergrass 1984 ¹³²	diagnostic EL = III	100	women; menstruating Country: USA	measurement of MBL	Direct weight methods permits recovery of 97% to 98% of menstrual sample.	Funding source: Not stated Study summary: Reliable method, but includes all menstrual material, not just blood.

Bibliographic information	Study type and evidence level	No. of patients and prevalence	Population characteristics	Type of test and reference standard	Sensitivity, specificity, PPV and NPV	Source of funding and additional comments
Reid 2000 ¹³⁷	Diagnostic EL = II	103 women	women; 16–47 years; referred to menorrhagia clinic; no hormonal contraceptives or IUDs Country: UK	alkaline haematin test; PBAC	Of 103 women: MBL range was 10.2 to 389.4 ml, 63 had MBL > 80 ml. PBAC scores ranged from 61 to 545, 5 women had PBAC < 100. Correlation coefficient = 0.4659 (95% CI 0.3–0.6). At PBAC > 100 sensitivity was 97%, specificity = 7.5%, PPV = 62%, NPV = 60%. Up to 10× difference in ml and PBAC scores.	Funding source: Leiras Oy Study summary: PBAC has not been validated, and should not be used.
Shaw 1972 ¹²⁸	diagnostic EL = III	6	women Country: USA	measurement of MBL	Alkaline haematin: accuracy 95–105% recovery. Precision: 99.5–101.5%.	Funding source: Not stated.
van Eijkeren 1986 ¹²⁹	Diagnostic test EL = II	21	women; Country: Netherlands	calculation of MBL	Recovery rate from alkaline haematin test by added blood using existing equation (see paper): 10 ml (<i>n</i> = 4) recovered 10.9 ml (109%); 40 ml (<i>n</i> = 4) recovered 41.4 (104%); 80 (<i>n</i> = 4) recovered 77.1 (96%); 140 (<i>n</i> = 3) recovered 132.3 (95%); 200 (<i>n</i> = 3) recovered 181 (91%). New equation (see paper) 10 ml (<i>n</i> = 4) recovered 9.8 ml (98%); 40 ml (<i>n</i> = 4) recovered 40.7 (102%); 80 (<i>n</i> = 4) recovered 78.3 (98%); 140 (<i>n</i> = 3) recovered 139.1 (99%); 200 (<i>n</i> = 3) recovered 196.2 (98%).	Funding source: Not stated Study summary: Study shows alkaline haematin test is accurate and precise method.
Vasilenko 1988 ¹³⁰	Diagnostic EL = III	10	women; non-pregnant Country: USA	Spectrometer	Extraction efficiency of used pad vs blood alone = 96.9%. Variation between sanitary product used.	Funding source: Study summary: Study shows objective measurement of MBL is accurate and precise.
Wyatt 2001 ¹³³	Diagnostic EL = II	121: 62 subjective menorrhagia; 59 subjective controls. 13 failed to complete study.	women; presenting with menorrhagia Country: UK	PBAC; alkaline haematin	PBAC compared with alkaline haematin: sensitivity = 86% and specificity = 88% (assume at 80 ml cut-off). Inclusion of extraneous blood loss – during change of pads or other loss – included. No extraneous estimated: 22 of 61 presenting with menorrhagia had MBL > 80 ml. Including extraneous estimation – 45 of 61 had MBL > 80 ml. No correlation between extraneous blood loss and pad blood loss, <i>r</i> = 0.58.	Funding source: West Midlands Locally Organised Research Scheme and North Staffordshire Medical Institute Study summary: Study shows that PBAC provides a simple alternative to alkaline haematin. Study highlights the need to measure extraneous blood loss.
Shaw 1998 ¹⁰⁰	Diagnostic EL = 2–		Country:		Six domains developed with total score of 100 (best) – 0 (worst) – practical difficulties (14), social life (10), psychological health (14), physical health (21), working life (18), family life (23).	Funding source: Study summary: Study shows patient preferences from treatment for menorrhagia based on individual health beliefs. Study does not show how to estimate MBL.

Heavy menstrual bleeding

Table 4.3 Estimation of menstrual blood loss and quality of life – non-comparative studies

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Chapple 2001 ¹²⁶	Qualitative interviews EL = 3	How to measure MBL in general practice	73	GPs Country: UK		Main themes: Most GPs tried to estimate MBL using duration of menses or pad use, but not see as accurate. Objective measurement using alkaline haematin not practical due to workload. PBAC a more practical option. MBL not the important factor, that MBL is interfering with life is the important issue.	Funding source: Not stated Study summary: Study highlights disagreement within general practice about assessment of HMB, and need for guidance on this issue.
Hefnawi 1979 ⁴⁵	Physiological study EL = 3	factors associated with MBL	812 – 774 participated	Women; aged 14 – 49; regular menstrual bleeding Country: Egypt	MBL correlates	Mean MBL = 25.6, median MBL = 20.2 MBL and age: $r = +0.06$ (NS). MBL and parity $r = +0.21$. MBL and systolic blood pressure $r = +0.18$. MBL and diastolic blood pressure, $r = +0.12$.	Funding source: Not stated
Jenkinson 1996 ⁹⁷	Non-comparative cohort EL = 3	Testing reliability and validity of SF-36 in menorrhagia population.	348	women; 30–49 years; complaint of HMB Country: UK	internal reliability and validity of SF-36 on women with menorrhagia	Of 8 scales in SF-36 two (mental health and general health perceptions) had lower internal reliability with menorrhagia patients compared with general population: 0.5 vs 0.83 and 0.51 vs 0.8. Coefficients similar for all other scales. SF-36 not menorrhagia or period specific enough.	Funding source: Not stated Study summary: SF-36 not specific enough for a cyclical issue such as menorrhagia.
Santer 2005 ¹²²	Postal survey EL = 3	Examination of association between reporting of symptoms and reporting of health problem associated with symptoms	4610 questionnaires sent out, 2833 returned	Women Country: UK	Prevalence of menstrual symptoms; reporting of problem periods.	Reporting of menstrual symptoms: Heavy loss = 30% Very heavy loss = 5% Painful period = 15% Period lasting > 8 days = 7% Reporting of periods as a problem: Overall = 22% Of those with heavy periods = 37% Of those with very heavy periods = 83% Of those with painful periods = 75% Of those with periods lasting > 8 days = 61% OR for reporting of heavy periods by: age = 1.11 (0.91 to 1.36) parity = 1.20 (1.00 to 1.44) socioeconomic status = 1.17 (1.00 to 1.36) long-standing illness = (1.66 (1.12 to 2.46)	Funding source: Not stated Study summary: Reporting heavy or painful periods was common but reporting problem periods was less so. Reporting severe pain was at least as strongly associated with problem periods as very heavy periods and severe pain affected many more women than very heavy periods. Therefore the clinical preoccupation with heavy periods does not reflect the epidemiology of menstrual symptoms or problem.
Shapley 1995 ¹²¹	Cross-sectional community survey EL = 3	MBL measurement using PBAC	311 – 283 completed survey	women; age > 40; invited to 'well women' clinic Country: UK	MBL – PBAC	Of 283 women 140 had PBAC score > 100 (menorrhagia).	Funding source: not stated
Snowden 1983 ¹²³	cohort EL = 3	Assessment of menstruation cycles	5292	women; menstruating Country: Worldwide	MBL – subjective self-assessment; duration of menses – days; length of cycle – days	MBL estimation: 'light' = 870 (16.5%); moderate = 3375 (64%); heavy = 1008 (19.5%) Amount of MBL by duration of menses: 'light' ($n = 870$) – 1–2 days = 17%, 3–4 days = 61%, 5–6 days = 17%, 7+ days = 5%; 'moderate' ($n = 3375$) – 1–2 days = 3%, 3–4 days = 51%, 5–6 days = 37%, 7+ days = 10%. 'Heavy' ($n = 1008$) – 1–2 days = 1%, 3–4 days = 27%, 5–6 days = 42%, 7+ days = 30%. Preference and behaviour related to menses by MBL (% wanting factors by MBL class – light, moderate, heavy): no amenorrhoea – 68%, 75%, 61%; less blood loss – 13%, 15%, 54%; more blood loss – 34%, 6%, 8%; work less during menses – 13%, 17%, 23%; rest taken – 22%, 27%, 34%; mood change prior to menses – 34%, 33%, 44%; mood change during menses – 42%, 43%, 57%; discomfort prior to menses – 53%, 55%, 61%; discomfort during menses – 48%, 52%, 66%	Funding source: WHO Study summary: Large WHO study shows variation in menstrual patterns from worldwide populations.

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Warner 2004 ¹¹¹	Cohort EL = 3	Relationship of MBL or symptoms	952	Women; referred for HMB Country: UK	MBL – alkaline haematin; menstrual symptoms – pain, mood, etc.	<p>Reported problems of HMB ($n = 865$): period pain = 33%, mood change = 32.8%, blood loss greater than previously = 29.1%, duration of periods too long = 25.3%, Blood loss = 24.6%, interruption of daily life = 24.2%, feel unwell/tired due to period = 23.4%, Other changes = 22.6%, blood leakage uncontrollable = 20.1%.</p> <p>Relationship between MBL and symptoms based on 4 groupings (< 50 ml, 50–79 ml, 80–119 ml, > 120 ml): negative relationships – pain and MBL, $P = 0.015$, pain around period, $P = 0.003$, mood change around period, $P = 0.002$, unpredictable onset of periods, $P = 0.012$, any cyclic changes, $P = 0.007$. Positive relationships: accidents are severe problem, $P < 0.001$; impact of daily life causes help seeking, $P = 0.046$; extra laundry as a severe problem, $P = 0.029$. No relationship: feeling unwell/tired, volume of bleeding, worried that something is wrong.</p> <p>No correlation between MBL and factors between 50–79 ml and 80–199 ml groups.</p>	<p>Funding source: Chief Scientist's Office grant</p> <p>Study summary: Little difference between two groups around 80 ml. 80 ml definition is of limited clinical usefulness.</p>
Barer 1936 ⁴⁶	Cohort EL = 3	Normal MBL estimation	100	women; 15–43 years; anaemia excluded USA	MBL – alkaline haematin	<p>For group ($n = 100$) MBL = 6.55 to 178.69 ml, mean = 50.55 (SD 25.73) (though results skewed). 50% within 23.21 to 68.43 ml range.</p> <p>No relationship between MBL and age.</p> <p>Relationship between duration and MBL; 3 days = 24.3 and 6 days = 58.66 ml. No stats given. Relationship between number of pads and MBL. No stats given</p>	<p>Funding source: Eli Lilly</p> <p>Study summary: Study shows a wide variation in 'normal' menstrual blood loss.</p>

Table 4.4 Tests for exclusion of underlying conditions – comparative studies

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Baxter 2002 ¹⁵⁶	randomised; single-blind; concealed EL = Ib	96 asked to enter study, 83 entered study, 40 in flexible and 43 in rigid group.	Population characteristics: Women; referred for hysteroscopy due to AUB; > 16 years old; not pregnant. Baseline characteristics (flexible vs rigid): Age = 49 vs 47 Pre-menopausal = 26 vs 25 Reason for referral: Menorrhagia = 17 vs 8 Post-menopausal bleeding = 9 vs 10 Post-coital bleeding = 1 vs 1 Intermenstrual bleeding = 0 vs 2 Irregular bleeding = 8 vs 13 Abnormal bleeding on HRT = 5 vs 7 Part of trial = 0 vs 2 Country: UK	Flexible hysteroscopy; rigid hysteroscopy	30 minutes	Pain levels	Pain level (10 cm VAS scale): Immediately after procedure = 1.8 vs 4.0, $P = 0.0001$ 30 minutes after procedure = 1.0 vs 1.7, $P = 0.031$	Funding source: Not stated
Clark 2002 ¹⁵⁵	Systematic review EL = 2++	3486 studies identified, 208 retrieved for detailed analysis, 65 primary studies included in review.	Population characteristics: Search undertaken on Cochrane; MEDLINE; EMBASE, and hand searching of existing reviews. Country: UK	Hysteroscopy for identifying endometrial cancer and hyperplasia.	N/A	sensitivity, specificity, PPV, PNV	Endometrial cancer: sensitivity = 86.4 (95% CI 84 to 88.4); specificity = 99.2% (95% CI 99.1 to 99.3). Pre-test prevalence = 3.9%; pre-test likelihood ratio: positive 60.9, negative 0.15. post-test probability: positive = 71.8%; post test negative = 0.6%. Endometrial disease: sensitivity = 78%; specificity = 95.8%. Pre-test prevalence = 10.6%; pre-test likelihood ratio: positive = 10.4 and negative = 0.24. post-test probability: positive = 55.2%; post-test negative = 2.8%. Biopsy or hysterectomy or D&C pathology used as reference standards. Majority of studies use mixture of post- and pre-menopausal women Higher quality studies show lower likelihood ratio and outcome probability. All studies ($n = 61$) show pre-test likelihood ratio of endometrial cancer: positive = 60.9 and negative = 0.15; post-test probability – positive = 71.8, negative = 0.6. However, high quality studies only ($n = 11$) show pre-test likelihood ratio: positive = 34.8, negative = 0.21, and post-test probability: positive = 58.6, and negative = 0.8 respectively. For endometrial disease all studies ($n = 71$) show pre-test likelihood ratio: positive = 10.4 and negative = 0.2; post-test = 55.2, 2.8, and high quality show ($n = 12$) pre-test likelihood ratio: positive = 5.5, negative = 0.31; post-test probability: positive = 39.4, negative = 3.5. Factors such as study setting, study population and patient selection impact on results.	Funding source: University of Birmingham Interdisciplinary Research Fund and Birmingham Women's Hospital R&D fund Study summary: hysteroscopy is good at identifying endometrial cancer, but less so for identifying endometrial disease.
De Kroon 2003 ¹⁵⁴	Diagnostic; meta-analysis	109 studies identified, 24 included in review	Population characteristics: Search strategy: MEDLINE, EMBASE, DARE, Cochrane library, ISI – current	Saline contrast hysterosonography for AUB	No follow-up	Sensitivity, specificity, PPV, PNV	Pooled results for studies where hysterectomy was the reference method – 2 studies, $n = 96$ – positive likelihood ratio = 16.8, negative likelihood ratio = 0.05, positive post-test probability = 0.93,	Funding source: Not stated Study summary: SIS is an accurate method for

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
	EL = Ib		contents Studies examining saline contrast hysterosonography in AUB Country: Netherlands				negative post-test probability = 0.04 Pooled results for studies were verification bias avoided (quality measure) – 16 studies, $n = 877$ – sensitivity = 0.95, specificity = 0.88, positive likelihood ratio = 8.23, negative likelihood ratio = 0.06, positive post-test probability = 0.91, negative post-test probability = 0.07 Pooled results for studies for identification fibroids – sensitivity = 0.87, specificity = 0.92, positive likelihood ratio = 11.0, negative likelihood ratio = 0.07 Pooled results for studies for identification endometrial polyps – sensitivity = 0.86, specificity = 0.81, positive likelihood ratio = 5.23, negative likelihood ratio = 0.12 Success rate for SIS in 24 studies = 93%. 5 complications reported in 2278 procedures.	evaluating uterine cavity in women with AUB.
Dueholm 2002 ¹⁵²	Systematic review EL = Ib	18 papers	Population characteristics: MEDLINE search – 1982 to 2001, English language, diagnostic accuracy of transvaginal ultrasound, hysterosonographic examination, hysteroscopy, magnetic resonance imaging. Country: Denmark	Accuracy of transvaginal ultrasound, hysterosonographic examination, hysteroscopy, magnetic resonance imaging.	No follow-up	Accuracy of test – sensitivity, specificity	TVS ($n = 11$ studies) overall diagnostic accuracy – sensitivity = 87% (range 24% to 96%), specificity = 82% (range = 29% to 93%). For identification of polyps – sensitivity = 80% (range = 31% to 94%). For identification of submucous myomas – sensitivity = 94% (range 62% to 100%). Hysterosonographic examination overall diagnostic accuracy – sensitivity = 94% (range 83% to 100%), specificity = 85% (range = 72% to 99%) For identification of polyps – sensitivity = 93% (range 67% to 100%), specificity = 96% (range 93% to 100%). Hysteroscopy – no combined results reported. MRI – no combined results shown. Highlights that many studies use endometrial sampling as gold-standard which is inappropriate.	Funding source: Not stated
Farquhar 2003 ¹⁵¹	systematic review; diagnostic EL = Ib	19 papers	Population characteristics: MEDLINE and EMBASE 1980 to 2001. Search terms and MeSH terms used. Standard inclusion/exclusion criteria used. Standard quality assessment used. Standard data extraction used Country: New Zealand	Transvaginal ultrasound; sonohysterography; hysteroscopy; histopathology – operative hysteroscopy or hysterectomy	No follow-up	Accuracy of diagnostic method – sensitivity, specificity, PPV, NPV, +LR, -LR; patient discomfort	Transvaginal ultrasound vs histopathology or hysteroscopy for identification of intrauterine pathology ($n = 10$): Sensitivity range = 48% to 100%, specificity range = 12% to 100%, LR+ range 1.0 to 51.6, -LR range = 0.05 to 0.79. Transvaginal ultrasound vs histopathology or hysteroscopy for identification of submucous fibroids: Sensitivity range = 21% to 100%, specificity range = 53% to 100%, LR+ range 1.6 to 62.3, -LR range = 0.03 to 0.47. Transvaginal ultrasound vs histopathology or hysteroscopy for identification of hyperplasia: Sensitivity range = 33% to 100%, specificity range = 79% to 100%, LR+ range 2.6 to 679, -LR range = 0.04 to 1.00. Sonohysterography vs histopathology or hysteroscopy for identification of intrauterine pathology ($n = 11$): Sensitivity range = 85% to 100%, specificity range = 50% to 100%, LR+ range 2.0 to 80.3, -LR range = 0.04 to 0.38. Sonohysterography vs histopathology or hysteroscopy for identification of submucous fibroids:	Funding source: Not stated Study summary: Although high degree of variation in studies, all tests were moderately accurate at identifying pathology.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							<p>Sensitivity range = 57% to 100%, specificity range = 96% to 100%, LR+ range 21.3 to 80.3, -LR range = 0.06 to 0.47.</p> <p>Sonohysteroscopy vs histopathology or hysteroscopy for identification of endometrial hyperplasia: Sensitivity range = 29% to 80%, specificity range = 82% to 100%, LR+ range 1.6 to 70.4, -LR range = 0.14 to 29.</p> <p>Hysteroscopy vs histopathology or hysteroscopy for identification of intrauterine pathology ($n = 3$): Sensitivity range = 90% to 97%, specificity range = 62% to 93%, LR+ range 2.55 to 14.56, -LR range = 0.03 to 0.11.</p> <p>Hysteroscopy vs histopathology or hysteroscopy for identification of submucous fibroids: Sensitivity range = 53% to 100%, specificity range = 97% to 100%, LR+ range 10.4 to 41.0, -LR range = 0.08 to 0.48.</p> <p>Hysteroscopy vs histopathology or hysteroscopy for identification of endometrial hyperplasia: Sensitivity range = 90% to 100%, specificity range = 99% to 100%, LR+ range 47.0 to 111.7, -LR range = 0.02 to 0.15.</p> <p>Discomfort with transvaginal ultrasound – one study reported 2% of people found it unpleasant, and 40% experienced some discomfort.</p> <p>Discomfort with sonohysterography – study reported 13% found it unpleasant and 53% had discomfort</p> <p>Discomfort with hysteroscopy – 1.6% procedures not completed due to intolerance, and 3.6% of people would not have procedure again due to pain.</p> <p>Safety infrequently reported in studies for any test.</p>	
Guyatt 1992 ¹⁵⁰	Systematic review EL = 2++	55 articles included	Population characteristics: MEDLINE Two searches designed. Inclusion/exclusion criteria systematically applied. Systematic quality assessment	Testing for anaemia	N/A	Likelihood of anaemia	<p>55 studies identified.</p> <p>Serum ferritin ($n = 2579$) Area under ROC curve = 0.95 (95% CI 0.94 to 0.96). Likelihood ratio at serum ferritin levels ($\mu\text{g/l}$): $> 100 = 0.08$ $45 \text{ to } 100 = 0.54$ $35 \text{ to } 44 = 1.83$ $25 \text{ to } 34 = 2.54$ $24 \text{ to } 15 = 8.83$ $< 15 = 51.85$</p> <p>Red cell protoporphyrin ($n = 288$) Area under ROC curve = 0.77 (0.71 to 0.83) Likelihood ratio at red cell protoporphyrin levels ($\mu\text{g/l}$): $< 50 = 0.12$ $51 \text{ to } 150 = 0.56$ $151 \text{ to } 250 = 2.01$ $251 \text{ to } 350 = 6.05$ $> 351 = 8.31$</p> <p>Mean cell volume ($N = 436$) Area under ROC curve = 0.76 (0.72 to 0.80) Likelihood ratio at mean cell volume levels (μm^3):</p>	<p>Funding source: Not stated</p> <p>Study summary: Serum ferritin radioimmunoassay is powerful test in identification of iron-deficiency anaemia</p>

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							<p>> 90 = 0.29 85 to 89 = 0.76 80 to 84 = 0.91 75 to 79 = 1.00 70 to 74 = 3.33 < 70 = 12.47</p> <p>Trans-ferrin saturation ($n = 764$) area under ROC curve = 0.74 (0.70 to 0.78)</p> <p>Likelihood ratio at transferrin saturation level (%):</p> <p>> 50 = 0.15 30 to 49 = 0.43 20 to 29 = 0.52 10 to 19 = 0.81 5 to 9 = 2.54 < 5 = 10.46</p> <p>Red cell volume distribution ($n = 273$) area under ROC curve = 0.62 (0.55 to 0.69)</p> <p>Likelihood ratio at red cell volume distribution level:</p> <p>< 15 = 0.61 15 to 16 = 0.84 17 to 20 = 1.78 > 21 = 2.72.</p>	
James 2004 ¹⁴⁵	systematic review; diagnostic studies EL = 2-	107 articles identified	Population characteristics: MEDLINE. 1990 to 2003. Keyword search only. Country:	Testing for von Willebrand disease in menorrhagia	N/A	Prevalence of vWD or platelet abnormalities; sensitivity; specificity	<p>5 studies showed prevalence of vWD of 5.3% to 20%. Samples sizes from 19 to 150.</p> <p>6 studies showed sensitivity of between 79% and 100%</p> <p>4 studies showed specificity of between 80% to 95%</p>	<p>Funding source: Dade-Behring</p> <p>Study summary: Inadequate evidence to support routine testing for vWD in menorrhagia</p>
Krassas 1994 ⁵²	Epidemiology EL = 2+	428: 214 with thyroid disease; 214 matched controls	Population characteristics: Women; with or without thyroid disease Country: Greece	Association between thyroid condition and menstrual disorders	No follow-up	Presence of thyroid condition – TT3 and TT4 levels; menstrual disorders; smoking status; BMI	<p>Of the 214 patients, 168 (78.5%) had regular menstrual cycles and 46 (21.5%) irregular cycles. Out of 214 normal controls, matched for age and weight, 196 (91.6%) had normal menstruation and 18 (8.4%) irregular cycles. 2 (4.5%) and 2 (11%) of thyrotoxic and normal controls had menorrhagia.</p> <p>No statistical difference between groups.</p>	<p>Funding source: Not stated</p> <p>Study summary: These data demonstrate that hyperthyroidism in women is less frequently associated with menstrual abnormalities than was previously believed.</p>
Philipp 2003 ⁵⁶³	Cohort; epidemiology EL = 2+	126: 74 menorrhagia; 52 controls	Population characteristics: patient group: women; physician-diagnosed menorrhagia; known pathology excluded; scheduled for hysterectomy during study period; those taking pharmaceutical treatments asked to stop. Mean age – 40.4 (range 17 to 55) Controls: women; same as above but no menorrhagia. Country: USA	platelet functional defects association with menorrhagia		MBL – PBAC; platelet function test	<p>Of 59 PBACs returned by study group: 51 had score > 100; 37 had score > 185.</p> <p>Platelet aggregation and ATP release, comparison between study ($n = 74$) and control ($n = 52$) groups. Platelet aggregation: epinephrine 16 vs 2 ($P = 0.005$); ristocetin 20 vs 4 ($P = 0.007$); collagen 9 vs 2 ($P = 0.105$); ADP 3 vs 1 ($P = 0.5$); arachidonic acid 6 vs 1 ($P = 0.13$). ATP release: ADP 30 vs 7 ($P = 0.0009$); arachidonic acid 16 vs 1 ($P = 0.001$); collagen 18 vs 5 ($P = 0.04$); thrombin 1 vs 0 (N/A).</p>	<p>Funding source: Association of Teachers Preventative Medicine grant</p> <p>Study summary: Underlying platelet problems in majority of women with unexplained menorrhagia. Suggests need for screening for inherited blood disorders and platelet problems in women with menorrhagia.</p>

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Shankar 2004 ⁴⁸	Systematic review EL = 2-	11 studies included in review	Population characteristics: Women; menorrhagia; screened for von Willebrand disease Search undertaken on MEDLINE only using keyword search. Country:	vWD as risk factor in menorrhagia	N/A	Prevalence of von Willebrand disease	11 studies: 988 women with menorrhagia and vWD prevalence of 131 (13%, 95% CI 11 to 15.6%). Studies reported range from 5% to 24% of vWD. 4 studies from Europe, 5 from North America, 2 from elsewhere. 6 studies based on gynaecology outpatient clinics, 1 on coagulation clinic, 1 on administrative database, 2 on population study, 1 not stated. Menorrhagia state based on history in 5 studies, PBAC in 2, Alkaline Haematin in 2, and not stated in 2. vWF:Ag test only one used across studies, RiCof was second most common. Cut-off for vWD varied between studies. Different study designs and inclusion criteria probably account for differences between studies.	Funding source: Not stated

Table 4.5 Tests for exclusion of underlying pathology – diagnostic studies

Bibliographic information	Study type and evidence level	No. of patients and prevalence	Population characteristics	Type of test and reference standard	Sensitivity, specificity, PPV and NPV	Source of funding and additional comments
Anastasiadis 2000 ¹⁵⁷	retrospective; comparison EL = III	1415	women; scheduled for D&C for AUB. Aged 23–85 years Country: Greece	Transvaginal ultrasound (TVS); Sonohysterography (SH); D&C pathology – reference	Sensitivity, specificity, PPV, NPV for identification of hyperplasia or polyps by TVS in pre-menopausal women: 74%, 91%, 62%, 91% Sensitivity, specificity, PPV, NPV for identification of hyperplasia or polyps by TVS in post-menopausal women: 94%, 96%, 94%, 96% Sensitivity, specificity, PPV, NPV for identification of hyperplasia or polyps by SH: 95%, 96%, 90%, 98% No assessment of acceptability of tests. Tests undertaken in different groups.	Funding source: No stated
Arslan 2003 ¹⁵⁸	diagnostic; comparison EL = III	138 – 105 were postmenopausal, 33 peri-menopausal	women; AUB; HRT or tamoxifen excluded Country: Turkey	Colour Doppler ultrasonography to determine blood flow; endometrial thickness; histopathology	Results for endometrial thickness correlation with endometrial carcinoma: Endometrial thickness > 5 mm – neoplastic = 18, non-neoplastic = 75; ≤ 5 mm – neoplastic = 1, non-neoplastic = 11. Sensitivity = 95%, specificity = 37%, PPV = 19%, NPV = 97%.	Funding source: Not stated
Ash 1996 ⁷⁷	diagnostic; retrospective EL = III	310	Women; diagnosed with DUB; pre-menopausal status; undergone endometrial sampling by Pipelle; Women in menopause excluded Average age 39 years (17–53) Country: Canada	Pipelle endometrial biopsy	Pipelle outcome: 266 (85.8%) normal, 8 (2.6) hyperplasia, 9 (2.9) complex hyperplasia, 4 (1.3%) hyperplasia with atypia. 23 (7.4%) biopsies were insufficient for diagnosis. Logistic regression of risk factors for hyperplasia: irregular menses: OR = 73.5 (95% CI 14.6 to 370.4), $P = 0.0001$. Hypertension: OR = 4.94 (0.95 to 25.84), $P = 0.58$. Age > 40: OR = 3.97 (1.22 to 12.95), $P = 0.022$.	Funding source: Not stated Study summary: All women with irregular menstruation should have endometrial biopsy.
Badawy 1996 ¹⁵⁹	diagnostic; retrospective; case series; part-blinded EL = II	100	women; seen for menstrual disorders Country: UK	Ultrasonography – transvaginal or trans-abdominal; hysteroscopy; histopathology – reference; patient treatment/management – based on having ultrasound results, hysteroscopy results, or both.	Pathology identified: Ultrasonography: normal = 47, fibroids = 28, thickened endometrium = 11, adnexal pathology = 4 Hysteroscopy: normal = 68, fibroids = 19, polyps = 13 Histopathology: normal = 77, atrophic endometritis = 8, polyps = 10, hyperplasia = 3, chronic endometritis = 1, endocervical polyp = 1 Comparison of management strategies: no difference between management strategies based on information available from tests. Trend towards more surgery where both ultrasound and hysteroscopy data available.	Funding source: Not stated Study summary: Study shows that ultrasound and hysteroscopy provide complementary information.
Bain 2002 ²²¹	Randomised; blinded; controlled; diagnostic EL = Ib	460 eligible – 377 recruited, 83 did not enter trial – 370 randomised, 7 withdraw from trial – 186 received hysteroscopy, 184 received endometrial biopsy – 178 hysteroscopy completed study, 167 endometrial biopsies completed study	women; referred for menstrual problems. Hysteroscopy and Biopsy group: age 43.2, parity = 2, length of menses = 7.5. Endometrial biopsy alone: age 42.8, parity = 2, mean length of menses = 7.9 Country: UK	hysteroscopy and biopsy; endometrial biopsy alone	Outcomes: Semantic differential scale (12 item scales of bipolar terms rated from –3 [best] to +3 [worst], e.g. good–bad, to assess patient views of test). Items where $P < 0.05$ was for happy–sad – biopsy = –0.16 (SD 1.07), hysteroscopy = –0.045 (SD 1.19), $P = 0.01$. For McGill pain score: No difference between biopsy or hysteroscopy pain scores ($P = 0.62$, 2.58 vs 2.54, respectively). Initial management of groups: No difference between management strategies used on each group. Endometrial group had 9 hysterectomies vs hysteroscopy with 8 hysterectomies, relative risk = 1.14 (not significant).	Funding source: Not stated Study summary: Study shows that hysteroscopy is acceptable method to patients, and provide immediate reassurance. However, study shows hysteroscopy has not impact on management of patients compared with biopsy alone.
Ben-Baruch 1994 ²¹⁵	diagnostic comparison EL = II	269 – 172 Pipelle curette, 97 had D&C (45 from	women; non-pregnant; referred for investigation due to AUB	Pipelle curette; D&C; Hysterectomy	Of 172 Pipelle's attempted 170 (98.8%) were successful. 154 of 170 (90.6%) samples provided enough information for histology. 66 of 97 (68%) of D&C's provided enough material for histology.	Funding source: Not stated Study summary: Study shows Pipelle curettage is

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients and prevalence	Population characteristics	Type of test and reference standard	Sensitivity, specificity, PPV and NPV	Source of funding and additional comments
		Pipelle group later had histology available).	Country: Israel		Difference between groups was significant ($P < 0.0001$) Of 45 Pippelles where D&C or hysterectomy were later performed, the diagnosis was the same in 43 (95.5%).	useful meted for diagnosis of endometrial pathology.
Ben-Yehuda 1998 ¹⁶⁰	diagnostic; comparative; retrospective EL = III	373	women; AUB; undergone D&C and hysteroscopy for identification of hyperplasia or endometrial cancer Country: USA	Hysteroscopy; D&C – reference	Comparison of hysteroscopy and D&C for identification of hyperplasia and endometrial cancer: In 25 hysteroscopies no diagnosis made compared with 33 for D&C. True positive = 54, false positive = 115, false negative = 50, true negative = 154.	Funding source: Not stated
Bernard 1997 ¹⁶¹	prospective; comparison EL = III	163. 159 completed. 3 excluded.	women; AUB; pre- and post-menopausal; excluded if infection or cervical abnormality Country: France	Saline contrast sonohysterography (SCSH); hysteroscopy or hysterectomy as reference	Pathology ($n = 159$): Atrophy = 10 Normal = 36 Hystertrophy = 20 Polyp = 36 Submucosal myoma = 30 Intramural myoma = 15 Adenomyosis = 10 Cancer = 2 All pathology: True negative – 13; true negative – 1; false positive – 4; true positive- 91 Sensitivity (%) and specificity (%): Hypertrophy – 88.8, 95.6 Polyp – 87.8, 90.7 Submucosal myoma – 89.6, 95 Cancer – 40, 100	Funding source: Not stated Reviewer comments: Study included in the Farquhar review. Study shows saline sonography is useful method for identifying pathology.
Bettocchi 2001 ⁵⁶⁸	diagnostic; comparative; retrospective EL = III	399	Women; AUB; diagnostic D&C; underwent hysterectomy within 2 months due to persistent symptoms. Country: Italy	D&C; hysterectomy pathology – reference	Accuracy of D&C compared with histopathology for identification of intrauterine abnormalities: sensitivity = 46%, specificity = 100%, PPV = 100%, NPV = 7.1%	Funding source: Not stated Study summary: D&C is an inadequate method for diagnosis in AUB.
Breitkopf 2004 ¹⁶²	Diagnostic; retrospective; case series EL = III	206 – 6 patients procedure failed.	women; referred for AUB; pre-menopausal women aged 18 to 53 years Country: USA	Sonohysteroscopy; histopathology – reference	Pathology available for 97 patients. Sonohysteroscopy compared with histology for identification of intra-cavity masses had a sensitivity of 99%, specificity of 98%. Accuracy of endometrial thickness compared with sonohysteroscopy for identification of pathology, at 5 mm cut-off: sensitivity 74%, specificity = 46%, PPV = 37%, NPV = 80%, +LR = 1.35, -LR = 0.58.	Funding source: Not stated Study summary: Study shows that endometrial thickness has limited correlation with pathology.
Bronz 1997 ⁷³	diagnostic; comparative; prospective EL = II	139	women; referred due to AUB; 83 women pre-menopausal, 56 post-menopausal Country: Switzerland	transvaginal sonography; saline infusion sonography; histology – reference	Results for pre-menopausal women: Benign polyps identified in 33 women by histology, TVS identified 21, SCHS identified 32. Submucous fibroids identified in 22 women by histology, TVS identified 21, SCHS identified 21. Endometrial hyperplasia identified in 5 women by histology, TVS identified 5, SCHS identified 2. No endometrial carcinoma reported Reviewer calculated: For TVS: Sensitivity = 48/62 = 0.77 Specificity = 19/21 = 0.90 For SCHS:	Funding source: not stated Study summary: Both TVS and SCHS are highly accurate methods at diagnosing pathology

Bibliographic information	Study type and evidence level	No. of patients and prevalence	Population characteristics	Type of test and reference standard	Sensitivity, specificity, PPV and NPV	Source of funding and additional comments
					Sensitivity = 58/62 = 0.94 Specificity = 17/21 = 0.81	
Cepni 2005 ¹⁵³	diagnostic; prospective; cohort; comparison EL = II	240 entered study, 223 completed all three tests	Women; referred for AUB. 165 were pre-menopausal, 58 were postmenopausal Country: Turkey	transvaginal ultrasound; saline infusion sonography; hysteroscopy; Biopsy or D&C – reference	All for pre-menopausal women group: Accuracy of TVS for identification of endometrial polyps compared with pathology: sensitivity = 72.0, specificity = 50.8, PPV = 69.2, NPV = 54.1, LR+ = 1.46, LR- = 0.55. Accuracy of SIS for identification of endometrial polyps compared with pathology: sensitivity = 91.8, specificity = 61.2, PPV = 77.6, NPV = 83.7, LR+ = 2.37, LR- = 0.13. Accuracy of hysteroscopy for identification of endometrial polyps compared with pathology: sensitivity = 94.4, specificity = 58.6, PPV = 80.8, NPV = 85.0, LR+ = 2.28, LR- = 0.10. Accuracy of TVS for identification of submucous fibroids compared with pathology: sensitivity = 58.3 specificity = 94.8, PPV = 46.7, NPV = 96.7, LR+ = 11.16, LR- = 0.44. Accuracy of SIS for identification of submucous fibroids compared with pathology: sensitivity = 81.3, specificity = 98.0, PPV = 81.3, NPV = 98.0, LR+ = 40.35, LR- = 0.19. Accuracy of hysteroscopy for identification of submucous fibroids compared with pathology: sensitivity = 90.9 specificity = 95.8, PPV = 76.9, NPV = 98.6, LR+ = 21.67, LR- = 0.10.	Funding source: No stated
Chittacharoen 2000 ¹⁶³	prospective; cohort; diagnostic; non-blinded EL = III	55	Women; AUB; previous ultrasound suggested pathology Country: Thailand	sonohysterography; pathology – via D&C or hysterectomy or operative hysteroscopy	Comparison of sonohysterography and pathology: true positive = 45, false positive = 1, false negative = 1, true negative = 5 Sensitivity = 97.82, specificity = 83.33, PPV = 97.82, NPV = 83.33%	Funding source: Not stated
Critchley 2001 ⁶⁹	diagnostic; randomised – block; prospective; statistical analysis blinded EL = Ib	1767 assessed, 1027 eligible, 683 recruited – 200 high risk, 326 moderate risk, 157 low risk	women; referred due to AUB; excluded pregnant women. Women divided into groups based on risk factors for pathology – age, history, pre- or post menopausal High risk = post-menopausal Moderate risk = pre-menopausal, < 40, no risk factors – family history Low risk = pre-menopausal, < 40 High-risk group: age = 57.6, 1% with HMB, 30% on HRT, 22% sterilised. Moderate-risk group: age = 45.2, 68% with HMB, 9% on HRT, 38% sterilised. Low-risk group: age = 33.9, 57% with HMB, 0% on HRT, 28% sterilised. Country: UK	hysteroscopy plus biopsy – Tao Brush or Pipelle, blind biopsy; transvaginal ultrasound; no investigation	Randomised groups: High-risk group: Biopsy (Tao and/or Pipelle) and ultrasound = 100; biopsy and hysteroscopy = 100. Moderate risk group: Biopsy = 80; Biopsy and ultrasound = 80; Hysteroscopy and biopsy = 84; (Hysteroscopy or biopsy) and ultrasound = 82 Low-risk group No evaluation = 62; Pipelle only = 17; Tao only = 15; Hysteroscopy or Pipelle = 17; Hysteroscopy or Tao = 14; Ultrasound = 32 Investigations successfully undertaken: Moderate risk group: hysteroscopy, ultrasound and biopsy = 65 (79%); Hysteroscopy and biopsy = 71 (85%); ultrasound and biopsy = 60 (75%); biopsy = 67 (84%). Low-risk group: Hysteroscopy and Tao Brush = 10 (71%); hysteroscopy and Pipelle = 11 (65%); Ultrasound = 31 (97%); Tao Brush = 12 (80%); Pipelle = 14 (82%); None = 62 (100%). NEO questionnaire: General population averages for adult women – neuroticism = 20, extraversion = 28, openness = 27, agreeableness = 34, conscientiousness = 35 For moderate risk group – neuroticism = 21, extraversion = 28, openness = 27, agreeableness = 34, conscientiousness = 35 For low risk group – neuroticism = 21, extraversion = 28, openness = 25, agreeableness = 33, conscientiousness = 34 GHQ questionnaire scores: moderate-risk group: Somatic symptoms = 7.0, anxiety = 7.0, social dysfunction = 7.0, depression = 0.0, total = 21 low-risk group: Somatic symptoms = 6.0, anxiety = 6.0, social dysfunction = 7.0, depression = 0.0, total = 20 Difference between groups: Somatic symptoms, $P = 0.001$, anxiety $P = 0.001$, social dysfunction $P = 0.197$,	Funding source: Health Technology Assessment, NHS Study summary: Ultrasound provides higher visualisation rates than hysteroscopy ($P = 0.002$). Tao Brush outperforms Pipelle in post-menopausal women. Polyps better identified with hysteroscopy, and fibroids by ultrasound. Hysteroscopy and biopsy more likely than ultrasound to be classified 'unpleasant'.

Heavy menstrual bleeding

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					<p>depression $P = 0.044$, total $P = 0.001$.</p> <p>Moderate-risk group:</p> <p>Visualisation – hysteroscopy ($n = 84$): 84 subjects, 10 not possible, 74 possible, 3 not undertaken for other reasons, 71 completed, 64 successful visualisation. Ultrasound ($n = 80$): 0 not possible, 80 possible, 3 not undertaken for other reasons, 77 completed, 73 successful visualisation. Hysteroscopy and Ultrasound ($n = 82$): 7 and 0 not possible, 75 and 82 possible, 3 and 7 not undertaken for other reasons, 72 and 75 completed, 63 and 71 successful visualisation.</p> <p>Biopsy:</p> <p>Hysteroscopy and Pipelle: 84 subjects, 78 possible, 76 undertaken, 71 successful. Hysteroscopy and Tao Brush: 84 subjects, 78 possible, 75 undertaken, 63 successful. Ultrasound then 'blind' Pipelle: 80 subjects, 64 possible, 64 undertaken, 59 successful. Ultrasound then 'blind' Tao Brush: 80 subjects, 64 possible, 64 undertaken, 55 successful.</p> <p>Success of visualisation and biopsy: hysteroscopy and Pipelle = 82%, hysteroscopy and Tao Brush = 78%, ultrasound and Pipelle = 76%, ultrasound and Tao Brush = 71%.</p> <p>High- and moderate-risk groups combined:</p> <p>Success of visualisation and biopsy: hysteroscopy = 77%; hysteroscopy and Pipelle = 70%, hysteroscopy and Tao Brush = 80%, ultrasound = 88%, ultrasound and Pipelle = 60%, ultrasound and Tao Brush = 67%.</p> <p>Low-risk group:</p> <p>Visualisation – hysteroscopy ($n = 31$): 5 not possible, 26 possible, 2 not undertaken for other reasons, 24 completed, 20 successful visualisation. Ultrasound ($n = 32$): 0 not possible, 32 possible, 1 not undertaken for other reasons, 31 completed, 31 successful visualisation.</p> <p>Biopsy:</p> <p>Hysteroscopy and Pipelle: 17 subjects, 13 possible, 12 undertaken, 10 successful. Hysteroscopy and Tao Brush: 14 subjects, 13 possible, 12 undertaken, 12 successful. Ultrasound then 'blind' Pipelle: 17 subjects, 14 possible, 14 undertaken, 14 successful. Ultrasound then 'blind' Tao Brush: 15 subjects, 13 possible, 12 undertaken, 11 successful.</p> <p>Abnormalities identified by visualisation:</p> <p>Moderate group:</p> <p>Endometrial/uterine polyp – hysteroscopy = 19, ultrasound = 7</p> <p>Uterine fibroids – hysteroscopy = 31, ultrasound = 59.</p> <p>cervix suspicious – hysteroscopy = 0, ultrasound = null.</p> <p>Cervical polyp – hysteroscopy = 7, ultrasound = null</p> <p>Low-risk group:</p> <p>Endometrial/uterine polyp – hysteroscopy = 1, ultrasound = 2</p> <p>Uterine fibroids – hysteroscopy = 1, ultrasound = 6.</p> <p>Cervical polyp – hysteroscopy = 1, ultrasound = null</p> <p>Abnormalities identified by biopsy:</p> <p>High-risk group:</p> <p>Endometrial cancer = 5. Hyperplasia = 2. Atrophic endometrium = 12. Inactive endometrium = 106. Cyclic endometrium = 26. Other = 27</p> <p>moderate-risk group:</p> <p>Endometrial cancer = 3. Hyperplasia = 3. Atrophic endometrium = 0. Inactive endometrium = 19. Cyclic endometrium = 213. Other = 59</p> <p>Low-risk group:</p> <p>Endometrial cancer = 0. Hyperplasia = 0. Atrophic endometrium = 0. Inactive endometrium = 2. Cyclic</p>	

Bibliographic information	Study type and evidence level	No. of patients and prevalence	Population characteristics	Type of test and reference standard	Sensitivity, specificity, PPV and NPV	Source of funding and additional comments
					<p>endometrium = 91. Other = 0</p> <p>Sensitivity (%), specificity (%), PPV (%), PNV (%) of investigations for endometrial cancer:</p> <p>Ultrasound ($n = 64$) = 66.7 (20.8 to 93.9), 55.7 (43.3 to 67.5), 6.9 (1.9 to 22.0), 97.1 (85.5 to 99.5).</p> <p>Hysteroscopy ($n = 254$) = 20 (3.6 to 62.4), 98.8 (96.5 to 99.6), 25.0 (4.6 to 69.9), 98.4 (96.0 to 99.4)</p> <p>Pipelle ($n = 473$) = 70.0 (39.7 to 89.2), 100 (99.2 to 100), 100 (64.6 to 100), 99.4 (98.1 to 99.8)</p> <p>Tao Brush ($n = 478$) = 90.0 (59.6 to 98.2), 100 (99.2 to 100), 100 (70.1 to 100), 99.8 (98.8 to 100).</p> <p>Adverse events:</p> <p>Ultrasound = 0, hysteroscopy = 12, blind biopsy = 9</p> <p>Investigation 'unpleasant':</p> <p>Hysteroscopy = 27%, ultrasound = 11%, biopsy = 29%. (rates higher for low-risk group).</p>	
De Crespigny 1997 ¹⁶⁴	diagnostic; comparative; prospective EL = III	60. 55 completed	women; referred for investigation; 43 menorrhagia/intermenstrual bleeding; 6 postmenopausal bleeding; 5 infertility; 3 suspected Asherman syndrome; 1 tamoxifen treatment; 1 recurrent abortions; 1 exclusion of uterovesical fistula. Country: Australia	Saline Infusion Sonohysterosalpingography (SIS); transvaginal ultrasound (TVS); hysteroscopy – reference, not whole sample	<p>55 of 60 examinations completed.</p> <p>Disagreement between SIS and TVS: 12 polyps identified on SIS but not TVS; 7 had endometrial polyp on TVS but not on SIS.</p> <p>11 hysteroscopies avoided due to SIS. 15 of 16 hysteroscopies agreed with SIS.</p>	Funding source: not stated
De Vries 2000 ¹⁶⁵	Diagnostic; prospective; cohort EL = II	62	Women; pre-menopausal; AUB; scheduled for hysteroscopy Country: Netherlands	Transvaginal Sonography; Saline Infusion Sonography; Hysteroscopy	<p>Accuracy of TVS at identifying intrauterine pathology compared with hysteroscopy: sensitivity = 60% (12 of 20), specificity = 93% (39 of 42), +LR = 8, -LR = 0.43</p> <p>Accuracy of SIS at identifying intrauterine pathology compared with hysteroscopy: sensitivity = 68% (14 of 16), specificity (39 of 41) = 95%, +LR = 10, -LR = 0.13</p>	Funding source: Not stated Study summary: SIS was more accurate test than TVS for identifying uterine pathology.
Dijkhuizen 2000 ²²²	systematic review; meta-analysis EL = II	1768 articles identified. 39 studies included in review.	Search on MEDLINE. Keyword search only	Endometrial sampling for carcinoma or hyperplasia	<p>Identification of endometrial carcinoma:</p> <p>31 studies reported sensitivities ranging between 25% to 100%, and specificity between 93% to 100%.</p> <p>Sample size-weight combined sensitivities were 68%, 78%, and 81% where hysterectomy, D&C or both were, respectively, used as reference method. The specificities were 99.7%, 99.6% and 99.9%, respectively.</p> <p>Study quality criteria – blinding, prospective – had no impact on study outcomes.</p> <p>Identification of atypical hyperplasia:</p> <p>19 provided sensitivities, and 17 provided specificities. Sensitivity varied between 39% and 100%, and specificity between 93% and 100%</p> <p>Sample size-weight combined sensitivities for identification of hyperplasia, were 74%, 75%, and 45% where hysterectomy, D&C or both were, respectively, used as reference method. The specificities were 100%, 99.1% and 100%, respectively.</p> <p>Studies show statistically significant ($P = 0.01$) differences between Pipelle method and others in terms of sensitivity and specificity for identification of hyperplasia.</p>	Funding source: Not stated Study summary: Pipelle biopsy is superior to other methods in identification of endometrial cancer and hyperplasia.
Dijkhuizen 1996 ¹⁶⁶	diagnostic; blinded EL = II	136	women; metrorrhagia or postmenopausal bleeding Country: Netherlands	transvaginal ultrasonography; hysteroscopy	<p>Hysteroscopic pathology for pre-menopausal: insufficient sample = 1, atrophy = 3, proliferative/secretory = 30, polyp = 17, submucous myoma = 10, hyperplasia = 6, carcinoma = 0.</p> <p>Ultrasound: sensitivity = 88%, specificity = 68%, PPV = 73%, NPV = 85%, PLR = 2.8, NLR = 0.18</p>	Funding source: Not stated Study summary: Limited use in women with irregular menstrual bleeding

Heavy menstrual bleeding

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Dijkhuizen 2000 ¹⁶⁷	diagnostic; prospective; cohort EL = II	50 – received both transvaginal ultrasound and saline infusion sonography	women; scheduled for hysterectomy. Age range 35 to 59. 26 had menorrhagia, 24 had metrorrhagia Country: Netherlands	transvaginal ultrasound; saline infusion sonography; histopathology from hysterectomy – reference	Transvaginal ultrasound: Accuracy of TVS compared with histopathology for identification of pathology: sensitivity = 61%, specificity = 96%, +LR = 16, –LR = 0.41 Saline infusion sonography: Accuracy of SIS compared with histopathology for identification of pathology: sensitivity = 100%, specificity = 85%, +LR = 6.8, –LR = 0.0. In 2 patients SIS could not be performed.	Funding source: Not stated Study summary: The diagnostic accuracy of SIS is higher than TVS.
Dueholm 2001 ¹⁶⁸	diagnostic; prospective; cohort; comparative EL = II	470 women referred for bleeding disorders. 189 had operative hysteroscopy or hysterectomy after tests.	women; referred for bleeding disorders; pre-menopausal; aged less than 55 years. Country: Denmark	Transvaginal sonography; saline contrast sonohysteroscopy; endometrial sample – reference	Diagnostic accuracy of transvaginal ultrasound compared with pathology for identification of polyps or submucous myomas: sensitivity = 92%, specificity = 62%, PPV = 80%, NPV = 82% Diagnostic accuracy of transvaginal ultrasound compared with pathology for identification of any abnormality (including hyperplasia at > 12 mm cut-off): sensitivity = 93%, specificity = 54%, PPV = 79%, NPV = 82% Diagnostic accuracy of saline contrast sonohysteroscopy compared with pathology for identification of polyps or submucous myomas: sensitivity = 99%, specificity = 72%, PPV = 85%, NPV = 98% Diagnostic accuracy of saline contrast sonohysteroscopy compared with pathology for identification of any abnormality (including hyperplasia at > 12 mm cut-off): sensitivity = 99%, specificity = 57%, PPV = 81%, NPV = 97% In 18 cases saline contrast sonohysteroscopy could not be performed. In 28 cases the visualisation was use-optimal. There were no complaints of pain by any patients, but 42 reported discomfort.	Funding source: Not stated
Dueholm 2001 ¹⁶⁹	Diagnostic; prospective; comparative EL = II	355	Women; referred for AUB; pre-menopausal; Aged < 55 years; scheduled for hysteroscopy, hysterectomy, or endometrial sampling Country: Denmark	Transvaginal ultrasound; histological findings – reference	Mean average endometrial thickness by pathology outcome: Hyperplasia = 11.52 (SD 4.97), $P = 0.005$ (from normal) Polyp = 11.75 (5.08), $P = < 0.001$ (from normal) Submucous myomas = 7.08 (SD 3.41) $P = 0.01$ (from normal) Normal = 8.37 (SD 3.85) Pre-test probability of hyperplasia or polyps = 0.20 (0.16 to 0.25) (66 of 329). Post-test probability of hyperplasia or polyps = 0.084 where endometrial thickness ≤ 4 mm and 0.077 where ≤ 7 mm. Pre-test probability of any abnormal finding ($n = 173$) = 0.42 (0.37 to 0.48). Post-test probability of abnormal finding = 0.16 (0.11 to 0.23) with normal sonogram (excluding endometrial thickness)	Funding source: Not stated Study summary: Study shows that endometrial thickness does correlate with presence of polyps and hyperplasia, but using cut-offs does not exclude pathology.
Eldred 1994 ¹⁴³	Epidemiology; case-control EL = II	42	women; presenting with subjective menorrhagia; no pathology or coagulation disease. Country: UK	Pituitary and ovarian hormone levels association with menorrhagia	20 patients had MBL > 80 ml, 22 had MBL < 80 ml. No difference between groups in hormone levels – FSH, LH-FSH and E2 No correlation between MBL and hormone levels.	Funding source: Not stated Study summary: No association between hormone levels and menstrual blood loss
Emanuel 1997 ¹⁷⁰	Diagnostic; comparative; prospective EL = III	131	women; referred for AUB; undergone D&C; scheduled for hysteroscopy Country: Netherlands	D&C; hysteroscopy – reference	Comparison of D&C and hysteroscopy for identification of uterine pathology: True positive = 17, false positive = 11, false negative = 47, true negative = 56. Pre-test probability = 0.49, post-test probability + = 0.61, post-test probability – = 0.46, +LR = 1.69, –LR = 0.87	Funding source: Not stated Study summary: D&C is an obsolete method for diagnosing intrauterine disorders.
Emanuel 1995 ¹⁷¹	diagnostic comparison; prospective EL = II	279 – 19 not evaluable	women; referred by GP due to AUB Country: Netherlands	Transvaginal ultrasonography; hysteroscopy – reference	Patient population ($n = 260$): menorrhagia = 109; metrorrhagia = 104; postmenopausal bleeding = 47 Sonogram results by hysteroscopy: 135 were true negative, 4 were false negative; intrauterine structure – 76 true positive, 9 false positive; endometrium – 14 true positive, 1 false positive; both – true positive = 2, false positive = 6; inconclusive – 13 = true positive, 6 = false positive. Sensitivity of sonogram = 0.96 (95% CI 0.91 to 0.99); specificity = 0.89 (0.83 to 0.94); pre-test probability = 0.42, post-test probability normal = 0.03, post-test probability abnormal = 0.87; likelihood ratio normal result = 0.04, likelihood ratio abnormal result = 9.09.	Funding source: Not stated Study summary: Transvaginal sonography effective at excluding pathology in AUB

Bibliographic information	Study type and evidence level	No. of patients and prevalence	Population characteristics	Type of test and reference standard	Sensitivity, specificity, PPV and NPV	Source of funding and additional comments
Fedele 1992 ⁷⁸	diagnostic; pre- and post treatment EL = II	43	women; recurrent menorrhagia; enlarged uterus; no evidence of leiomyomas on examination; scheduled for hysterectomy; . Country: Italy	transvaginal ultrasound; histopathology post-hysterectomy – reference	Ultrasonography results: 22 of 43 had adenomyosis, 4 had leiomyomas > 10 cm. Pathologist: 20 had adenomyosis, confirming 16 US findings, 6 were excluded, 4 new cases. US sensitivity = 80%, specificity = 74%, PPV 73%, PNV = 81%.	Funding source: Not stated
Fedele 1991 ¹⁷²	diagnostic; comparative EL = Ib	71	women; scheduled for hysterectomy due to fibroids; aged 37 to 54 Country: Italy	transvaginal sonography; hysteroscopy	65 of 71 sonographs successful. 6 unsuccessful due to enlargement of uterus. 'Success' of sonography at identifying submucous fibroids: sensitivity = 100%, specificity = 94%, PPV = 81% PNV = 100%	Funding source: not stated Study summary: Sonography offers alternative to sonography for identifying pathology, but cannot differentiate between type of pathology.
Ferry 1993 ²¹⁸	diagnostic; comparative EL = II	37	women; scheduled for hysterectomy; confirmed diagnosis of endometrial cancer Country: Australia	Pipelle endometrial biopsy	25 (67%) of 37 biopsy samples were positive for endometrial cancer	Funding source: Not stated Study summary: Study shows poor results when using Pipelle biopsy to diagnose endometrial cancer.
Fothergill 1992 ¹⁷³	Diagnostic; comparison EL = II	187	women; scheduled for D&C Country: UK	Pipelle biopsy; D&C	164 of 187 results were the same. All carcinomas were identified	Funding source: Not stated
Fukuda 1993 ¹⁷⁴	diagnostic; comparative EL = III	36	women; hypomenorrhoea, dysmenorrhoea, anaemia; attending women's clinic Country: Japan	Transvaginal sonography (TVS); endometrial balloon catheter and saline (TVHS); hysterectomy or hysteroscopy – reference standard	TVS identified – 22 submucous myomas, 10 intramural myomas, 4 endometrial polyps. TVHS identified – 20 submucous myomas, 12 intramural myomas, 4 endometrial polyps. Hysterectomy/hysteroscopy identified – 13 misdiagnoses with TVS: 7 submucous myomas were intramural myomas, 5 intramural myomas were submucous myomas, 1 myomas was adenomyosis. 1 misdiagnoses with TVHS – 1 submucous myomas was adenomyosis. Misdiagnosis rates were: 36% for TVS, an 2.8% for TVHS. Sensitivity: TVS = 73.7%, TVHS = 100% Specificity: TVS = 52.9%, TVHS = 93.8% PPV: TVS = 63.6%, TVHS = 95% PNV: TVS = 64.3%, TVHS = 100%	Funding source: Not stated Study summary: TVHS better than TVS for diagnosis of fibroids.
Garuti 2001 ¹⁷⁵	diagnostic; comparison; retrospective EL = III	1500	Women; referred due suspected endometrial pathology. 694 post-menopausal, 806 pre-menopausal. 310 with menorrhagia Country: Italy	hysteroscopy; histopathology – reference (when available)	128 cases hysteroscopy were unsatisfactory or incomplete. 43 cases of biopsy inadequate tissue. Hysteroscopy compared with histopathology: False negative hysteroscopy in 30 cases (16.2%) of 185 hyperplasia. False negative hysteroscopy in 1 of 102 endometrial carcinomas 116 false positive results in 927 women with normal histopathology. Sensitivity, specificity, NPV and PPV for distinguishing normal from abnormal endometrium: 94.2%, 88.8%, 96.3%, and 83.1%. Sensitivity, specificity, NPV and PPV for distinguishing endometritis: 77.7%, 99.3%, 99.5%, 67.7% Sensitivity, specificity, NPV and PPV for distinguishing endometrial polyps: 95.3%, 95.4%, 98.9%, 81.7% Sensitivity, specificity, NPV and PPV for distinguishing endometrial hyperplasia: 70.0%, 91.6%, 9.3%, 60.6% Sensitivity, specificity, NPV and PPV for distinguishing endometrial cancer: 85.7%, 99.5%, 98.7%, 93.5%	Funding source: Not stated
Gimpelson 1988 ²¹⁷	diagnostic; comparative; retrospective	276	women; referred for investigation due to AUB, postmenopausal bleeding,	hysteroscopy direct biopsy; D&C	220 of 265 the biopsy and D&C results were the same. 44 cases (16%) biopsy provided improved results. Endometrial polyp = 15, submucous myoma= 13, endometrium = 7, adenomatous hyperplasia = 2, atypical	Funding source: Not stated Study summary: Study shows direct biopsy better

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients and prevalence	Population characteristics	Type of test and reference standard	Sensitivity, specificity, PPV and NPV	Source of funding and additional comments
	EL = III		suspected myoma; infertility Country: USA		hyperplasia = 1, other = 6 9 cases (3%) biopsy provided reduced results. In 8 cases D&C missed diagnosis.	than D&C at identifying pathology.
Goldchmit 1993 ⁵⁶⁹	Diagnostic; comparison EL = II	176 – 41 postmenopausal, 135 premenopausal	women; scheduled for D&C Country: Israel	Pipelle biopsy; D&C; sonography	Sensitivity, specificity, PPV, NPV for Pipelle biopsy compared with histology for identifying pathology: 82%, 99%, 93%, 98% Sensitivity, specificity, PPV, NPV for Pipelle biopsy and endometrial thickness > 5 mm compared with histology for identifying pathology: 92%, 96%, 92%, 96% Pipelle vs curettage (reference): True positive = 57, false positive = 15, true negative = 102, false negative = 2.	Funding source: Not stated Study summary: Study shows Pipelle biopsy alone is accurate method of identifying pathology.
Goldstein, 1997 ¹⁷⁶	Diagnostic; screening EL = III	433	women; referred for assessment due to AUB – menorrhagia, metrorrhagia, etc.; perimenopausal; > 39 years of age; using contraceptives or pregnant excluded Country: USA	Endovaginal ultrasound	Results of Ultrasound: 280 (65%) had thin, distinct, symmetric endometrial echo < 5 mm = diagnosed with DUB. 153 (35%) had saline sonohysterography – 44 due to inadequate ultrasound, 109 due to endometrium > 5 mm. Sonohysterography results: 61 (40%) endometrium < 3 mm, 58 (38%) polyps, 22 (7%) submucous myomas, 10 (7%) thick symmetric endometrium > 3 mm; 2 (1%) inadequate scan.	Funding source: Not stated Study summary: Imaging allows for identification of pathology that is potentially missed by biopsy alone.
Güven 2004 ¹⁷⁷	diagnostic; randomised; non-blinded EL = Ib	197 – 139 premenopausal, 67 postmenopausal	Women; presenting with history of AUB Country: Turkey	Transvaginal ultrasonography; hydrososonography; surgical histopathology – reference	Diagnostic accuracy of transvaginal sonography: sensitivity = 56%, specificity = 68%, PPV = 75%, NPV = 48% Diagnostic accuracy of hydrososonography: sensitivity = 81%, specificity = 73%, PPV = 83%, NPV = 70% No data on acceptability or success of methods	Funding source: No stated Study summary: Hydrososonography is more accurate than TVS in detection of uterine pathology.
Harmanli 2005 ¹⁷⁸	Comparative diagnostic study EL = II	333	Women scheduled who had undergone ultrasound due to menorrhagia, pelvic pain and suspected uterine fibroids; scheduled for hysterectomy. Country: USA	Ultrasound; histopathology (after hysterectomy)	Ultrasound vs histopathology. Of 333 women. 24 false positive for fibroids, 12 false negative for fibroids, true positive and true negative not given. Any type of ultrasound: Sensitivity = 95.9% Specificity = 42.5% PPV = 92.4% NPV = 58.6% Adenomyosis was present in 70.8% of false positive and 83.3% of false negative results.	Funding source: Not stated Study summary: Adenomyosis is the most common final diagnosis in women with inaccurate ultrasound reports for uterine leiomyomas
Hunter 2001 ⁵⁷⁰	Diagnostic; comparative; prospective EL = III	100	women; referred for D&C; not pregnant or have cancer. Average age: 48.5 Country: UK	Ultrasound and biopsy; hysteroscopy and biopsy – reference	Comparing ultrasound and biopsy with hysteroscopy and biopsy for identification of any uterine pathology: sensitivity = 75%, specificity = 90%, PPV = 40%, NPV = 98%	Funding source: Not stated
Indman 1995 ¹⁷⁹	diagnostic; comparative EL = II	238	women; referred for evaluation of AUB; aged 25 to 75 Country: USA	transvaginal ultrasound; hysteroscopy; curettage	Hysteroscopy vs ultrasound: For all findings: hysteroscopy = 97 normal vs ultrasound 51 normal, 33 equivocal, 13 abnormal. Hysteroscopy = 141 abnormal vs ultrasound = 6 normal, 45 equivocal, 90 abnormal. For abnormal findings: myoma = 74 abnormal vs 1 normal; polyps = 42 abnormal vs 5 abnormal; myoma and polyps = 8 abnormal vs 0 normal; thickened endometrium = 5 abnormal vs 0 normal; septum = 4 abnormal vs 0 normal; cancer = 2 abnormal vs 0 normal; total = 135 abnormal vs 6 normal. Ultrasound sensitivity = 94%, specificity = 89%, PPV = 87%, NPV = 89%.	Funding source: not stated Study summary: Transvaginal ultrasound provides excellent diagnostic outcome.

Bibliographic information	Study type and evidence level	No. of patients and prevalence	Population characteristics	Type of test and reference standard	Sensitivity, specificity, PPV and NPV	Source of funding and additional comments
Kavak 1996 ¹⁸⁰	diagnostic; comparative; cohort EL = II	78	women; referred for D&C Aged 35 to 71, Mean 50.8. Parity = 2.5. 43.6% pre-menopausal, 56.4% post-menopausal Country: Turkey	vaginal ultrasonography; Pipelle biopsy; D&C	Sonography results: Endometrial thickness ranged from 0 mm to 18 mm, mean = 6.99 (\pm 3.4 mm). No disease group, mean = 7.04 (\pm 2.9 mm) Benign disease group, mean = 7.45 (\pm 3.4 mm) Carcinoma group, mean = 15 (\pm 1.4 mm) ($P < 0.01$ for carcinoma group vs others). Sensitivity for endometrial disease = 88.5% based on 5 mm cut-off. Pipelle results: 68 of 78 (87.1%) agreement between D&C and Pipelle results. 9 cases Pipelle did not provide enough material. 8 cases both Pipelle and D&C did not provide enough material. Reviewer Calculated: For Pipelle compared with histology: sensitivity = 22/23 specificity = 38/38 PPV = 22/22 PNV = 38/39 excluding insufficient material	Funding source: Not stated
Kelekci 2005 ¹⁸¹	Randomised; double blind; no mention of concealment EL = II	50 enrolled	Included if – Women scheduled for hysterectomy; with and without AUB; not pregnant; normal cervical pathology; aged > 35 years. Excluded if – Previous cervical surgery, previous problems with investigations, post-menopausal, received hormonal treatment within 1 month. Country: Turkey	Transvaginal Ultrasound (TVS); Saline Infusion Sonography (SIS); Office hysteroscopy (OHS); Reference = Histopathology (after hysterectomy)	TVS vs SIS vs OHS Identification of correct final diagnosis (outcome (95% CI)): Sensitivity: 56.3 (41 to 71.9) vs 81.3 (69 to 93) vs 87.5 (77 to 97) Specificity: 72.0 (58 to 85) vs 100 vs 100 PPV: 56.3 (41 to 71.9) vs 100 vs 100 NPV: 72.0 (58 to 85) vs 88.9 (79 to 97) vs 92.6 (84 to 100)	Funding source: Not stated Study summary: The diagnostic accuracy of SIS was equal to that of OHS in diagnosing intra-cavity abnormalities. Moreover, SIS was less painful than OHS for patients.
Kent 1998 ¹⁸²	Diagnostic; comparative; prospective EL = II	1022 with AUB, 177 had transcervical resection	Women; AUB Country: UK	Undirected biopsy; transcervical resection pathology results – reference	30% of pathology results differed from blind biopsy results. For any pathology: True positive = 4, false positive = 4, false negative = 50 (2 from insufficient material but abnormal), true negative = 119 Sensitivity = 7.4%, specificity = 96.4% For submucous fibroids: True positive = 3, false positive = 2, false negative = 12 (2 from insufficient material but abnormal), true negative = 41 Sensitivity = 20%, specificity = 95% Reviewer calculated	Funding source: Not stated Reviewer comments: Study used other diagnostic techniques in addition to those study, as patient safety and outcome were paramount.
Khanna 2001 ¹⁸³	diagnostic; cohort; comparative EL = III	70	women; AUB; excluded if pregnant; unmarried with pelvic infection, endocrine problems or coagulation disorder. Women aged 20> years;	Transvaginal ultrasound, saline infusion sonography; hysteroscopy – reference	Transvaginal ultrasound compared with histopathology for identification pathology at 5 mm cut-off in pre-menopausal women: true positive = 11, false positive = 2, true negative = 43 (15 with atrophy), false negative = 9 – reviewer calculated Sensitivity = 55%, specificity = 95.5% Saline infusion sonography compared with histopathology for identification of pathology: true positive = 19,	Funding source: Not stated

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients and prevalence	Population characteristics	Type of test and reference standard	Sensitivity, specificity, PPV and NPV	Source of funding and additional comments
			9 of 70 had menorrhagia Country: India		false positive = 6, true negative = 43, false negative = 2 (15 with atrophy) – reviewer calculated Sensitivity = 90.4%, specificity = 87.5% Hysteroscopy compared with histopathology for identification of pathology: sensitivity = 97.2%, specificity = 90.6%, PPV = 92.1%, NPV = 96.6%	
Koonings 1990 ¹⁸⁴	Diagnostic; comparison; RCT EL = Ib	149 – 74 Pipelle, 75 Tis-u-trap	women; scheduled for hysterectomy Country: USA	Pipelle biopsy; Tis-u-trap biopsy; hysterectomy histology	Pipelle biopsy: 9 of 74 inadequate tissue (12.2%). 45 of 74 samples good to excellent. Tis-u-trap: 12 of 75 (16%) inadequate tissue. 49 of 75 had good to excellent samples.	Funding source: Not stated Study summary: Pipelle equivalent to Tis-u-trap in effectiveness and cheaper.
Koss 1984 ²¹⁹	Epidemiological study EL = III	2586. 1567 re-examined at 1 year.	women; > 45 years of age; intact uterus; absence of genital tract symptoms; willingness to participate Country: USA	Endometrial sampling – Mi-Mark or Isaac devices	Success of device: Mi-Mark successful in 1117 (86.39%) of cases. Isaac successful in 1194 (92.34%) of cases ($P < 0.001$) Acceptability of devices: moderate to severe discomfort – upon insertion = 21.37% for Mi-Mark vs 16.76% for Isaacs. During procedure: Mi-Mark = 21.18% vs 12.05% for Isaacs After procedure: Mi-Mark = 7.36% vs 4.31% for Isaacs. Prevalence of carcinoma: 16 occult carcinomas, 2 missed carcinomas from 2586 women. 6.96 per 1000. Prevalence of Hyperplasia: 17 hyperplasia, 4 polyps with hyperplasia from 2586. 8.12 per 1000. Incidence of carcinoma = 1.71 per 1000. Incidence of hyperplasia = 1.71 per 1000. Risk-factors: White vs non-white OR = 1.65:1 (NS). Parity OR = 1.07:1 (NS). Onset of menopause: < 49 = 5.1 per 1000, > 56 = 32.3 per 1000. ($P < 0.04$). Obesity OR = 1.26:1 (NS). Estrogen OR = 1.31:1 (NS).	Funding source: National Cancer Institute Study summary: Study shows the risk factors for endometrial cancer.
Krampl 1997 ¹⁸⁵	Diagnostic EL = III	324	women; undergone Pipelle biopsy followed by TCRE or hysterectomy. Mean age = 48.02 (± 7.01), 287 were pre-menopausal. Country: Norway	Pipelle biopsy; histology via TCRE or hysterectomy.	Pipelle vs TCRE ($n = 249$), average age = 46.59 \pm 5.83. Pipelle vs hysterectomy ($n = 75$), average age = 52.75 \pm 8.43. PPV for Pipelle identifying endometrial malignancy = 100% (95% CI 73.5 to 100%) Hyperplasia identified in 38 women. 14 found by surgery, 22 endometrium was functional and 2 it was atrophic. Functional endometrium identified in 261. 232 found by surgery, 21 showed hyperplasia, 8 showed atrophy. Insufficient material collected in 5 cases. All shown to be benign by surgery	Funding source: Not stated Study summary: Adequate preoperative histological assessment is possible using Pipelle biopsy.
Krampl 2001 ¹⁸⁶	diagnostic; prospective; comparative; blind assessment EL = Ib	100	Women referred for AUB; excluded if had biopsy within 12 months, multiple, large fibroids causing discomfort Country: Norway	transvaginal ultrasonography; sonohysterography; operative hysteroscopy; histology – reference	Sensitivity, specificity, PPV, PNV (all %) for identification of abnormal endometrium (benign and atypical hyperplasia): TVS = 33.3%, 88.6%, 25.0%, 92.1% SH = 33.3%, 92.4%, 33.3%, 92.4% HSC = 22.2%, 87.3%, 16.7%, 90.1% Sensitivity, specificity, PPV, PNV (all %) for identification of focal pathology (polyps/fibroids): TVS = 23.5%, 93.0%, 44.4%, 83.5% SH = 94.1%, 84.5%, 59.3%, 98.4% HSC = 100%, 87.3%, 65.4%, 100%	Funding source: Not stated Study summary: Sonohysterography has considerably better results than transvaginal ultrasound.
Laughead 1997 ¹⁸⁷	diagnostic EL = II	124 – 114 underwent saline solution infusion sonohysterography . 10 with thin endometrium (< 4 mm) not given saline infusion	women; attending for AUB aged 36 to 70 Country: USA	Saline infusion sonohysterography; endometrial biopsies; histological evaluation	Saline solution sonohysterography: 56 uterine leiomyomas (1 to 13.7 cm); 48 intramural and 8 submucous. In patients with thickened endometrium, 18 people with polyps identified – all hysteroscopic confirmed. 19 patients with thickened endometrium had no polyps. Pathology showed 2 simple hyperplasia, 12 disordered endometrium and 2 atypical adenomatous.	Funding source: Not stated Study summary: Saline infusion sonohysterography is useful in management of AUB

Bibliographic information	Study type and evidence level	No. of patients and prevalence	Population characteristics	Type of test and reference standard	Sensitivity, specificity, PPV and NPV	Source of funding and additional comments
Law 1993 ¹⁸⁸	Diagnostic EL = II	191	women; pre- and post-menopausal Country: UK	Pipelle biopsy; D&C	In 118 of 191 Pipelle and D&C provided same result. In 15 cases Pipelle did not provide sufficient material. In 5 cases D&C did not provide enough material. In 53 cases neither provided enough material.	Funding source: Not stated
Lipscomb 1994 ¹⁸⁹	Diagnostic; comparison; randomised; blind EL = Ib	248 – Pipelle = 85, Accurette = 81, Explora = 82	Women; AUB; referred for biopsy Country: USA	Pipelle; Accurette; Explora – biopsies	In pre-menopausal women: Pipelle – failed on 4 (4.7%), insufficient material on 12 (14.8%). Accurette – failed on 15 (18.5%), insufficient material on 19 (27.5%). Explora – failed on 2 (2.4), insufficient material on 12 (14.6%).	Funding source: Not stated Study summary: Pipelle and Explora can be recommended.
Litta 1996 ¹⁹⁰	diagnostic EL = III	629	women; persistent AUB. 60.4% were pre-menopausal, 39.6% were postmenopausal Country: Italy	Hysteroscopy; targeted biopsy – reference	Accuracy not calculated by authors, so done by reviewer (atrophic counted as normal; all based on pathology vs no pathology, rather than correct diagnosis, so likely to over-estimate accuracy). In pre-menopausal women ($n = 378$): True positive = 144, true negative = 164, false positive = 52, false negative = 18 Sensitivity = 89%, specificity = 76%, PPV = 73.5%, NPV = 90%	Funding source: Not stated
Loffer 1989 ⁸⁴	Diagnostic; comparison EL = II	187	women; AUB – 47 post-menopausal, 192 menorrhagia, 20 metrorrhagia, 18 metrorrhagia Country: USA	D&C; hysteroscopy	Pathology identified: Menorrhagia = 68 normal, 13 polyps, 16 fibroids, 3 hyperplasia, 0 cancer, 2 endometriosis. Sensitivity, specificity, PPV, NPV of D&C compared with histology: 65% (32/49), 100% (102/102), 100% (32/32), 17% (17/102) Sensitivity, specificity, PPV, NPV of hysteroscopy with tissue sample compared with histology: 98% (48/49), 100% (102/102), 100% (48/48), 1% (1/102) In 91 patients with negative hysteroscopy only 1 had pathology identified by biopsy.	Funding source: Not stated Study summary: Study shows value of hysteroscopy for identification of uterine pathology.
MacKenzie 1978 ⁷²	Diagnostic EL = III	1029	Women; undergoing D&C; excluded if for evacuation of retained products of conception or for hysterectomy or vaginal repair. Country: UK	D&C	Histopathology results: Proliferative phase = 310 (30.1%) Secretory phase = 274 (26.6%) Mixed = 8 (0.8%) Menstrual = 35 (3.4%) Hyperplastic = 57 (5.5%) Decidua = 12 (1.2%) Atrophic endometrium = 8 (0.8%) Endometritis = 8 (0.8%) Endometrial polyps = 21 (2.0%) Endometrial carcinoma = 15 (1.4%) Inadequate sample = 85 (8.3%) No curettings = 153 (14.9%) No report = 43 (4.2%) Figures varying by indication for D&C. Mean stay in hospital = 1.8 days.	Funding source: Not stated Study summary: improved selection of patients for D&C could greatly reduce number of unnecessary procedures.
Mancini 2002 ¹⁹¹	Diagnostic; comparative; non-blinded EL = II	216 – 106 sterile women, 53 AUB, 57 post-menopausal bleeding	Women; previous transvaginal ultrasound results showing increased endometrial thickness. Country: Italy	Sonohysteroscopy; hysteroscopy – reference	Accuracy of sonohysteroscopy for identifying any pathology: sensitivity = 99.3%, specificity = 98.6%, PPV = 99.3%, NPV = 98.6%. Pain was described as 'mild' by 32 and 'intense' by 19 women undergoing hysteroscopy. Pain was described as 'mild' by 15 and 'intense' by 6 women undergoing Sonohysteroscopy. Difference between groups ($P < 0.05$) 8 hysteroscopy and 1 sonohysteroscopy patient had adverse reactions to tests.	Funding source: Not stated Study summary: Sonohysteroscopy is an accurate method for diagnosis.
Mathew 2000 ¹⁹²	Diagnostic; prospective; cohort	110	Women; presenting with AUB 70 with menorrhagia, 29	Transvaginal ultrasound; hysteroscopy – reference	Accuracy of TVS against hysteroscopy for identifying pathology: sensitivity = 54%, specificity = 100%, PPV = 100%, NPV = 81.1%.	Funding source: Not stated

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients and prevalence	Population characteristics	Type of test and reference standard	Sensitivity, specificity, PPV and NPV	Source of funding and additional comments
	EL = II		with metrorrhagia, 11 were post-menopausal bleeding Country: Oman			
Mihm 2002 ¹⁹³	diagnostic; comparison; cohort; blinded EL = Ib	143 underwent SIS and biopsy, 113 also underwent surgical from which pathology could be determined	Women; aged 25 to 69; AUB; failed medical treatment Country: USA	Saline sonohysterography and biopsy; surgery – D&C, hysteroscopy, hysterectomy (reference)	SIS and biopsy compared with histopathology ($n = 113$): True positive = 64, false positive = 14, false negative = 2, true negative = 33 Sensitivity = 97%, specificity = 70%, PPV = 82.1%, NPV = 94.3%	Funding source: R&D grant from University of Virginia Study summary: SIS and biopsy is an accurate method for identification of pathology.
Miller 2001 ⁵⁶⁴	Epidemiological cohort EL = III	246: 123 cases – 51 Caucasian; 70 African-American, 123 controls – 45 Caucasian; 76 African-American	women; treated for menorrhagia Country: USA	test for von Willebrand disease	African-Americans had higher vWF:Ag ($P = 0.001$), FVIII ($P = 0.008$) and vWF:Act ($P = 0.006$) than Caucasian population. vWF:RiCof, bleeding time and partial thromboplastin did not differ between racial groups. In Caucasian group 0 control and 7 cases had vWD, in African-American group 1 control and 1 case had vWD. In both racial groups those with type O blood differed from those with ABO blood type.	Funding source: not stated Study summary: Study shows higher levels of vWF factors in African-American population compared with Caucasian population. This suggests tests should take account of these differences
Nagele 1996 ⁷¹	Diagnostic EL = III	2500	Women referred for outpatient hysteroscopy Country: UK	hysteroscopy	Hysteroscopy successful in 96.4%. 89% completed, 7.4% incomplete, and 3.6% failed. Diagnostic outcomes: menorrhagia ($n = 1120$) 583 (52.1%) normal, 334 (29.8%) fibroids, 112 (10%) polyps, 8 (0.7%) atrophy, 29 (2.6%) irregular endometrium, 3 (0.3%) endometrial carcinoma, 51 (4.6%) miscellaneous. Total ($n = 2409$) 1172 (48.6%) normal, 585 (24.3%) fibroids, 272 (11.3%) polyps, 87 (3.6%) atrophy, 64 (2.7%) irregular endometrium, 11 (0.5%) endometrial carcinoma, 218 (9%) miscellaneous.	Funding source: Not stated Study summary: Hysteroscopy, unlike ultrasound, allows optimum assessment of patient prior to potential surgery.
Nagele 1996 ¹⁹⁴	diagnostic; randomised (alternate) EL = II	157	women; referred for investigation for AUB – all had previous examination and ultrasound Country: UK	hysteroscopy with either saline or carbon dioxide distension.	Mean age of groups: saline = 43.4 vs 42.3 for CO ₂ Requiring cervical dilation for hysteroscopy: saline = 17.9% vs 35.4% for CO ₂ Visualisation: OR of poor or very poor = 1.94 (95% CI 0.61 to 6.74) Hysteroscopy unsuccessful in 2 saline and 4 CO ₂ patients. Pain during procedure was: 4 for saline group and 11 for CO ₂ group (OR = 0.33, 95% CI 0.08 to 1.20)	Funding source: Not stated Study summary: Saline is equivalent to CO ₂ in terms of use for distension for hysteroscopy.
Nanda 2002 ¹⁹⁵	diagnostic; prospective; comparative EL = II	50	women; referred for hysterectomy – 23 for DUB and 27 for fibroids Country: India	saline infusion sonography (SIS); transvaginal ultrasound (TVS); histology	Sensitivity, specificity, LR+, LR– for identification of submucous fibroids by TVS: 70.0%, 96.7%, 21.2%, 0.3% Sensitivity, specificity, LR+, LR– for identification of submucous fibroids by SIS: 89.5%, 100%, N/A, 0.1% Sensitivity, specificity, LR+, LR– for identification of endometrial polyps for TVS: 66.7%, 100, N/A, 0.3% Sensitivity, specificity, LR+, LR– for identification of endometrial polyps for SIS: 100%, 97.8%, 45.4%, 0.0% No assessment of acceptability of methods.	Funding source: Not stated Study summary: SIS is more accurate than TVS at identifying fibroids and polyps.
Ossola 1999 ¹⁹⁶	Diagnostic; comparative; prospective EL = III	55 – 33 pre-menopausal, 22 postmenopausal	Women; referred with AUB; aged between 28 and 73 (average 49) Country: Italy	Transvaginal ultrasound; Saline infusion sonography; hysteroscopy; endometrial biopsy or operative hysteroscopy – reference	TVS: Sensitivity, specificity, PPV, NPV of TVS for identifying all pathology: 91%, 12%, 86%, 20%. Polyps: 35%, 70%, 61%, 45%. Myomas: 21%, 100%, 100%, 76% SIS: Sensitivity, specificity, PPV, NPV of SIS for identifying all pathology: 97%, 50%, 92%, 80%. Polyps: 96%, 56%, 75%, 92%. Myomas: 57%, 100%, 100%, 85% Hysteroscopy: Sensitivity, specificity, PPV, NPV of hysteroscopy for identifying all pathology: 95%, 62%, 93%, 71%. Polyps: 96%, 70%, 81%, 94%. Myomas: 53%, 97%, 88%, 84% No problems or adverse events report with any method.	Funding source: Not stated Study summary: SIS is accurate method for diagnosis, being similar to hysteroscopy.

Bibliographic information	Study type and evidence level	No. of patients and prevalence	Population characteristics	Type of test and reference standard	Sensitivity, specificity, PPV and NPV	Source of funding and additional comments
Paschopoulos 2001 ¹⁹⁷	diagnostic; retrospective; case series EL = III	397 – 164 menorrhagia; 152 metrorrhagia, 81 postmenopausal bleeding	women; referred with AUB Country: Greece	Transvaginal ultrasound (TVS); vaginoscopic hysteroscopy; histopathology – reference	Transvaginal sonography: sensitivity = 67%, specificity = 87%, pre-test probability = 0.5, Likelihood ratio of abnormal result = 5.15, likelihood ratio of normal results = 0.38 Vaginoscopic hysteroscopy: sensitivity = 92%, specificity = 95%, pre-test probability = 0.5, Likelihood ratio of abnormal result = 18.4, likelihood ratio of normal results = 0.08 Vaginoscopic hysteroscopy was unsuccessful in 18 women (4.3%) No data on acceptability of methods.	Funding source: Not stated
Pascual 2005 ¹⁹⁸	Prospective; cohort EL = II	272	Women; referred for assessment due to AUB (metrorrhagia or menorrhagia). Mean age: 44 years. Country: Spain	Colour Doppler transvaginal ultrasound; hysteroscopy (reference)	Table for CDTU vs hysteroscopy: Figures presented are the hysteroscopy findings for normal, polyp, myoma, hyperplasia, synechia, neoplasia, total. Normal = 106, 11, 6, 4, 3, 0, 130 Polyp = 12, 59, 0, 9, 1, 1, 82 Myoma = 2, 3, 36, 0, 0, 0, 41 Hypertrophy = 2, 7, 0, 7, 0, 0, 16 Neoplasia = 1, 1, 0, 1, 0, 0, 3 Total = 123, 81, 42, 21, 4, 1, 272 Outcomes for any pathology: Sensitivity = 83.9% (95% CI 76.2 to 89.2) specificity = 86.2% (95% CI 78.5 to 91.5) PPV = 88.0% (95% CI 81.3 to 92.7) NPV = 81.5% (95% CI 73.6 to 87.6)	Funding source: Not stated
Pasqualotto 2000 ¹⁹⁹	Retrospective; diagnostic EL = III	375	Women; referred with AUB. Patient characteristics: average age = 49.4 (\pm 13.5); BMI = 28.5 (\pm 8.1); 211 pre-menopausal, 164 post-menopausal; pathology – 105 had myoma, 172 had polyps, 21 had hyperplasia, 4 had cancer and 71 had normal endometrium Country: USA	Office hysteroscopy; Transvaginal Ultrasound; Saline Infusion Sonography; endometrial Pipelle biopsy; hysteroscopic surgery – reference	Sensitivity of diagnostic tool for identifying polyps or submucosal myomas: TVS (n = 236) = 39%, SIS (n = 94) = 96%, Hysteroscopy (n = 273) = 99%, Pipelle biopsy (n = 171) = 10% Sensitivity of diagnostic tool for identifying hyperplasia: TVS = 90%, SIS = 13%, Hysteroscopy = 27%, Pipelle biopsy = 33% Different methods used in different patients No assessment of acceptability or success of methods.	Funding source: Not stated
Pasija 2004 ²⁰⁰	diagnostic; cohort EL = III	58	women; AUB; > 40 years; not treatment for AUB within 3 months; normal uterus. 52 pre-menopausal, 6 post-menopausal Country: India	transvaginal ultrasound; saline infusion sonohystography; endometrial sampling (reference)	Transvaginal ultrasound accuracy compared with histopathology: sensitivity = 84.8%, specificity = 79%, PPV = 82.4%, NPV = 82%. Saline infusion sonohysteroscopy compared with histopathology: sensitivity = 94.1%, specificity = 88.5%, PPV = 91.4%, NPV = 92%	Funding source: Not stated
Philipp 2005 ⁵⁷¹	diagnostic comparison EL = II	81	women; subjective menorrhagia (> 7 days bleeding); pathology or IUD excluded. Non-pregnant. NSAIDs or anti-platelet treatments	Haemostatic testing: platelet function analyser (PFA-100); bleeding time (BT)	Sensitivity, specificity, PPV and NPV of PFA-100 compared with haematology for identifying vWD = 80%, 89%, 33%, 98% Sensitivity, specificity, PPV and NPV of BT compared with haematology for identifying vWD = 60%, 68%, 12%, 96% Based on vWF = vWF/RiCcof and/or vWF:Ag below ABO type specific range.	Funding source: Association of Teachers Preventative Medicine Study summary: Neither PFA-100 or BT are accurate methods of classifying VWD

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients and prevalence	Population characteristics	Type of test and reference standard	Sensitivity, specificity, PPV and NPV	Source of funding and additional comments
			discontinued for 14 days. Age 13 to 55 Race: 57 white, 15 black, 9 other Blood group: 43 O-group, 38 non-O group PBAC = 306, 47 were > 100 Country: USA			
Pungetti 1990 ²⁰¹	Diagnostic, non-comparative EL = III	150	Women; referred for investigation for various gynaecological issues. Indications for investigation: AUB = 71 Peri/postmenopausal bleeding = 34 Infertility = 17 Suspected myoma = 7 Suspected polyp = 2 Other = 19 Country: Italy	Hysteroscopy; D&C	No assessment of myoma or polyps. Concordance: Functional endometrium = 88.5% Hypo/atrophic endometrium = 95% Dysfunctional endometrium = 66.6% Low-risk hyperplasia = 66.6% High-risk hyperplasia = 33.3% Sensitivity and specificity could not be calculated due lack of data.	Funding source: Not stated
Reinhold 1996 ²⁰²	diagnostic; comparison; prospective; blinded EL = Ib	147 – 28 excluded due to protocol violations. 119 included in analysis	Women; aged 29 to 83; 64 pre-menopausal and 55 post-menopausal; scheduled for hysterectomy; University Hospital Country: Canada	Endovaginal Ultrasound; Magnetic Resonance Imaging; Histopathology examination – reference	Of 119 women – histopathologic found 28 (24%) had adenomyosis. Endovaginal US found 25 cases and absence in 81. 10 false positives and 3 false negatives. Sensitivity = 89%, specificity = 89%, PPV = 71%, PNV = 96%. MRI found 24 cases and excluded 73. 13 false positive and 4 false negative. Sensitivity = 86%, specificity = 86%, PPV = 65%, PNV = 95%. Differences between sensitivities ($P = 0.65$) and specificities ($P = 0.75$). Primary pathology by histopathology: 42 leiomyomas, 26 endometrial carcinoma 26, 11 endometrial polyps, 9 ovarian carcinoma, 8 cervical carcinoma, 6 adenomyosis (usually a secondary diagnosis, hence 28 in total but 6 here), 7 miscellaneous, 10 no major pathology.	Funding source: Canadian Association of Radiologists fellowship Study summary: Endovaginal US was as accurate as MRI at identifying adenomyosis.
Ryu 2004 ²⁰³	comparative; diagnostic; retrospective EL = III	414 patients seen for AUB; 105 had TVS or HS	Women; referred for AUB; Age range from 27 to 73, average 44.3 47 were post-menopausal, 58 were pre-menopausal. Country: Korea	Transvaginal ultrasound; hysterosonography; D&C, hysterectomy and biopsy, hysterectomy (reference)	Accuracy of transvaginal ultrasound compared with pathology for identification uterine pathology: sensitivity = 0.79, specificity = 0.46, PPV = 0.83, NPV = 0.39 Accuracy of hysterosonography compared with pathology for identification uterine pathology: sensitivity = 0.95, specificity = 0.83, PPV = 0.95, NPV = 0.83	Funding source: Not stated Study summary: hysterosonography provide better information to physician than transvaginal ultrasound.
Saidi 1997 ²⁰⁴	Diagnostic; randomised; trial; non-blinded EL = II	68 – 34 transvaginal ultrasound; 34 sonohysterography	Women; referred for AUB Patient characteristics: Group A: age = 49.35 parity = 1.97 gravidity = 2.44 Group B:	Transvaginal ultrasound; sonohysterography; diagnostic hysteroscopy; operative hysteroscopy – reference	Sonohysterography – sensitivity = 90.0%, specificity = 83.3%, PPV = 16.7%, NPV = 90.9% Ultrasound – sensitivity = 95.7%, specificity = 63.6%, PPV = 12.5%, NPV = 84.6% Diagnostic hysteroscopy – sensitivity = 82.2%, specificity = 65.2%, PPV = 45.5%, NPV = 78.3%	Funding source: Not stated

Bibliographic information	Study type and evidence level	No. of patients and prevalence	Population characteristics	Type of test and reference standard	Sensitivity, specificity, PPV and NPV	Source of funding and additional comments
			age = 53.2 parity = 1.70 gravidity = 1.97 Country: USA			
Salim 2005 ²⁰⁵	Diagnostic; double-blind EL = Ia	49	women; referred due to menorrhagia; symptomatic submucous fibroids; average age = 39; 21 women were nulliparous Country: UK	3D saline infusion sonohysterography (3D SIS); hysteroscopy – reference	3D SIS identified 61 fibroids, hysteroscopy identified 61 fibroids. Agreement between methods on classification = 89%, kappa = 0.8	Funding source: Not stated Study summary: Study show good agreement between 3D SIS and hysteroscopy.
Scarpellini 1994 ²⁰⁶	diagnostic; comparative EL = II	157	women; referred for investigation for menstrual problems Country: Italy	transvaginal ultrasound; histology	40 of 157 had endometrial hyperplasia after histological test. Ultrasound identified 29 hyperplasia, which was confirmed in 19 cases (67.85%).	Funding source: not stated
Schwarzler 1998 ²⁰⁷	Diagnostic; comparison; prospective; partial-blinded EL = II	104 – 6 unable to complete, 98 assessed	Women; post- and pre-menopausal; diagnosed with irregular or excessive uterine bleeding; resistant to medical treatment Country: UK	Transvaginal ultrasound; sonohysterography; diagnostic hysteroscopy; operative hysteroscopy – reference; discomfort and acceptability of tests	Sensitivity, specificity, PPV, NPV of TVS for identification of any pathology compared with operative hysteroscopy: 67%, 89%, 88%, 71%. Polyps: 56%, 97%, 86%, 87%. Fibroids: 82%, 98%, 82%, 96% Sensitivity, specificity, PPV, NPV of sonohysterography for identification of any pathology compared with operative hysteroscopy: 87%, 91%, 92%, 86%. Polyps: 84%, 97%, 91%, 85%. Fibroids: 94%, 98%, 89%, 99% Sensitivity, specificity, PPV, NPV of diagnostic hysteroscopy for identification of any pathology compared with operative hysteroscopy: 90%, 91%, 92%, 89%. Polyps: 92%, 100%, 100%, 97%. Fibroids: 88%, 100%, 100%, 98%. Discomfort with TVS – 58% had no discomfort, 40% had slight discomfort and 2% found treatment unpleasant. Discomfort with sonohysterography – 34% had no discomfort, 53% had slight discomfort, 13% found the test unpleasant. This resulted in 1% of sonohysteroscopies being halted. No data on hysteroscopy.	Funding source: Austrian FWF Foundation Study summary: Study shows that sonohysterography is an alternative to hysteroscopy, and better than transvaginal ultrasound.
Smith 1991 ²⁰⁸	diagnostic; comparative EL = III	45	women; postmenopausal bleeding Country: USA	Transvaginal ultrasound; Histopathology	Ultrasound compared with histopathology: normal-normal = 22, normal-abnormal = 0, abnormal-normal = 14, abnormal-abnormal = 9	Funding source: Not stated Study summary: Ultrasound may be a useful initial diagnostic method for assessing endometrial pathology
Stovall 1991 ⁷⁶	randomised; comparative; blind EL = Ia	275 – 126 Novak biopsy, 149 Pipelle biopsy	women; referred for AUB; excluded if pregnant. Novak group: aged 44, parity 4, indication for biopsy – AUB = 83.3%, postmenopausal bleeding = 16.7% Pipelle group: aged 40, parity = 4, indication for biopsy – AUB = 89.9%, postmenopausal bleeding = 10.1% Country: USA	Novak curette; Pipelle endometrial sampling; Histology from subsequent hysterectomy	Patient pain: for Novak group mean pain score was 4.36 vs 3.21 for Pipelle group ($P < 0.05$). Failure of test: insufficient sample – Novak group = 12 (9.5%) vs 19 (12.8) for Pipelle group (NS) Sampling outcomes: Endometriosis: Novak = 23 (18.3%) vs 23 (15.4%) in Pipelle Hyperplasia: Novak = 15 (11.9%) vs 11 (7.4%) in Pipelle. Proliferative or secretory: Novak = 76 (60.3%) vs 96 (64.4%) for Pipelle Histology confirmed results in 48 of 50 (96%) of patients.	Funding source: Not stated Study summary: Study suggests that Pipelle is as effective as Novak.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients and prevalence	Population characteristics	Type of test and reference standard	Sensitivity, specificity, PPV and NPV	Source of funding and additional comments
Tahir 1999 ²²⁰	diagnostic; randomised EL = Ib	411 – 11 declined randomisation; 200 inpatient; 200 in outpatient group	women; > 35 years old; referred for AUB (menorrhagia, postmenopausal, irregular bleeding, etc.) Country: UK	inpatient – hysteroscopy and curettage; outpatient – vaginal ultrasound, outpatient hysteroscopy – reference, Pipelle endometrial biopsy.	<p>Patient population: menorrhagia – inpatient = 75 and outpatient = 88, total = 163 (40.75%)</p> <p>Hysteroscopy findings (all patients): inpatients – normal = 104, fibroids = 46, polyp = 31, atrophy = 15, carcinoma = 4; outpatients – normal = 100, fibroid = 52, polyp = 26, atrophy = 11, carcinoma = 4.</p> <p>Endometrial biopsy results: inpatient (curettage) – normal = 131, atrophic = 17, benign polyp = 31, hyperplasia = 1, Adenocarcinoma = 6, inadequate tissue = 14, failed = 0; outpatient (Pipelle) – normal = 134, atrophic = 15, benign polyp = 0 (26 with hysteroscopy), hyperplasia = 2, Adenocarcinoma = 5, inadequate tissue = 16, failed = 2</p> <p>Outpatient vs inpatient results:</p> <p>Inpatient – normal = 99, fibroid = 46, polyp = 31, atrophy = 17, endometrium – hyperplasia = 1, carcinoma = 6. Outpatient: normal = 100, fibroid = 52, polyp = 26, atrophy = 15, endometrium – hyperplasia = 2, carcinoma = 5.</p> <p>TVS and Pipelle alone (no hysteroscopy) missed 14 benign lesions (18%) (McNemar chi-squared, $P = 0.0076$), but detected 2 hyperplasia and 1 carcinoma not found on hysteroscopy.</p> <p>Patient pain (VAS) = inpatient median score = 1.5, outpatient = 3.5 ($P < 0.0001$)</p> <p>Patient anxiety (VAS) = inpatient median score = 4, outpatient = 4.</p> <p>patient acceptability (VAS) = inpatient median score = 5, outpatient = 5.</p>	<p>Funding source: Not stated</p> <p>Study summary: Combined Pipelle and transvaginal should be used as initial investigation for AUB in over 35s</p>
Taylor 2001 ²⁰⁹	diagnostic; health service research; cohort EL = III	264	women; pre-menopausal; AUB Country: UK	Ultrasound – abdominal or vaginal; hysteroscopy – reference; bleeding pattern	<p>Comparison of ultrasound with hysteroscopy for identification of pathology: true positive = 15, false positive = 16, true negative = 140, false negative = 25</p> <p>Sensitivity = 37.5%, specificity = 89.7%</p>	<p>Funding source: Not stated</p> <p>Study summary: Ultrasound had no additional impact on patient management, in those with normal findings.</p>
Teal 1998 ²¹⁶	Diagnostic EL = III	114	women; referred for investigation – 44% for postmenopausal bleeding, 39% for DUB, 6% for HRT problems, 11% for other reasons. Country: UK	Pipelle endometrial suction curette	<p>Of 114 patients:</p> <p>112 procedures attempted</p> <p>95 successful entry to endometrial cavity (83%)</p> <p>9 no sample obtained (8%)</p> <p>17 Unsuccessful entry to endometrial cavity (15%)</p> <p>62 Adequate material for histology (54.4%)</p> <p>24 material inadequate for histology (21%)</p> <p>Of which 2 were later found to have cancer (1.8%)</p> <p>Subsequent D&C/H&C 40 (35%)</p>	<p>Funding source: Not stated</p> <p>Study summary: Successful Pipelle curette is a useful diagnostic tool, but when unsuccessful or ambiguous then a more definitive method must be used.</p>
Torrejón 1997 ²¹⁰	Comparative; case series; retrospective EL = III	1398 selected patients	Women; referred for AUB who underwent hysteroscopy then later D&C. Country: Spain	hysteroscopy; D&C – reference	<p>In pre-menopausal women the accuracy of hysteroscopy compared with D&C for identification of pathology was: sensitivity = 71.8%, specificity = 96.4%, PPV = 79.3%, NPV = 94.7%</p>	<p>Funding source: Not stated</p> <p>Study summary: In AUB population, hysteroscopic is a should be a basic diagnostic tool.</p>
Towbin, 1996 ²¹¹	diagnostic EL = II	149	women; referred for excessive menstrual bleeding; Country: USA	transvaginal ultrasonography; office hysteroscopy; inpatient hysteroscopy/hysterectomy – reference	<p>140 of 149 underwent endometrial biopsy; 124 of 149 underwent ultrasonography; 149 of 149 underwent hysteroscopy.</p> <p>Hysteroscopy identified: 42 as normal; 53 myoma; 36 endometrial polyps; 6 hyperplasia; 17 adenomyosis; 2 atrophic endometrium.</p> <p>Ultrasonography identified: 59 as normal; 52 with leiomyoma; 11 with thickened uterine wall; 2 polypoid lesions.</p> <p>Hysteroscopy: sensitivity = 79%, specificity = 93%</p> <p>Ultrasonography: sensitivity = 54%, specificity = 90%</p>	<p>Funding source: not stated</p> <p>Study summary: Study shows office hysteroscopy is a suitable method for investigating excessive menstrual bleeding</p>
Valle 1981 ⁷⁴	Diagnostic EL = II	553	women; AUB; Age range from 20 to 75	Hysteroscopy; Hysteroscopic biopsy; D&C	<p>Pre-menopausal women ($n = 419$):</p> <p>Number of pathologies identified via hysteroscopy; hysteroscopic biopsy; curettage histology.</p> <p>Endometrial polyps = 165, 150, 15</p>	<p>Funding source: Not stated</p> <p>Study summary: Hysteroscopy provides a</p>

Bibliographic information	Study type and evidence level	No. of patients and prevalence	Population characteristics	Type of test and reference standard	Sensitivity, specificity, PPV and NPV	Source of funding and additional comments
			Country: USA		Submucous leiomyoma = 68, 8, 0 Adenomatous hyperplasia = 16, 10, 4 Intrauterine adhesions = 9, 2, 0 Intrauterine foreign body = 7, 7, 0 Uterine septum = 7, 0, 0 Caesarean section scar defect = 5, 0, 0. Post-menopausal women (<i>n</i> =134) Number of pathologies identified via hysteroscopy; hysteroscopic biopsy; curettage histology: Endometrial polyps = 37, 29, 5 Submucous leiomyoma = 12, 2, 0 Atrophic endometrium = 17, 15, 12 Adenomatous hyperplasia = 6, 5, 1 Adenocarcinoma = 3, 3, 1	useful method for identifying intrauterine pathology not available using 'blind' D&C
Vercellini 1997 ⁷⁰	Diagnostic EL = II	793	women; referred for AUB to Centre for Menorrhagia; PBAC > 100; those on hormonal treatment excluded; those who had D&C or hysteroscopy within 3 months excluded Country: Italy	Ultrasonography; hysteroscopy; hysterectomy/resection – reference	Ultrasonography: 300 normal, 417 abnormal, 53 doubtful. Hysteroscopy: 325 normal, 445 abnormal (234 submucous myomas, 155 endometrial polyps, 76 endometrial hyperplasia, 2 endometrial carcinoma). Sensitivity, specificity, PPV, PNV of ultrasonography compared with hysteroscopy = 96%, 86%, 91%, 94% Sensitivity, specificity, PPV, PNV of hysteroscopy compared with hysterectomy (<i>n</i> = 234): submucous myomas – 95%, 81%, 85%, 93%; endometrial polyps = 86%, 94%, 91%, 90%; endometrial hyperplasia = 45%, 99%, 38%, 94%.	Funding source: Not stated Study summary: Considering good specificity and NPV of transvaginal ultrasonography, it should be considered for initial investigation of pre-menopausal women.
Vercellini 1998 ⁷⁹	diagnostic study EL = Ib	115 – 13 excluded, 102 included in analysis	women; undergoing hysterectomy due to menorrhagia and/or dysmenorrhoea; women with known pathology excluded. Country: Italy	transvaginal ultrasonography; myometrial needle biopsy; post-hysterectomy pathology assessment – reference	Biopsy: 29 cases of adenomyosis identified (28%) Sonography: 48 cases of adenomyosis; 24 confirmed; 5 missed Sensitivity, specificity, PPV, PNV = 82.7%, 67.1%, 50%, 90.7% Needle: 16 cases; 13 confirmed; 16 missed. Sensitivity, specificity, PPV, PNV = 44.8%, 95.9%, 81.2%, 81.4%	Funding source: Not stated Study summary: Both tests produced suboptimal test results, and combined did not improve results.
Widrich 1996 ²¹²	Diagnostic; prospective; blinded EL = Ib	130 – 113 both diagnostic procedures – 64 pathology results	women; referred for investigation Country: USA	Saline infusion sonography; hysteroscopy; pathology – reference	SIS compared with hysteroscopy (<i>n</i> = 113): abnormalities, sensitivity, specificity, PPV, NPV. Polyps = 34 vs 30, 0.87, 0.9, 0.76, 0.95. myoma = 25 vs 26, 0.93, 0.99, 0.96, 0.98. Hyperplasia = 9 vs 4, 1.00, 0.95, 0.44, 1.00. All findings = 61 vs 56, 0.96, 0.88, 0.89, 0.96. SIS vs pathology (<i>n</i> = 64): abnormalities, sensitivity, specificity, PPV, NPV. Polyp = 25 vs 16, 1.00, 0.81, 0.64, 1.00. Myoma = 13 vs 13, 0.92, 0.98, 0.92, 0.98. Hyperplasia = 8 vs 7, 0.86, 0.97, 0.75, 0.98. All findings = 40 vs 34, 1.00, 0.80, 0.85, 1.00. Hysteroscopy vs pathology (<i>n</i> = 64): abnormalities, sensitivity, specificity, PPV, NPV. Polyp = 20 vs 16, 0.94, 0.90, 0.75, 0.98. Myoma = 15 vs 13, 1.00, 0.96, 0.87, 1.00. Hyperplasia = 3 vs 7, 0.43, 1.00, 1.00, 0.93. All findings = 35 vs 34, 0.97, 0.93, 0.94, 0.97.	Funding source: Not stated Study summary: SIS was well tolerated method. Both hysteroscopy and SIS had advantages and disadvantages in terms of diagnosis power.
Wood, 1993 ²¹³	diagnostic EL = II	97	women; menorrhagia; non-responsive to medical treatment Country: Australia	vaginal ultrasound; surgical assessment of uterus	Transvaginal ultrasound: normal 33, bulky uterus 4, bicornuate uterus 2, adenomyosis 13, intracavity fibroid/polyp 9, intramural or subserous fibroid 36. Surgical diagnosis: normal 42, bulky uterus 4, bicornuate uterus 2, adenomyosis 7, intracavity fibroid/polyp 8, intramural or subserous fibroid 34 Reviewer calculation: PPV = 31/33 = 0.94 NPV = 53/64 = 0.83 Sensitivity = 31/42 = 0.74 Specificity = 53/55 = 0.96	Funding source: not stated Study summary: Routine use of ultrasound in menorrhagia recommended

Heavy menstrual bleeding

Table 4.6 Tests for exclusion of underlying conditions – non-comparative studies

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
ACOG 2001 ²¹⁴	Recommendations of ACOG EL = 4	Recommendations for vWD testing in women with menorrhagia		Country: USA		vWD screening recommended amongst women with menorrhagia but no pathology prior to any surgical intervention.	
Andrade 1991 ¹⁴⁸	cohort EL = 3	haematological against total MBL	309	women; aged 15–48 years – average 29.4; parity = 2.4; suitable for entry into IUS study Country: Brazil	haematological assay – haemoglobin, serum iron, and serum ferritin; MBL – alkaline haematin	Haematological results by MBL (MBL – haemoglobin, serum iron, serum ferritin): < 20 ml ($n = 130$) – 13.3, 78.8, 28.5; 21–40 ($n = 95$) – 13.5, 75.6, 23.4; 41–60 ($n = 50$) = 12.8, 57.3, 18.6; 61–80 ($n = 24$) – 13, 75.9, 14.5; > 80 ($n = 10$) = 12, 47.3, 10.6; All ($n = 309$) – 13.2, 72.2, 23. Normal (< 60 ml) vs Heavy (> 60 ml). Age = 29.2 (SD 6.5) vs 30.6 (SD 6.4); weight = 55.9 (SD 9.7) vs 42 (SD 8.8); height = 155.3 (SD 6) vs 157 (SD 6.8); parity = 2.4 (SD 1.9) vs 3.6 (SD 2.8) $P < 0.05$.	Funding source: Not stated Study summary: Women become anaemic when MBL reaches 80 ml not 60 ml.
Claessens 1981 ¹⁴⁶	Epidemiology EL = 3	Testing for coagulation disorders	83 – 59 included, 24 excluded as menorrhagia not the main presenting symptom	women; hospitalised for menorrhagia at Hospital for Sick Children (assume young adults). Study undertaken between 1971 to 1980. Country: Canada	Prevalence of coagulation disorders	44 of 59 (74%) were found to have DUB. 11 of 59 (19%) were found to have coagulation disorder – 4 had idiopathic thrombocytopenic disorders, 3 had vWD, 2 had Glanzmann's disease, 1 had thalassaemia, 1 had Fanconi's anaemia. 9 (15%) of 59, but 5 (45%) of 11 with coagulation disorders had life-threatening uterine blood loss.	Funding source: Not stated Study summary: Suggested that girls referred for HMB have in-depth history and blood test.
Decloedt 1999 ⁸⁵	diagnostic; epidemiology; retrospective EL = 3	hysteroscopy	673 hysteroscopies in 665 patients	women; AUB – menorrhagia, post-menopausal bleeding, etc; average age 47 years Country: Belgium	Pathology identification; failure rate	Failure rate of 6% for hysteroscopies. 336 (50%) women had menorrhagia – 128 (19%) < 40 and 208 (31%) > 40. Normal cavity: Menorrhagia < 40 years = 79% (96); menorrhagia > 40 years = 68% (138). Whole population = 68% (431) Fibroids and polyps: menorrhagia < 40 – submucosal fibroids = 11% (13), endometrial polyps = 7% (9). Menorrhagia > 40 – submucosal fibroids = 21% (43), endometrial polyps = 20% (10). Whole population = 12% and 17%, respectively.	Funding source: Not stated Study summary: High level of pathology suggests need for hysteroscopies in AUB patients, except menorrhagia in < 30 year olds.
Gao 1987 ¹⁴⁹	epidemiological cohort EL = 3	Epidemiology of MBL and blood haematology – alkaline haematin methods	421	Women; 18 to 44 years; regular menstruation; normal pelvic examinations; no history of hormonal contraceptives. Country: China	MBL levels; haematology levels	MBL (ml): range 4.1 to 273.6 ml, mean 54.2 (SD 37). 5th and 95th percentiles = 14.2 and 124.1. 2SD range = 11.3 to 169. Haemoglobin (g/dl): range = 8.3 to 16.7, mean 13.2 (SD 1.1). 5th and 95th percentiles = 11.5, 14.9. 2SD = 11. to 15.4 Ferritin (ng/ml): range 1.2 to 180. Mean = 22.8 (SD 18.3). 5th to 95th percentile = 3.6 to 55.8. 2SD = 3.49 to 83.8. Results by MBL: MBL, % haemoglobin < 12 g/dl, % ferritin < 16 ng/ml, % with both. < 20 ml ($n = 48$) 0%, 16.7%, 0% 20 to 40 ($n = 1445$) 4.1%, 27.6%, 2.1% 40 to 60 ($n = 92$) 9.8%, 33.7%, 3.3% 60 to 80 ($n = 53$) 18.9%, 54.7%, 17% 80 to 100 ($n = 37$) 13.5%, 70.3%, 13.5% > 100 ($n = 46$) 30.4%, 82.6%, 26.1%.	Funding source: United Nations Fund for Population Activities Study summary: Study shows higher average MBL than with European and US populations
Hallberg 1966 ²⁵	Cross-sectional survey EL = 3	Menstrual patterns	748 approached – data available on 476. Women either refused or were	women; age stratified 15–50; menstruating Country: Sweden	MBL – alkaline haematin; blood tests	MBL (ml) by age: (mean, SD, 90th percentile) 15 = 33.8, 2.4, 65.1; 23 = 38.9, 3.7, 77.8; 30 = 49.7, 8.6; 40 = 44.5, 5.7, 87.1; 45 = 42.7, 4.5, 88.1; 50 = 62.4, 13.2, 133.1; All = 43.4, 2.3; 83.9. MBL (ml) by age of 'series B' – subjective assessment of 'normal', haemoglobin > 12 g/100 ml, plasma iron > 80 µg/100 ml, MCHC > 30%: (mean, SD) 15 = 32.9, 2.6; 23 = 38.8, 4.8; 30 = 29.7, 3.9; 40 = 29.8, 3.0; 45 = 31.7, 3.7; 50 = 52, 7.5; All = 33.2,	Funding source: Swedish Medical Council Study summary: MBL > 80 ml is seen as abnormal based on average MBL and change in blood counts.

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
			excluded.			1.6. All subjects: Haemoglobin concentration decrease ($P < 0.01$) at > 80 ml MBL. MHC decrease ($P < 0.01$) at > 80 ml. Iron concentration decrease ($P < 0.01$) at > 80 ml. Series B – 95th percentile = 76.4 ml	
Haynes 1979 ¹⁴⁴	cohort EL = 3	pattern of MBL	50 women	Women; MBL > 80 ml Country: UK	Description of MBL	Daily MBL ($n = 11$) – 70% by 2nd day and 92% by 3rd. Duration of menses and MBL: no association between duration and total MBL.	Funding source: Not stated Study summary: No association between length of menses or distribution of MBL and having menorrhagia. No gross ovarian pituitary pathology in majority of patients.
Janssen 1998 ²⁶	Epidemiological; Cohort EL = 3	measurement of MBL	313	Women; aged 18–50; no amenorrhea. Country: Netherlands	MBL – alkaline haematin; haemoglobin; anaemia; ferritin; subjective assessment of heavy bleeding	Haemoglobin significantly decreased ($P < 0.05$) at 60ML. Anaemia increased rapidly at 60 ml and then again at 120 ml. Ferritin decreased at 20 ml. Low ferritin at 40 ml. Anaemia levels with MBL: 1–20 = 1.5%, 21–40 = 5.9%, 41–60 = 5.3%, 61–80 = 10.3%, 81–100 = 18.8%, 101–120 = 16.7%, 121–160 = 37.5%, 161–240 = 50%, $> 240 = 93.8$	Funding source: Not stated Study summary: Risk of developing anaemia increases substantially at 120 ml, not 80 ml. Suggests that 80 ml definition of menorrhagia needs to be revised upwards.
Kadir 1998 ⁴⁹	Cohort; epidemiology EL = 3	testing for inherited blood disorders	208 assessed. 58 with PBAC < 100 excluded. 150 included	Women; PBAC score > 100 ; regular bleeding; known blood or endocrine disorders excluded; use of hormonal treatment within 2 months excluded; identified pathology excluded. Country: UK	MBL – PBAC; inherited blood disorder presence.	Of 150 – 123 had no inherited disorder, 20 had vWD, 6 had FXI deficiency. Menorrhagia since menarche in 11, 13 ($P = 0.001$), and 4 ($P < 0.001$) respectively.	Funding source: Not stated Study summary: Routine testing for inherited bleeding disorders suggested in women presenting with menorrhagia.
Looker 1997 ¹⁴⁷	Epidemiology EL = 3	Blood test – haemoglobin levels, serum iron levels; questionnaire – socio-economic-cultural variables	24894	Men and women; Part of National Health and Nutrition Survey; > 1 year of age Country: USA	Prevalence of iron deficiency by risk factors	Prevalence of iron deficiency and iron deficiency anaemia by age and sex: Females: 12–15 ($n = 786$) – 9%, 2% 16–19 ($n = 700$) – 11%, 3% 20–49 ($n = 4495$) – 11%, 5% 50–69 ($n = 2034$) – 5%, 2% > 70 ($n = 1630$) – 7%, 2% Males : 12–15 ($n = 691$) – 1%, $< 1\%$ 16–19 ($n = 658$) – $< 1\%$, $< 1\%$ 20–49 ($n = 4048$) – $< 1\%$, 1% 50–69 ($n = 1929$) – 2%, 1% > 70 ($n = 1437$) – 4%, 2% Univariate analysis showed racial minorities, poor, lower educated, and higher parity. Multivariate analysis showed racial group and parity were significant risk factors, but poverty and education did not.	Funding source: Not stated Study summary: Study shows a high prevalence of iron deficiency amongst women in USA. Reviewer comment: Large epidemiological study shows that anaemia is significant problem in USA, and this is likely to be higher in women with menorrhagia.
Rodeghiero 1987 ⁵⁰	epidemiology; cohort EL = 3	Test for von Willebrand factors and family history of bleeding orders	1218	children; both sexes; aged 11 to 14; one province Country: Italy	Prevalence of vWD	Of 1218 children, between 7 (0.57%) and 14 (1.15%) could be classified as having vWD. This was based of being below 90th% confidence interval of whole group. 8 of 14 were female 9 of 14 were in type O blood group.	Funding source: Health Department of Veneto Region Study summary: Prevalence of vWD in population may be higher than previously thought.

Table 5.1 Patient education – comparative studies

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Cheung 2003 ²⁴²	randomised EL = 1–	96 – 48 in cognitive group, 48 in information only group	Population characteristics: Women; scheduled for hysterectomy Groups comparable at baseline Country: China	Cognitive training – distraction and reappraisal; information booklet	N/A	Anxiety; pain scores; analgesic use; patient satisfaction	Anxiety, pain scores, and patient satisfaction all better in cognitive group ($P < 0.05$). No difference in analgesic use. Anxiety scores: cognitive = 60.17 (SD 6.56) vs 62.77 (SD 5.77), $P < 0.05$ Pain score (VAS): cognitive = 7.10 (SD 0.72) vs information = 7.35 (SD 0.56), $P < 0.05$ Patient satisfaction: cognitive = 47.38 (SD 3.89) vs information = 45.75 (SD 3.52), $P < 0.05$	Funding source: Not stated
Garrud 2001 ²⁴⁰	randomised EL = 1–	40 – 20 old leaflet, 20 risk information	Population characteristics: Women scheduled for laparoscopy; aged 23 to 41 Country: UK	Provision of risk information	N/A	Anxiety; knowledge; satisfaction	No difference between groups for anxiety, but significant difference for knowledge ($P = 0.002$) and satisfaction ($P < 0.001$)	Funding source: Not stated Study summary: Providing detailed information improves patient satisfaction
Kennedy 2003 ²³⁶	Randomised – block; concealed allocation; no blinding EL = 1+	1301 invited to join study, 407 refused randomisation, 894 were randomised. 298 to control, 296 to information, 300 to information with interview. 204, 206 and 215 available long-term, respectively	Population characteristics: Women; referred for non-urgent menorrhagia. Average age: control = 40.0, information = 40.0, interview = 41.0 Knowledge of available treatments (0 to 100): 68, 66, 65, respectively Menorrhagia severity score: 47, 47, 48, respectively Country: UK	control – no information; information – received information booklet; interview – received information booklet and had interview to elicit and discuss treatment preferences intervention vs intervention	24 months	QoL – SF-36, EQ-5D, patient satisfaction; patient preferences; patient knowledge	Baseline results: Patient preferences: Control ($n = 285$) – 130 stated a preference. 59 wanted hysterectomy, 6 wanted ablation, 2 wanted unspecified surgery, 13 wanted drug therapy, 7 wanted other treatment, 2 wanted no treatment. Information ($n = 285$) – 117 stated a preference. 49 wanted hysterectomy, 9 wanted ablation, 2 wanted unspecified surgery, 6 wanted drug therapy, 5 wanted other treatment, 2 wanted no treatment. Interview ($n = 292$) – 139 stated a preference. 46 wanted hysterectomy, 6 wanted ablation, 4 wanted unspecified surgery, 5 wanted drug therapy, 6 wanted other treatment, 1 wanted no treatment. Post-consultation preference: Control ($n = 235$) – 113 had a preference. 56 wanted hysterectomy, 2 wanted ablation, 1 wanted unspecified surgery, 8 wanted drug therapy, 7 wanted other treatment, 3 wanted no treatment. Information ($n = 240$) – 145 had a preference. 46 wanted hysterectomy, 12 wanted ablation, 2 wanted unspecified surgery, 23 wanted drug therapy, 10 wanted other treatment, 4 wanted no treatment. Trend for information group not to want treatments compared with control group. Interview ($n = 233$) – 160 had a preference. 50 wanted hysterectomy, 22 wanted ablation, 3 wanted unspecified surgery, 19 wanted drug therapy, 8 wanted other treatment, 5 wanted no treatment. Interview group were less likely to want hysterectomy (OR 95% CI 0.35 to 0.85) or drug therapy (OR 95% CI 0.24 to 0.82) than control group. Trend towards wanting ablation more than control group. Information (OR 95% CI 1.46 to 4.20) and interview (OR 95% CI 1.72	Funding source: HTA programme Study summary: Information provision and patient preference interview do not improve outcomes, but do improve patient satisfaction, knowledge and receiving preferred treatment.

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							<p>to 5.13) groups more likely to have treatment preference after consultation than control group.</p> <p>Trend towards those in information and interview groups to change preference.</p> <p>Knowledge and satisfaction:</p> <p>Trends towards those in information (OR 95% CI 1.08 to 1.84) and interview (OR 95% CI 0.97 to 2.00) groups having greater perceived knowledge. than control group.</p> <p>No difference between groups in terms of perceived involvement in treatment choice.</p> <p>Trend towards information (OR 95% CI 0.42 to 1.01) and interview (OR 95% CI 0.49 to 1.23) groups being less satisfied that their opinions important in decision-making, than the control group.</p> <p>Short-term follow-up:</p> <p>Quality of life outcomes:</p> <p>No difference between groups on SF-36 scores or EQ-5D scores or menorrhagia outcome scores</p> <p>Likelihood that treatment undergone matched stated preference:</p> <p>Trend towards information (OR 95% CI 1.20 to 2.97) and interviews (OR 95% CI 0.62 to 2.01) getting their preferred treatments compared with control group.</p> <p>Patient satisfaction:</p> <p>Trend towards those in information (OR 95% CI 1.04 to 1.86) and interviews (OR 95% CI 0.99 to 2.25) to feel more involved in treatment decision than control group.</p> <p>No difference between groups in satisfaction with treatment outcome.</p> <p>Long-term follow-up:</p> <p>Quality of life outcomes:</p> <p>No difference between groups on SF-36 scores or EQ-5D scores or menorrhagia outcome scores.</p> <p>Likelihood that treatment undergone matched stated preference:</p> <p>Trend towards information (OR 95% CI 0.99 to 2.28) and interviews (OR 95% CI 0.69 to 2.36) getting their preferred treatments compared with control group.</p> <p>Patient satisfaction:</p> <p>Trend towards those in information (OR 95% CI 0.91 to 1.69) and interviews (OR 95% CI 1.11 to 2.01) to feel more involved in treatment decision than control group.</p> <p>Those in interview group were more satisfied with their treatment than those in the control group (1.03 to 2.01). No difference between information and control groups.</p>	
O'Connor 2002 ²³⁵	Systematic review EL = 1+	11995 articles identified, 35 studies included.	Population characteristics: 1) searching electronic medical and social science databases; 2) scanning the tables of contents	Decision aids in healthcare	N/A	Decision regret; anxiety; persistence with choice; general health outcome; satisfaction with	<p>Among the trials comparing decision aids to usual care, decision aids performed better in terms of:</p> <p>a) greater knowledge 18.75 [13.14, 24.35]</p> <p>b) more realistic expectations (RR 1.4, 95%CI 1.1 to 1.9);</p>	Funding source: Canadian Institute of Health Research (formally MRC) CANADA

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			<p>in publications that have frequently reported decision aid studies (Health Expectations; Medical Decision Making; and Patient Education and Counselling) from the journal's inception date up to August 2002;</p> <p>3) searching personal files; and</p> <p>4) contacting known developers and evaluators through a shared decision making list-serve and e-mail contacts in May 2002.</p> <p>We searched the following electronic databases: MEDLINE (1966–August 2002); EMBASE (1980–April 2001); PsycINFO (1979–August 2002); CINAHL (1983–August 2002); Aidsline (1980–December 2000); CancerLit (1983–August 2002); and the Cochrane Controlled Trials Register (2002, Issue 3). As of 2001, MEDLINE is expanded to include unique citations from AIDSLINE, BIOETHICS, HealthSTAR, HISTLINE, POPLINE, and SPACELINE).</p>			<p>decision; disease specific symptom outcomes</p>	<p>c) lower decisional conflict related to feeling informed (WMD -9.1 of 100, 95%CI -12 to -6);</p> <p>d) increased proportion of patient that controlled decision making (RR 1.49 95% CI 0.99, 2.25);</p> <p>e) reduced practitioner controlled decision making (RR = 0.68 [0.53, 0.89]) and</p> <p>f) reduced proportion of people who remained undecided post intervention RR = 0.43 [0.27, 0.70].</p> <p>When simpler were compared with more detailed decision aids, the relative improvement was significant in:</p> <p>a) knowledge (WMD 4 out of 100, 95% CI 3 to 6);</p> <p>b) more realistic expectations (RR 1.5, 95% CI 1.3 to 1.7); and</p> <p>c) greater agreement between values and choice.</p> <p>Decision aids appeared to do no better than comparisons in affecting satisfaction with decision making, anxiety, and health outcomes. Decision aids had a variable effect on which healthcare options were selected.</p>	<p>Study summary: Trials indicate that decision aids improve knowledge and realistic expectations; enhance active participation in decision making; lower decisional conflict; decrease the proportion of people remaining undecided, and improve agreement between values and choice. The effects on persistence with chosen therapies and cost-effectiveness require further evaluation. Finally, optimal strategies for dissemination need to be explored.</p>
Redman 1986 ⁵⁷²	prospective; cohort EL = 2-	43 – 19 in information group, 24 in control group	<p>Population characteristics: Women; schedule for abdominal hysterectomy.</p> <p>Country: UK</p>	Information booklet about hysterectomy	N/A	<p>Patient satisfaction with operation; patient satisfaction with communication; patient knowledge of hysterectomy</p>	<p>Patient satisfaction: no difference between groups</p> <p>Satisfaction with communication: $P < 0.01$ in favour of information group.</p> <p>Knowledge of hysterectomy: $P < 0.01$ in favour of information group.</p>	Funding source: Not stated
Ridgeway 1982 ²⁴¹	randomised EL = 1-	60 – 20 to information, 20 to cognitive help, 20 to control. Plus 10 who had no information.	<p>Population characteristics: Women; scheduled for abdominal hysterectomy</p> <p>Country: UK</p>	Cognitive assessment – reassurance and positive attitude; information booklet	4 post-operation interviews	<p>Pre-operative symptoms; post-operative symptoms</p>	<p>Pre-operative symptoms: Cognitive group had less worries, but less knowledge than information group. Both groups had less anxiety, less worries and better knowledge than control group.</p> <p>Post-operative results: Cognitive group had fewer symptoms, and fewer days of pain than information group, same total activities.</p>	Funding source: Not stated
Vuorma 2003 ²³⁷	randomised EL = 1-	569 – 206 in pre-treatment cohort (178 at 12 months), 184 (156 at 12 months) in randomised	<p>Population characteristics: Women; subjective menorrhagia.</p> <p>Groups were comparable at baseline.</p> <p>Country: Finland</p>	Information booklet; no information	12 months	<p>Treatment preference; treatment received.</p>	<p>Treatment preference at baseline: Information group ($n = 184$): 49% wanted hysterectomy, 32 wanted conservative treatment, 19% had no clear preference.</p> <p>Control group ($n = 179$): 45% wanted hysterectomy, 37% wanted conservative medical treatment, 18% had no clear preference.</p> <p>Treatment plan at 3 months:</p>	<p>Funding source: Not stated</p> <p>Study summary: More women had clear preference after being given information.</p>

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
		information, 179 (159 at 12 months) in control group					<p>Intervention group ($n = 184$): 54% hysterectomy, 21% minor surgery or LNG, 2% change in birth control, 18% oral medication, 4% no decision, 1% no clinic visit.</p> <p>Control group ($n = 179$): 49% hysterectomy, 29% minor surgery or LNG, 2% change in birth control, 8% oral medication, 11% no decision, 2% no clinic visit.</p> <p>Significantly less minor surgery, more oral medication, and fewer undecided in information group ($P < 0.05$)</p> <p>No difference between information and control groups for knowledge, satisfaction with clinic or anxiety.</p>	
Vuorma 2004 ²³⁸	randomised; concealed; blinding not possible EL = 1–	1880 approached, 962 willing to participate, 569 eligible – 206 to pre-trial group, 184 to intervention group, 179 to control group	<p>Population characteristics: Women; aged 35 to 54 years; referred due to menorrhagia or fibroids.</p> <p>Average age = 44.4, 47% sterilised, 63% had heavy flow, 24% had irregular periods, 46% had pelvic pain.</p> <p>Country: Finland</p>	Decision aid booklet (about menorrhagia and treatments); no treatment	12 months	<p>SF-36; VAS perceived health, anxiety and psychosomatic symptoms; menstrual symptoms, Sexuality; satisfaction with treatment.</p>	<p>Differences between groups on SF-36 scores, VAS perceived health, anxiety and psychosomatic symptoms; menstrual symptoms, Sexuality; satisfaction with treatment.</p> <p>No statistical difference between intervention and control group, except for emotional role ($P = 0.01$), where intervention group improved more.</p> <p>Both groups significantly improved from baseline for all outcomes, except sexuality scores.</p> <p>No statistically significant differences between groups in terms of health service use or cost.</p>	<p>Funding source:</p> <p>Study summary: Study shows that patient information booklet had not impact on treatment outcome.</p>

Table 5.2 Patient education – non-comparative studies

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Augustus 2002 ²²⁷	Qualitative; interviews EL = 3	Patient beliefs about hysterectomy	30	women; African-American; had undergone hysterectomy Average age = 49 years 60% had up to high school education 60% of women were single Country: USA	Patient beliefs about hysterectomy	64.3% of women did not get a second opinion prior to surgery. 96.7% of women would recommend operation to friends Main themes relating to hysterectomy were: Myths, fears and sexual symbolism related to hysterectomy – fear for sexual identity and relationship with partners Freedom from pain and embarrassment – women no longer had to plan lives around vaginal bleeding Improved sexuality and self-esteem – women surprised and relieved after surgery than sexuality was unchanged or improved.	Funding source: Not stated
Groff 2000 ²³¹	Qualitative; focus groups EL = 3	Women's views on hysterectomy	148	Women; aged 30 to 65; had not had hysterectomy; four groups of women – African-American, Hispanic, non-Hispanic white and lesbian. Country: USA	Themes related to hysterectomy	Three main themes: Outcome of hysterectomy; decision to have hysterectomy; opinions of healthcare providers. Outcomes of hysterectomy: Women identified benefit of symptoms relief. Women also want minimally invasive surgery, and quick recovery in order to return to work and family duties. Women concerned about side effects of surgery, both physical and mental. Decision to have surgery – women consulted friends and family about decision. Using others experience as a guide. Women wanted clear rationale for having surgery from health professionals. Women also concerned about loss of sexuality and male response to hysterectomy. Opinions on healthcare – women felt health professional only interested in financial gain. Women wanted female doctors as thought they were less likely to suggest hysterectomy. There were differences between sub-groups about above theme.	Funding source: Not stated
O'Connor 2002 ²³³	Decision support strategy EL = 4	Decision support system		Country: Canada	Decision support factors	Assess needs of woman: Perceptions of decision – knowledge, expectations, values, decisional conflicts, stage of decision making, predisposition towards options. Perceptions of others – perceptions of others, support, pressures, roles in decision making Resources to make decision – personal (skills, motivation, self-confidence, previous experience), external support networks. Demographic characteristics: client, practitioner. Provide decision support: provide information – health situation, options, outcomes, other opinions and choices. Re-align expectations of outcomes Clarify personal values for outcomes Provide guidance and coaching – steps in decision making, communicating with others, handling pressure, accessing support and resources. Evaluate: Decision making – reduce decisional conflict, improved knowledge, realistic expectations, clear values, agreement between values and choice, implementation of chosen option, self-confidence and satisfaction with decision making Outcomes of decision: Persistence with others, improved quality of life, reduced distress, reduced regret, informed use of resources.	Funding source: Not stated

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Scriven 1997 ²²⁶	Survey EL = 3	Written information provision		Hospitals in England ask to send written information that they give to patient relating to hysterectomy Country: UK	Quality of information provision	Written information produced by a variety of health professionals. 33% produced based on existing literature. 37% give information prior to admission, 36% on admission, 11 post-op, 16% no policy Most leaflets mention activities of daily living, but often imply health professional control over resumption of these activities. Variation in highlighting the main side effects of hysterectomy. Suggest strategy: 1. professional design and layout 2. get patient to help with piloting 3. realistic advice on potential side effects 4. evaluation of information 5. co-ordinated dissemination of information 6. Authors should critically assess their work 7. Information should empower patient 8. Information about why advice is important should be given – why lifting can be harmful.	Funding source: Not stated
Skea 2004 ²³²	Survey EL = 3	Patient views on information provision	104	Women; undergone hysterectomy for benign conditions. Country: UK	Patient opinions on information provision	Five factors relating to information provision examined: Advantages of hysterectomy Possible risks and side effects of hysterectomy Treatments other than hysterectomy Advantages of treatments other than hysterectomy Disadvantages of treatments other than hysterectomy. Patients felt not enough information about risks and disadvantages of surgery. Women sought information in addition to that provided for a number of reasons: About what hysterectomy involves What effect hysterectomy has on menstrual system Other effects of hysterectomy What other treatment options would involve What effect other treatments would have on period problems What may need to take after hysterectomy Reasons for finding additional information were: Help discuss and make decision Prepare for hysterectomy Discuss and understand other treatments Check right decision had been made Just wanted to know When asked questions about if doctor had been supportive during decision making between 15% to 30% were neutral or dissatisfied. When asked various questions about if hysterectomy was the right decision about 10% of women were neutral or disagreed.	Funding source: Not stated
Uskul 2003 ²²⁸	qualitative; interviews EL = 3	Women's experience of hysterectomy	29	Women; scheduled for hysterectomy Country: Canada	Factors important to women in relation to hysterectomy	Most women delayed seeking formal medical help for as long as possible, often using complementary therapy Women often tried to get information about condition as early as possible from various sources. Women received a lot of information about hysterectomy from health professional but little information on alternatives. A number of social and psychological factors account for women accepting hysterectomy. Women had hysterectomy on advice of gynaecologist, but often told to think about impact and wait to	Funding source: Not stated

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
						<p>have operation if social or psychological issues with operation.</p> <p>Women often still in decision-making process after they agreed to surgery.</p> <p>Women told to talk to family and friends about procedure before making decision.</p>	
Vuorma 2003 ²³⁹	Comparative; cohort EL = 3	Correlates with treatment choice	474 – 185 had hysterectomy, 113 had conservative treatment, 69 had no treatment, 107 unclear what treatment received	Women; aged 35 to 54; referred for HMB Country: Finland	Logistic regression correlates with treatment choice	<p>Items correlated with choosing hysterectomy over conservative treatment:</p> <p>Age, OR = 95% CI 1.00 to 1.16</p> <p>Wish for further pregnancies, 95% CI OR = 0.09 to 0.60</p> <p>Menstrual pain, OR = 95% CI 1.02 to 1.21</p> <p>Irregular periods, OR = 95% CI 1.07 to 3.96</p> <p>Education less than 12 years, OR = 95% CI 1.47 to 4.62</p> <p>Unemployed, OR = 95% CI 1.10 to 11.7</p> <p>Number of visits to gynaecologist for HMB, OR = 95% CI 1.21 to 2.47</p> <p>Factors, such as inconvenience caused by HMB were not significant.</p>	Funding source: Not stated
Wade 2000 ²³⁰	Case series; survey EL = 3	Patient opinions about hysterectomy	102	Women; undergone hysterectomy within past 2 years. Average age = 34.1 Average time since hysterectomy = 12.1 months 80.1% had hysterectomy and oophorectomy. Country: USA	Themes related to hysterectomy experience	<p>Seven major themes were identified:</p> <p>Positive aspects – 61 of 102 outlined positive aspects of hysterectomy, including relief from symptoms, accurate information, supportive physician, involvement in decision making.</p> <p>HRT – fears and concerns about using HRT based on lack of information.</p> <p>Insufficient information – 38 of 102 thought insufficient information had been given about hysterectomy and physical impact.</p> <p>Sexual concerns – 28 of 102 were concerned about changes caused by hysterectomy and lack of information about this.</p> <p>Structure of emotional support – 20 of 102 outlined need for systems to provide emotional and information support for women.</p> <p>Psychological sequelae – 17 of 102 talked about psychological distress caused by hysterectomy, including mood swings etc.</p> <p>Feelings of loss – 5 of 102 wrote about loss of femininity caused by hysterectomy, and the feeling of grief this caused.</p>	Funding source: Not stated
Webb 1986 ²²⁹	Qualitative interviews EL = 3	Experience of hysterectomy	50	women; scheduled for hysterectomy Country: UK	Patient experience factors	<p>Lack of information provision about nature and implications of hysterectomy.</p> <p>Most women were afraid of having major surgery.</p> <p>Women highlighted need for support networks.</p> <p>Most women had only general expectations about surgery</p> <p>Lack of information during recovery period.</p> <p>Women had a deficit between expected support and help, and what they actually received.</p>	Funding source: not stated
Williams 2000 ²³⁴	Cohort EL = 3	Experience of hysterectomy	38	Women; aged 30 to 76; hysterectomy within past 3 years for benign condition. Country: USA	Themes related to hysterectomy	<p>Three main themes: decision making about hysterectomy; outcome of hysterectomy; perceptions of male response.</p> <p>Decision making: had biophysical – pain and bleeding. Most women had had symptoms for a number of years and used variety of treatments to help symptoms and avoid surgery. Psychological – mood swing, depression. After years of symptoms women want relief, but fear about deciding to have operation and not having operation (fear of developing cancer)</p> <p>Sociological factors – advice from friends, family and health professionals. Advice on alternatives to hysterectomy.</p> <p>Spiritual domain – women used prayer and meditation to help them make a decision.</p>	Funding source: not stated

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
						<p>Outcome factors – range of responses depending on symptoms were relieved or not, but also about loss of fertility, loss of sexuality, and having to use HRT.</p> <p>Male response to hysterectomy – sub-set of women were concerned about male reaction to hysterectomy.</p>	
Wade 2000 ²³⁰	Case series; survey EL = 3	Patient opinions about hysterectomy	102	<p>Women; undergone hysterectomy within past 2 years.</p> <p>Average age = 34.1</p> <p>Average time since hysterectomy = 12.1 months</p> <p>80.1% had hysterectomy and oophorectomy.</p> <p>Country: USA</p>	Themes related to hysterectomy experience	<p>Seven major themes were identified:</p> <p>Positive aspects – 61 of 102 outlined positive aspects of hysterectomy, including relief from symptoms, accurate information, supportive physician, involvement in decision making.</p> <p>HRT – fears and concerns about using HRT based on lack of information.</p> <p>Insufficient information – 38 of 102 thought insufficient information had been given about hysterectomy and physical impact.</p> <p>Sexual concerns – 28 of 102 were concerned about changes caused by hysterectomy and lack of information about this.</p> <p>Structure of emotional support – 20 of 102 outlined need for systems to provide emotional and information support for women.</p> <p>Psychological sequelae – 17 of 102 talked about psychological distress caused by hysterectomy, including mood swings etc.</p> <p>Feelings of loss – 5 of 102 wrote about loss of femininity caused by hysterectomy, and the feeling of grief this caused.</p>	Funding source: Not stated

Table 5.3 Patient choice – comparative studies

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Longo 2006 ²⁵¹	Randomised at practice level EL = 1+	2585 approached, 1135 recruited, 1082 invited for consultation, 747 attended, 584 completed questionnaire	Population characteristics: People with menorrhagia, atrial fibrillation, menopausal symptoms, prostatism. Country: UK	Shared decision making; risk communication		Factors associate with ease of choice		Funding source: Not stated Study summary: Shared treatment decisions were valued less than some other attributes of a consultation. However, patient utilities for such involvement appeared responsive to changes in experiences of consultations. This suggests that SDM may gain greater value among patients once they have experienced it.
Cooper 1999 ²⁴³	Randomised; concealed EL = 1++	272 eligible, 187 recruited, 94 randomised to medical treatment, 93 to TCRE. By 2 years 86 medical and 87 TCRE patients remained in the study.	Population characteristics: Women; referred due to HMB; completed family; < 10 weeks size uterus; normal uterine pathology; referred for surgery. Baseline characteristics (medical vs TCRE): Age = 41.4 vs 41.9 Haemoglobin (g/dl) = 12.79 vs 12.61 Menstrual symptom rating: mild/moderate = 6 vs 4 Severe = 54 vs 52 Very severe = 26 vs 32 Bleeding score = 24.7 vs 24.8 Country: UK	Medical treatment; TCRE	2 years	QoL (SF-36); patient satisfaction; menstrual status; bleeding score	Outcomes for medical vs TCRE. QoL (SF-36): Baseline: Physical functioning = 78.67 vs 82.33 Social functioning = 68.35 vs 70.03 Role: physical = 53.01 vs 56.98 Role: emotional = 57.43 vs 55.03 Mental health = 58.20 vs 59.43 Energy/fatigue = 40.36 vs 41.49 Pain = 53.55 vs 58.14 General health = 68.17 vs 65.90 Change by 2 years: Physical functioning = 3.73 vs 5.00 Social functioning = 3.94 vs 10.59 Role: physical = 12.95 vs 18.60 Role: emotional = 11.25 vs 22.48 Mental health = 7.17 vs 9.98 Energy/fatigue = 10.06 vs 14.58 Pain = 11.38 vs 12.34 General health = -0.67 vs 1.69 No significant difference between groups. Patient satisfaction: Totally or generally satisfied with treatment = 48 (57%) vs 68 (79%), $P = 0.002$ Cure or acceptable improvement = 53 (61%) vs 69 (81%), $P = 0.017$ Treatment acceptable = 65 (77%) vs 79 (93%), $P = 0.004$ Menstrual status: No bleeding or light = 36 (42%) vs 50 (58%), $P = 0.04$ Unchanged or heavier = 16 (18%) vs 5 (6%), $P = 0.02$ Bleeding score = 6.8 (SD 9.9) vs 5.4 (SD 8.1)	Funding source: Scottish Office Department of Health Study summary: The results at 2 years consolidate the findings and conclusions based on the four-month follow up data. A policy of early TCRE is effective and safe and does not result in an increase in hysterectomies. It should not be routinely withheld in an effort to try alternative medical therapies. Reviewer comments: LNG-IUS not available as a medical treatment.

Table 5.4 Patient choice – non-comparative studies

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Augustus 2002 ²²⁷	Qualitative; interviews EL = 3	Patient beliefs about hysterectomy	30	women; African-American; had undergone hysterectomy Average age = 49 years 60% had up to high school education 60% of women were single Country: USA	Patient beliefs about hysterectomy	64.3% of women did not get a second opinion prior to surgery. 96.7% of women would recommend operation to friends Main themes relating to hysterectomy were: myths, fears and sexual symbolism related to hysterectomy – fear for sexual identity and relationship with partners Freedom from pain and embarrassment – women no longer had to plan lives around vaginal bleeding improved sexuality and self-esteem – women surprised and relieved after surgery than sexuality was unchanged or improved.	Funding source: Not stated
Bourdrez 2004 ²⁴⁴	Prospective; cohort EL = 3	Patient preferences for treatments	96	Women; DUB; scheduled for either hysterectomy, endometrial ablation and LNG-IUS. No statistical difference between groups for age or symptoms. Country: Netherlands	Importance of symptoms; reasons for treatment choice; patient preference to avoid hysterectomy	HMB was most serious symptom for 74% of IUD group, 77% of ablation group and 84% of hysterectomy group. Main reasons to choose treatment: IUD – Short or no admittance, fast recovery, no general anaesthetics, no hysterectomy, no oral contraceptive. Ablation – No IUD, No hysterectomy, No oral contraceptive, Advice from gynaecologist, Short or no admittance Hysterectomy – no complaints anymore, no oral contraceptive, No IUD, Advice of gynaecologist. Patient preference: 70% of women undergoing ablation preferred this to hysterectomy when success rate was presumed to be 50%. 95% of LNG-IUS patients preferred this to hysterectomy when success was presumed to be 50%	Funding source: Not stated Study summary: Study shows that the majority of women are willing to take a 50:50 chance of treatment success to avoid hysterectomy.
Coulter 1994 ²⁴⁶	Survey EL = 3	Correlation between socio-demographic factors and patient preferences for treatment	129 GPs and 483 women (425 returned questionnaire).	Women; consulting due to menstrual disorders. Country: UK		Patient had preference: Age at completion of full time-education: < 16 OR = 1, 17–18 OR = 1.02, > 19 OR = 3.35 (1.95 to 5.76) Previous consultation for menstrual problems: none OR = 1.00, 1> OR = 2.22 (1.38 to 3.60) Specialist gynaecological consultation within 1 year: none = 1.00, 1> = 1.94 (1.06 to 3.53) Preference for surgery: symptoms mild or moderate = 1.00, sever OR = 2.59 (1.21 to 5.76) GPs aware of patient preference in 34.4% Factors associated with referral for surgery ($P < 0.05$) were: GPs prediction of treatment, patient's preference, what GP thought patient wanted, previous surgery, age of patient, and sex of GP.	Funding source: Not stated Study summary: Study shows a mismatch between patient preferences and the management they receive.
Entwistle 2001 ²⁴⁸	Qualitative; interviews EL = 3	Women's decision making about hysterectomy	37	Women; scheduled for hysterectomy Country: UK	Factors that influence patient decision making	Women can be either passive, collaborative or active in decision making about hysterectomy, so difficult to provide single strategy to help women.	Funding source: Not stated
Entwistle, 2006 ²⁵²	Survey and interviews EL = 3	Patient experience of involvement in decision making	157 questionnaires, 20 interviews	Women; scheduled for hysterectomy for menstrual problems Country: UK	Recollection of information provision; recollection of involvement in decision making	Information provision about hysterectomy: Different kinds of hysterectomy = 68% Advantages of different types of hysterectomy = 40% Disadvantages of different types of hysterectomy = 32% Types of hysterectomy being undertaken = 75% Advantages of removing cervix = 28% Disadvantages of removing cervix = 24% Whether cervix is being removed = 46% Too little information provided: Different kinds of hysterectomy = 26%	Funding source: Not stated

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
						<p>Advantages of different types of hysterectomy = 36%</p> <p>Disadvantages of different types of hysterectomy = 44%</p> <p>Types of hysterectomy being undertaken = 26%</p> <p>Advantages of removing cervix = 60%</p> <p>Disadvantages of removing cervix = 65%</p> <p>Whether cervix is being removed = 41%</p> <p>Interviews:</p> <p>Most women reported having little input into decision about type of hysterectomy undertaken.</p>	
Fry 2001 ²⁵³	Survey EL = 3	Factors influencing decision to have oophorectomy	58 – 30 having oophorectomy, 28 ovarian screening	women Country: UK	Factors related to oophorectomy	<p>Frequency of item being rated high or extremely important:</p> <p>Reducing risk of ovarian cancer, reducing cancer worry, Age, worries about effectiveness of screening, partner's attitude, loss of periods. All at $P < 0.05$</p> <p>No difference for other factors – need for HRT, risks of surgery, recovery time, desire for children, etc.</p>	Funding source: Not stated
Groff 2000 ²³¹	Qualitative; focus groups EL = 3	Women's views on hysterectomy	148	Women; aged 30 to 65; had not had hysterectomy; four groups of women – African-American, Hispanic, non-Hispanic white and lesbian. Country: USA	Themes related to hysterectomy	<p>Three main themes: Outcome of hysterectomy; decision to have hysterectomy; opinions of healthcare providers.</p> <p>Outcomes of hysterectomy: Women identified benefit of symptoms relief. Women also want minimally invasive surgery, and quick recovery in order to return to work and family duties. Women concerned about side effects of surgery, both physical and mental.</p> <p>Decision to have surgery – women consulted friends and family about decision. Using others experience as a guide. Women wanted clear rationale for having surgery from health professionals.</p> <p>Women also concerned about loss of sexuality and male response to hysterectomy.</p> <p>Opinions on healthcare – women felt health professional only interested in financial gain. Women wanted female doctors as thought they were less likely to suggest hysterectomy.</p> <p>There were differences between sub-groups about above theme.</p>	Funding source: Not stated
Leung 2005 ²⁵⁴	Survey EL = 3	Patient preferences	324 questionnaires, 200 returned	Women; menorrhagia; Chinese Country: Hong Kong	Patient preferences and knowledge	<p>Of respondents:</p> <p>70.5% knew of drug therapies, 7.5% of LNG-IUS, 4.5% of ablation, 28% of hysterectomy.</p> <p>6% wanted amenorrhoea, 7.5% wanted oligomenorrhoea, 86.5% wanted eumenorrhoea.</p> <p>87% wanted drug treatment as first line treatment, 3% LNG-IUS, 3% ablation, 7% no treatment.</p> <p>45% wanted LNG-IUS if drug treatment failed, 16% ablation, 4.5% hysterectomy, 34.5% no treatment</p> <p>Main reason for not choosing a treatment was not knowing about it.</p>	Funding source: Not stated
Lindberg 2001 ²⁴⁹	Qualitative; interviews EL = 3	Patient decision-making process	10	Women; pre-menopausal prior to hysterectomy Country: USA	Decision-making process	<p>Women go through four phases in decision making:</p> <p>Seeking solutions – finding information on symptoms that occur via friends and family, health professionals etc.</p> <p>Hold on – changing lifestyle in order to cope with symptoms</p> <p>These factors act in a circular iterative process.</p> <p>Changing course – single event usually triggers women to seek solution to problem. This may result in rapid decision to have surgery.</p> <p>Taking charge – is period when women organises and prepares for hysterectomy.</p>	<p>Funding source: Not stated</p> <p>Study summary: Understanding of decision-making process can help health professionals aide patients.</p>
Marsh 2002 ²⁵⁵	Cross-sectional survey EL = 3	Outpatient hysteroscopy; day-case hysteroscopy	250 questionnaires sent, 189 questionnaires completed	Women; referred for hysteroscopic investigation. Country: UK	Patient preference	<p>52% wanted outpatient procedure, 26% wanted day-case, 17% wanted doctor to decide and 5% wanted further information.</p> <p>Reasons for preferring day case:</p> <p>No pain during procedure</p> <p>Likely not to need for repeat procedure</p> <p>Do not want to see procedure happening</p> <p>Reasons for not preferring day case:</p> <p>Fasting</p>	Funding source: Not stated

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
						Pre-assessment clinic visit needed Waiting for procedure in hospital Reasons for preferring outpatient: Quick process Able to see what is happening Able to see inside womb Reasons for not preferring outpatient: Procedure could be uncomfortable Procedure may have to be repeated Sitting in examination chair for 10 to 15 minutes	
Nevadunsky 2001 ²⁴⁷	Survey EL = 3	Patient reasons for wanting surgery	84	Women; referred for UAE; uterine fibroids Country: USA	sources of information; symptoms; impact of fibroids; reason for wanting surgery	Sources of information: Internet = 67%. Primary information source: literature = 40%, physician = 25%, television = 15%, internet = 13%, friend = 5%, other = 1% Knowledge of fibroids: well informed = 94% Knowledge of treatment options = 98% Symptoms related to fibroids: Bleeding = 73% Reason for wanting UAE: Avoid fibroid symptoms = 95% Avoid adverse events of other treatments = 90% Avoid prolonged recovery = 83% Avoid surgery = 78% Maintain self-image = 58% Maintain sexual image = 58% Uterus is source of femininity = 47% Maintain fertility = 30% Family advice = 29% Other medical condition = 28% Want children = 20% Religious beliefs = 15%	Funding source: not stated
O'Connor 2002 ²³³	Decision support strategy EL = 4	Decision support system		Country: Canada	Decision support factors	Assess needs of woman: Perceptions of decision – knowledge, expectations, values, decisional conflicts, stage of decision making, predisposition towards options. Perceptions of others – perceptions of others, support, pressures, roles in decision making Resources to make decision – personal (skills, motivation, self-confidence, previous experience), external support networks. Demographic characteristics: client, practitioner. Provide decision support: provide information – health situation, options, outcomes, other opinions and choices. Re-align expectations of outcomes Clarify personal values for outcomes Provide guidance and coaching – steps in decision making, communicating with others, handling pressure, accessing support and resources. Evaluate: Decision making – reduce decisional conflict, improved knowledge, realistic expectations, clear values, agreement between values and choice, implementation of chosen option, self-confidence and	Funding source: Not stated

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
						<p>satisfaction with decision making</p> <p>Outcomes of decision:</p> <p>Persistence with others, improved quality of life, reduced distress, reduced regret, informed use of resources.</p>	
Sculpher 1998 ²⁴⁵	Cohort EL = 3	Patient preferences for surgery	221	<p>Women; referred to specialist care with menorrhagia.</p> <p>Average age: 40.94</p> <p>Duration of menorrhagia = 18 months</p> <p>Country: UK</p>	Importance scores for patient outcomes	<p>Mean importance scores:</p> <p>Stops periods for good = 1.18</p> <p>Not removing womb = 0.71</p> <p>Back to usual activities as soon as possible = 1.07</p> <p>Removing womb = 0.47</p> <p>Least pain and discomfort = 0.68</p> <p>Hospital stay as short as possible = 0.59</p> <p>Reduce periods = 0.42</p> <p>Resume sex life as soon as possible = 0.59</p> <p>No worry about contraception = 0.14</p> <p>Not leaving scar = 0.14</p> <p>Patient preferences based on descriptions of surgery:</p> <p>abdominal hysterectomy = 43%</p> <p>endometrial resection = 41%</p> <p>Neither = 4%</p> <p>Unable to choose = 11%</p>	<p>Funding source: Not stated</p> <p>Study summary: Many women referred for surgery for menorrhagia have conflicting objectives from treatment.</p>
Uskul 2003 ²²⁸	qualitative; interviews EL = 3	Women's experience of hysterectomy	29	<p>Women; scheduled for hysterectomy</p> <p>Country: Canada</p>	Factors important to women in relation to hysterectomy	<p>Most women delayed seeking formal medical help for as long as possible, often using complementary therapy</p> <p>Women often tried to get information about condition as early as possible from various sources.</p> <p>Women received a lot of information about hysterectomy from health professional but little information on alternatives.</p> <p>A number of social and psychological factors account for women accepting hysterectomy.</p> <p>Women had hysterectomy on advise of gynaecologist, but often told to think about impact and wait to have operation if social or psychological issues with operation.</p> <p>Women often still in decision-making process after they agreed to surgery.</p> <p>Women told to talk to family and friends about procedure before making decision.</p>	Funding source: Not stated
Vuorma 2003 ²³⁹	Comparative; cohort EL = 3	Correlates with treatment choice	474 – 185 had hysterectomy, 113 had conservative treatment, 69 had no treatment, 107 unclear what treatment received	<p>Women; aged 35 to 54; referred for HMB</p> <p>Country: Finland</p>	Logistic regression correlates with treatment choice	<p>Items correlated with choosing hysterectomy over conservative treatment:</p> <p>Age, OR = 95% CI 1.00 to 1.16</p> <p>Wish for further pregnancies, 95% CI OR = 0.09 to 0.60</p> <p>Menstrual pain, OR = 95% CI 1.02 to 1.21</p> <p>Irregular periods, OR = 95% CI 1.07 to 3.96</p> <p>Education less than 12 years, OR = 95% CI 1.47 to 4.62</p> <p>Unemployed, OR = 95% CI 1.10 to 11.7</p> <p>Number of visits to gynaecologist for HMB, OR = 95% CI 1.21 to 2.47</p> <p>Factors, such as inconvenience caused by HMB were not significant.</p>	Funding source: Not stated
Wade 2000 ²³⁰	Case series; survey EL = 3	Patient opinions about hysterectomy	102	<p>Women; undergone hysterectomy within past 2 years.</p> <p>Average age = 34.1</p> <p>Average time since hysterectomy = 12.1 months</p>	Themes related to hysterectomy experience	<p>Seven major themes were identified:</p> <p>Positive aspects – 61 of 102 outlined positive aspects of hysterectomy, including relief from symptoms, accurate information, supportive physician, involvement in decision making.</p> <p>HRT – fears and concerns about using HRT based on lack of information.</p> <p>Insufficient information – 38 of 102 thought insufficient information had been given about hysterectomy and physical impact.</p>	Funding source: Not stated

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
				80.1% had hysterectomy and oophorectomy. Country: USA		Sexual concerns – 28 of 102 were concerned about changes caused by hysterectomy and lack of information about this. Structure of emotional support – 20 of 102 outlined need for systems to provide emotional and information support for women. Psychological sequelae – 17 of 102 talked about psychological distress caused by hysterectomy, including mood swings etc. Feelings of loss – 5 of 102 wrote about loss of femininity caused by hysterectomy, and the feeling of grief this caused.	
Webb 1986 ²²⁹	Qualitative interviews EL = 3	Experience of hysterectomy	50	women; scheduled for hysterectomy Country: UK	Patient experience factors	Lack of information provision about nature and implications of hysterectomy. Most women were afraid of having major surgery. Women highlighted need for support networks. Most women had only general expectations about surgery Lack of information during recovery period. Women had a deficit between expected support and help, and what they actually received.	Funding source: not stated
Williams 2000 ²³⁴	Cohort EL = 3	Experience of hysterectomy	38	Women; aged 30 to 76; hysterectomy within past 3 years for benign condition. Country: USA	Themes related to hysterectomy	Three main themes: decision making about hysterectomy; outcome of hysterectomy; perceptions of male response. Decision making: had biophysical – pain and bleeding. Most women had had symptoms for a number of years and used variety of treatments to help symptoms and avoid surgery. Psychological – mood swing, depression. After years of symptoms women want relief, but fear about deciding to have operation and not having operation (fear of developing cancer) Sociological factors – advice from friends, family and health professionals. Advice on alternatives to hysterectomy. Spiritual domain – women used prayer and meditation to help them make a decision. Outcome factors – range of responses depending on symptoms were relieved or not, but also about loss of fertility, loss of sexuality, and having to use HRT. Male response to hysterectomy – sub-set of women were concerned about male reaction to hysterectomy.	Funding source: not stated
Wu 2005 ²⁵⁰	Decision-tree EL = 4	Decision aide for hysterectomy	32 women in 2 phases	Women; pre-menopausal; fibroids Country: Taiwan	Decision tree	13 factors identified and combined in decision tree: Is condition immediately fatal? Immediate relief from physical symptoms? Overcome 'fear' of benign tumour becoming malignant? Fear negative outcome of operation? Worry about consequences of operation? Disadvantages of hysterectomy outweigh advantages? Hysterectomy is only choice? Overcome psychological obstacles to having operation? Sufficient faith in surgery? Willing to undergo myomectomy? Willing to use medical treatment only? Willing to wait until menopause to improve fibroids Tried non-medical methods to reduce fibroid?	Funding source: not stated

Table 8.1 LNG-IUS for treatment of HMB – comparative studies

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Barrington 2003 ²⁶⁰	randomised EL = 1+	50: 25 LNG-IUS; 25 Thermal balloon ablation. 2 LNG-IUS discontinued, 2 were lost to follow-up. 2 TBA lost to follow-up.	Population characteristics: women; menorrhagia; no pathology; cervical cavity > 12 cm Country: UK	LNG-IUS; thermal balloon ablation treatment vs baseline	6 months	MBL – PBAC	MBL (mean): IUS pre-treatment = 107 ml vs 31 ml post-insertion (~71%); Ablation pre-treatment = 122 ml vs 61 ml post-surgery (~50%). No difference between groups ($P = 0.689$). MBL (median): IUS pre-treatment = 75 ml vs 19 ml post-insertion; Ablation pre-treatment = 101 ml vs 27 ml post-surgery.	Funding source: not stated Study summary: Study shows LNG-IUS and thermal ablation are equivalent.
Busfield 2006 ²⁶¹	randomised; non-blinded; concealed EL = 1+	177 screened, 83 randomised, 42 to LNG-IUS, 41 to TBA. 37 in LNG-IUS and 31 in TBA completed 24 months follow-up	Population characteristics: Women; subjective HMB; aged 25 to 50; regular cycles. Excluded if – ultrasound abnormalities (including intramural fibroids > 3 cm in diameter), laboratory abnormalities, hysteroscopic abnormalities (endometrial polyps), irregular bleeding, chronic pelvic pain, severe dysmenorrhoea, medical contraindications to procedures, untreated abnormal cervical cytology. Baseline characteristics (LNG-IUS vs TBA): Age < 40 = 7 vs 13 Age 40 to 44 = 21 vs 16 Age 45 to 49 = 14 vs 12 BMI = 28.8 vs 29.7 Nulliparous = 1 vs 0 PBAC score = 490 (SD 419) vs 502 (SD 422) Country: New Zealand	LNG-IUS; Thermal Balloon Ablation (TBA)	24 months.	PBAC; Amenorrhoea; QoL (SF-36); Complications	PBAC (Mean (SD)): LNG-IUS vs TBA; P value. 3 months = 125.0 (SD 198.5) vs 220.8 (438.5); $P = 0.452$ 6 months = 72.1 (SD 118.6) vs 107.5 (SD 135.4); $P = 0.080$ 12 months = 41.1 (SD 86.5) vs 94.7 (SD 112.0); $P = 0.002$ 24 months = 20.6 (SD 28.8) vs 75.4 (SD 75.4); $P = 0.002$ Amenorrhoea: LNG-IUS vs TBA; P value. 3 months = 2 vs 5; $P = 0.236$ 6 months = 3 vs 1; $P = 0.613$ 12 months = 6 vs 2; $P = 0.254$ 24 months = 9 vs 1; $P = 0.025$ QoL (SF-36): LNG-IUS vs TBA: Baseline = 63.7 (SD 22.7) vs 63.7 (SD 14.4) 3 months = 77.7 (SD 17.0) vs 78.2 (SD 13.7) 12 months = 79.3 (SD 16.5) vs 76.9 (SD 16.8) 24 months = 77.5 (SD 20.1) vs 74.9 (SD 18.8) Complications: No major complications reported in either group.	Funding source: Not stated Study summary: At 12 and 24 months of follow up, women with heavy menstrual bleeding treated with the LNG-IUS have significantly lower PBAC scores than women treated with thermal balloon ablation. Both the treatments resulted in a significant increase in overall quality of life, but there were no significant differences between either treatment in quality of life, patient satisfaction or the number of women requesting an alternative treatment during 24 months of follow up.
Cameron 1987 ²⁶²	randomised EL = 1–	30 in total: 6 in danazol group; 8 in mefenamic acid group; 8 in norethisterone group; and 8 in coil group	Population characteristics: Women; MBL > 50 ml Age: danazol = 42, mefenamic acid = 40, norethisterone = 39, progesterone coil = 40 Parity: danazol = 2, mefenamic acid = 4, norethisterone = 4, progesterone coil = 2 Country: UK	Danazol (200 mg); mefenamic acid (500 mg × 3); norethisterone (5 mg × 2); progesterone coil treatment vs no treatment period	4 consecutive cycles – 2 with no treatment and 2 with treatment	MBL – alkaline haematin; length of cycle; PGE; PGF; PG concentrations	In the mefenamic acid group MBL changed from 85 (range 68–169) in no treatment period to 47 (39–210) in the treatment periods ($P = 0.05$); a –44.5% change. danazol: pre-treatment = 203 ml, treatment = 51 ml; a –75% change. Progesterone coil: pre-treatment = 64 ml ($P < 0.05$), treatment = 45 ml; a 30% change. Norethisterone: pre-treatment = 131, treatment = 110; a –16% change. Side effects not reported.	Funding source: Not stated Study summary: All treatments except norethisterone reduce MBL.
Coulter 1995 ²⁷³	Systematic review; meta-analysis EL = 1+		Population characteristics: Searches undertaken on MEDLINE	Review of evidence for treatment of HMB		MBL	Antifibrinolytics: Pooled result from 7 trials was a % reduction in MBL of 46.7 (95% CI 47.9–51.6). Reports on 4 RCT of etamsylate. Meta-analysis identifies a % blood loss reduction of 13.1 (95% CI 10.9–15.3). Norethisterone: 4 RCTs showed a reduction change in MBL of	Funding source: Not stated Study summary: Studies of this preparation report greater reductions in blood loss but slightly

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							<p>-3.6% (-6.1, 1.1)</p> <p>Danazol: 5 RCTs showed a combined reduction in MBL of 49.7% (47.9, 51.6)</p> <p>IUDs: 4 RCTs showed a combined reduction in MBL of 58.6 (56.7, 60.6)</p> <p>Mefenamic acid: Pooled results for 10 studies = -29% (95% CI 27.9-30.2). Diclofenac: 2 studies = -26.9% (23.3-30.6). Naproxen: 5 studies = -26.4% (24.6-28.3). Ibuprofen: 3 studies = -16.2% (13.6-18.7).</p> <p>OCP: 1 RCT - MBL reduction = 43%</p> <p>Side effects not reported.</p>	more side effects than mefenamic acid.
Crosgnani 1997 ²⁶³	randomised; open; prospective EL = 1+	97 assessed. 27 refused entry. 70 accepted entry to study - 35 in IUD group, 35 in endometrial resection group.	Population characteristics: women; 38 years or older; referred for hysterectomy; confirmed menorrhagia - PBAC > 100; pregnant or breast feeding excluded; using hormonal treatment in last 3 months; serious concomitant condition excluded. IUD group - age 43.8, parity = 1.8, BMI = 25.3 Endometrial resection group - age = 45.4, parity = 1.6, BMI = 24.0 Country: Italy	LNG-IUS; endometrial resection	12 months - 6 and 12 months	MBL - PBAC; SF-36	<p>MBL outcome: LNG-IUS (<i>n</i> = 30) baseline = 184.8 ml (SD 62.2), 12 months = 38.8 (SD 37.1) (<i>P</i> < 0.001). Endometrial resection (<i>n</i> = 30) baseline = 203.2 (SD 77.4), 12 months = 23.5 (SD 32.6) (<i>P</i> < 0.001).</p> <p>Difference between LNG-IUS and resection <i>P</i> = 0.015.</p> <p>Patient satisfaction: LNG-IUS: 29 (85%) satisfied. Endometrial resection: 33 (94%) satisfied.</p> <p>Mean SF-36 scores at 12 months (LNG-IUS vs Resection): Physical functioning = 78.0 vs 79.2. Role limitation = 72.5 vs 74.2 Bodily pain = 58.9 vs 70.3 General health = 64.1 vs 70.3 Vitality = 56.3 vs 54.8 Social functioning = 69.8 vs 69.7 Role limitation = 61.3 vs 72.4 Mental health = 60.1 vs 59.6</p> <p>Side effects reported by 19 of 34 in IUS group and 9 of 35 in resection group.</p> <p>1 LNG-IUS patient lost to follow-up.</p> <p>4 LNG and 3 resection patients had persistent menorrhagia after treatment and sought other treatment.</p>	<p>Funding source: National Research Council (Rome)</p> <p>Study summary: LNG-IUS produces slightly less satisfactory results than resection at 12 months.</p>
Halmesmaki 2004 ²⁶⁴	randomised; prospective EL = 1+	119 LNG-IUS vs 117 hysterectomy. 81 IUDs at 12 months - 24 hysterectomy, 10 removed, 5 used ERT. 107 hysterectomies undertaken at 12 months.	Population characteristics: Women; 35-49; menstruating; completed family. No fibroids, endometrial polyps, urinary or bowel symptoms, ovarian pathology. Hysterectomy: age 43.1, parity = 2.1, BMI = 26.6. LNG-IUS: age = 43.0, parity = 2.1, BMI = 25.1 Country: Finland	LNG-IUS; Hysterectomy Treatment vs baseline; treatment vs treatment	12 months	FSH serum levels; Kupperman index - menopausal symptoms - hot flushes, etc.	<p>FSH levels increased from 8.4 iu/ml at baseline to 13.8 iu/ml at 12 months vs 8.7 to 9.2 in LNG-IUS groups. (<i>P</i> = 0.005).</p> <p>No difference between or within groups on Kupperman index at 12 months (based on treatment use not intention-to-treat). Hot flushes increased in hysterectomy (<i>P</i> = 0.02) but not IUD; no difference between groups.</p>	<p>Funding source: Not stated</p> <p>Study summary: Hysterectomy may impair ovarian function.</p>
Hurskainen 2004 ¹⁰⁴	randomised; allocation concealed;	236: 119 LNG-IUS (57 had IUS; 10 nothing; 50 had	Population characteristics: women; menorrhagia; no pathology Country: Finland	LNG-IUS; hysterectomy treatment vs baseline; treatment vs treatment	5 years	QoL - EQ-5D, SF-36	<p>QoL at 5 years: change in EQ-5D was 0.08 for IUS vs 0.1 for hysterectomy from baseline of 0.76 (0.7, 0.8) and 0.78 (0.7, 0.8). No difference between groups (<i>P</i> = 0.6). SF-36: change</p>	<p>Funding source: Government grant</p> <p>Study summary: Study</p>

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
	controlled EL = 1++	hysterectomy by 5 years); 117 hysterectomy (109 had hysterectomy by 5 years). 5 LNG-IUS, 7 hysterectomy lost to follow-up.					<p>in general health = 3.6 vs 4.4 from baseline of 64 vs 65 ; physical functioning = -1.4 vs -2 from baseline of 83 vs 84; social functioning = 8.7 vs 9.0 from baseline of 72 vs 76. No difference between groups ($P = 0.8, 0.9, 0.9$).</p> <p>At 5 years: 50 LNG-IUS users had hysterectomy. Another 10 women were without LNG-IUS <i>in situ</i>. 7 Hysterectomy group had cancelled operation or had IUD fitted.</p> <p>Baseline figures: EQ-5D (LNG-IUS, Hysterectomy) – 0.76, 0.78; SF-36 general health – 64, 65; physical functioning – 83, 84; emotional well-being – 67, 70; social functioning – 72, 76; energy – 55, 57; pain 63, 62; role functioning – emotional – 65, 66; emotional – 61, 66. No data for entire population average.</p>	shows that at 5 years LNG-IUS offered effective alternative to hysterectomy.
Hurskainen 2001 ¹⁰⁵	randomised; allocation concealed EL = 1++	236: 117 LNG-IUS (24 had hysterectomy); 119 hysterectomy (107 underwent operation). 3 LNG-IUS and 5 hysterectomy patients were lost to follow-up.	Population characteristics: women; menorrhagia; no pathology – fibroids, cancer etc.; no previous failure with LNG-IUS; no acne Country: Finland	LNG-IUS; hysterectomy treatment vs baseline; treatment vs treatment	12 months	QoL – EQ-5D, SF-36	<p>Baseline QoL: EQ-5D: IUS = 0.76 (0.7 to 0.80), Hysterectomy = 0.78 (0.70 to 0.80)</p> <p>SF-36 scores: General health – IUS = 64 (60.6 to 67.4), Hysterectomy = 65 (61.0 to 69.0). Physical functioning – IUS = 83 (79.4 to 86.6), Hysterectomy = 84 (80.8 to 87.2). Emotional functioning – IUS = 67 (63.2 to 70.8), Hysterectomy = 70 (66.6 to 73.4). Social functioning – IUS = 72 (67.6 to 76.4), Hysterectomy = 76 (72.2 to 79.8). Energy – IUS = 55 (50.6 to 59.4), Hysterectomy = 57 (53.0 to 61.0). Pain – IUS = 63 (58.4 to 67.4), Hysterectomy = 62 (57.6 to 66.4). Role functioning – physical – IUS = 65 (57.5 to 72.3), Hysterectomy = 66 (58.9 to 73.1). Role functioning – emotional – IUS = 61 (53.5 to 68.5), Hysterectomy = 66 (58.7 to 73.3). General Health questionnaire – IUS = 73 (69.4 to 76.6), Hysterectomy = 75 (71.8 to 78.2). Anxiety – IUS = 32 (30.8 to 33.2), Hysterectomy = 31 (30.0 to 32.0). Depression – IUS = 5.2 (4.2 to 6.2), Hysterectomy = 4.2 (3.4 to 5.0). Sexual satisfaction – IUS = 23.6 (22.4 to 24.8), Hysterectomy = 23.7 (22.9 to 24.5). Sexual problems – IUS = 4.4 (4.0 to 4.8), Hysterectomy = 4.5 (4.1 to 4.9). Partner satisfaction – IUS = 11.2 (10.6 to 11.8), Hysterectomy = 11.6 (11.2 to 12.0).</p> <p>QoL at 12 months (intention-to-treat): all measured improved for both groups. EQ-5D by 0.1 in both groups ($P = 0.0001$) from baseline of 0.76 (0.7, 0.8) for LNG-IUS and 0.78 (0.7, 0.8) for hysterectomy. SF-36 General health – 5.5 for IUS and 6.2 for hysterectomy from baseline of 64 vs 65; physical</p>	<p>Funding source: Government funded. IUD provided free by Leiras.</p> <p>Study summary: Study shows LNG-IUS was effective alternative to hysterectomy at 12 months.</p>

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							functioning 4.8 vs 7.1 from baseline of 83 vs 84; social functioning 11.8 vs 12.4 from baseline of 72 vs 76. No difference between groups, except pain 11.8 vs 21.2 ($P = 0.01$). At 12 months – 24 LNG-IUS group had undergone hysterectomy. Another 10 women had had LNG-IUS removed. 5 hysterectomy group cancelled operation.	
Irvine 1998 ²⁶⁵	randomised, allocation concealed EL = 1+	44: 22 LNG-IUS, 22 norethisterone. 8 did not complete – 6 norethisterone, 2 IUS.	Population characteristics: women; 18–45 years; no pathology; no hormonal 3 months or injected contraceptives in 12 months. LNG-IUS group: av. 38.5 yr, 158.5 cm height, 69.9 kg weight. Norethisterone: 39 years, 159.5 cm, 71.4 kg. Country: UK	LNG-IUS; norethisterone (5 mg from day 5–26 of cycle) treatment vs baseline; treatment vs treatment	3 consecutive cycles	MBL; satisfaction; adverse events	LNG IUS: median MBL changed from pre-treatment = 105 to 6 a 3rd cycle. ($P < 0.001$) (–94%0 Norethisterone: median MBL changed from pre-treatment = 120 to 20 ml at 3rd cycle ($P < 0.001$) (–83%). Difference between groups $P = 0.56$. Satisfaction: 64% of LNG-IUS vs 22% of norethisterone were satisfied with treatment. Continuation of treatment: 77% LNG-IUS vs 22% of norethisterone. Period interfered with daily life: 90% (20/22) reduced to 31% (6/19) at 3 months for LNG-IUS vs 82% (18/22) reduced to 17% (2/12) for norethisterone. Mood swings, intermenstrual bleeding and breast tenderness all reduced more by norethisterone. Side effects: No difference between groups – weight gain	Funding source: Not sated Study summary: LNG-IUS is an alternative to hysterectomy and ablation.
Istre 2001 ²⁶⁶	Randomised EL = 1+	60: 30 LNG-IUS; 30 resection – 6 discontinued treatment by 12 months.	Population characteristics: women; menorrhagia (PBAC > 75); pre-menopausal; 30–49 years; regular uterine cavity < 10 cm; no pregnant or wanting to become so, breast feeding; large fibroid > 40 cm; pelvic disease; DVT; cancer; endometritis; liver disease; hormone therapy in 3 months Country: Norway	LNG-IUS; endometrial resection treatment vs baseline; treatment vs treatment	12 months	MBL = PBAC; duration of menstruation; haematological test; side effects	MBL (mean) – PBAC: LNG-IUS – baseline = 420 (SD 352), 12 months = 42 (SD 99) (–90%). TCRE – baseline = 404 (SD 480), 12 months = 7 (SD 15) (–98%). PBAC < 75 in 67% of LNG-IUS and 90% of TCRE patients at 12 months. ($P = 0.005$) Side effects: LNG-IUS 13 reported events – bleeding, abdominal pain, breast tenderness, headache, mood change. 6 discontinued treatment due to irregular bleeding, pain and acne.	Funding source: Leiras Oy Study summary: Resection reduces MBL more than IUS-LNG but only marginally.
Lahteenmaki 1998 ²⁶⁷	randomised, open, allocation concealed EL = 1++	56: 28 LNG-IUS, 28 control (standard medical treatment) from waiting list for hysterectomy	Population characteristics: women; menorrhagia; excluded if pathology; waiting for hysterectomy. Country: Finland	LNG-IUS; standard treatment treatment vs control	6 months	decision to undergo hysterectomy	64.3% (CI – 44.1, 81.4) of IUS vs 14.3% (CI – 4, 32.7) of control cancelled hysterectomy ($P < 0.001$) at 6 months. Menstrual effect on general well-being (VAS): control – baseline = 87 mm (77, 92) vs 79 mm (64, 87) at 6 months. LNG-IUS – 90 (74, 94) to 24 (14, 40). Difference at baseline (NS), at 6 months ($P < 0.001$). 12 ING-IUS discontinued use by 12 months, all for hysterectomy.	Funding source: Leiras Oy pharmaceutical Study summary: LNG-IUS group more likely to cancel operation than those in control group.
Lethaby 2004 ²⁵⁸	Systematic review; meta-analysis EL = 1++	10 RCTs	Population characteristics: (1) Electronic data bases Cochrane Menstrual Disorders and Subfertility Group Trials Register (see Review Group details for more information); this register is updated regularly by the trials search coordinator Cochrane Central Register of	LNG-IUS		MBL (objective and subjective); patient satisfaction; Adverse events	LNG-IUS vs placebo: No studies LNG-IUS vs any other medical treatment: Amenorrhoea (greater than three months) (1 RCT, $n = 35$) OR 8.67 [1.52, 49.35] favours LNG-IUS. Proportion of women satisfied with treatment (1 RCT, $n = 40$) OR 2.13 [0.62, 7.33]. Side effects – mood swings ($n = 31$, 1 RCT) OR 1.22 [0.28,	Funding source: No funding

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			<p>Controlled Trials (CENTRAL) (The Cochrane Library Issue 2, 2005)</p> <p>MEDLINE (1966 to July 2005)</p> <p>EMBASE (1980 to July 2005)</p> <p>Current Contents (1995 to July 2005)</p> <p>The National Research Register (NRR), a register of ongoing and recently completed research projects related to the United Kingdom's National Health Service (issue 2, 2005)</p> <p>Current Controlled Trials, comprising the ISRCTN Register (a database of randomised controlled trials with an International Standard Randomised Controlled Trial Number) (July 2005)</p> <p>MetaRegister of Controlled Trials (an international database combining registers of ongoing randomised controlled trials in all areas of healthcare) (searched July 2005)</p> <p>The NHS Centre for Reviews and Dissemination databases</p>				<p>5.24].</p> <p>Side effects – menstrual pelvic pain ($n = 51$) OR 4.53 [1.15, 17.83].</p> <p>Side effects – intermenstrual bleeding and menstrual irregularity ($n = 31$) OR 4.34 [1.01, 18.66].</p> <p>Side effects – breast tenderness ($n = 82$) OR 5.66 [2.02, 15.87].</p> <p>Side effects – nausea ($n = 51$) OR 0.50 [0.09, 2.69].</p> <p>Side effects – diarrhoea ($n = 51$) OR 0.28 [0.05, 1.76].</p> <p>Side effects – upper respiratory infection ($n = 51$) OR 1.05 [0.27, 4.12].</p> <p>Side effects – ovarian cysts ($n = 51$) OR 2.32 [0.56, 9.65].</p> <p>Side effects – headache ($n = 51$) OR 1.07 [0.35, 3.24].</p> <p>Withdrawal from treatment because of adverse events ($n = 44$) OR 0.37 [0.07, 1.82].</p> <p>Proportion unwilling to continue with treatment ($n = 91$) OR 0.27 [0.10, 0.67] in favour of LNG-IUS</p> <p>LNG-IUS vs Ablation:</p> <p>Success of treatment (PBAC score < 75) at 12 months ($n = 210$) OR 0.28 [0.14, 0.58].</p> <p>Amenorrhoea Up to 12 months ($n = 223$) OR 0.75 [0.36, 1.54] in favour of surgery.</p> <p>Proportion of women satisfied with treatment ($n = 136$) OR 0.61 [0.26, 1.46].</p> <p>Total proportion of women with side effects ($n = 201$) OR 3.09 [1.76, 5.42] in favour of surgery.</p> <p>No difference between groups for Endometritis, PID, Partial expulsion, Adenomyosis, Myometritis, Abnormal PAP, Oedema, Mastalgia, Headache, Leg pain, Dysmenorrhoea, Lower abdominal pain, Decreased libido, Hair loss, Anxiety or depression, Hypertension, or Pain before period.</p> <p>Difference between groups in favour of surgery for Weight gain (OR 2.92 [1.24, 6.90], Bloating (OR 4.52 [1.83, 11.17], Acne or greasy skin (OR 8.63 [2.23, 33.43], Nausea (OR 8.07 [1.09, 59.80], and Breast pain (OR 1.03 [0.14, 7.65].</p> <p>Need for further surgical treatment ($n = 110$) OR 1.33 [0.47, 3.81].</p> <p>LNG-IUS vs hysterectomy:</p> <p>Requirement for further surgery ($n = 232$) OR 12.56 [6.76, 23.35].</p> <p>Satisfaction with treatment ($n = 232$) OR 1.17 [0.41, 3.34]</p>	
Rauramo 2004 ²⁶⁸	randomised; open; equivalence EL = 1+	60: 30 LNG-IUS; 29 endometrial resection – 1 not randomised. 12 months – 6 LNG IUS vs 1 ablation discontinued or treatment failure. 36 months 5 vs 7	<p>Population characteristics: women; menorrhagia; not pregnant or lactating; finished family; normal uterine cavity; abnormal uterine bleeding; pathology.</p> <p>LNG-IUS: 41.4 years, 73.4 kg. TCRE: 42.1 years, 70.4 kg.</p> <p>Country: Norway</p>	LNG-IUS; endometrial resection treatment vs treatment; treatment vs baseline	3 years	<p>MBL = PBAC; duration of menstruation; haematological test; side effects</p> <p>Analysis based on intention-to-treat.</p>	<p>MBL:</p> <p>LNG-IUS (median)- baseline ($n = 30$) = 261.5 (60–1503), 1 year ($n = 24$) = 12, 2 years ($n = 20$) = 8.5, 3 years ($n = 19$) = 7.</p> <p>Resection – baseline ($n = 29$) = 311 (81–2506), 1 year ($n = 28$) = 8.5, 2 years ($n = 24$) = 10, 3 years ($n = 22$) = 4.</p> <p>Difference between groups not significant.</p> <p>Adverse events: 1 oedema from LNG, plus 3 endometriosis, 2 PID, 1 expulsion. 1 endometritis, 1 bleeding and pain from</p>	<p>Funding source: Schering AG</p> <p>Study summary: Both treatments effectively reduced MBL.</p>

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
		discontinued or treatment failure. 19 vs 22 at 36 months.					resection, plus 1 stroke	
Reid 2005 ²⁶⁹	randomised; non-blinded; concealed EL = 1+	391 assessed, 51 randomised, 25 to LNG-IUS, 26 to mefenamic acid. 4 in LNG-IUS and 5 in mefenamic acid group were lost to follow-up/discontinued.	Population characteristics: Women; aged 18 to 47 years; regular, ovulatory, menstrual cycles; idiopathic menorrhagia. Excluded if – AUB, abnormal test results, uterine fibroids > 5 cm ³ , hypertension, abnormal thyroid or liver test function, asthma, IUCD <i>in situ</i> , treated for menorrhagia or used hormonal treatments within 4 months. Baseline characteristics not described. Country: UK.	LNG-IUS (levonorgestrel 52 mg); mefenamic acid 9 (500 mg <i>t.i.d.</i>)	6 cycles	MBL (alkaline haematin); total fluid loss; PBAC score; adverse events	<p>MBL (alkaline haematin[ml]: median (range)):</p> <p>LNG-IUS:</p> <p>Baseline = 122 (81 to 375)</p> <p>Cycle 3 = 12 (0 to 240)</p> <p>Cycle 6 = 5 (0 to 45)</p> <p>(<i>P</i> < 0.005 for change between measurements)</p> <p>Mefenamic acid:</p> <p>Baseline = 121 (85 to 389)</p> <p>Cycle 3 = 94 (29 to 219) (<i>P</i> < 0.001 in favour of LNG-IUS)</p> <p>Cycle 6 = 100 (46 to 168) (<i>P</i> < 0.001 in favour of LNG-IUS)</p> <p>(<i>P</i> < 0.005 for change between measurements)</p> <p>Total fluid loss (ml; median (range)):</p> <p>LNG-IUS:</p> <p>Baseline = 183 (103 to 527)</p> <p>Cycle 3 = 53 (0 to 459)</p> <p>Cycle 6 = 27 (0 to 156)</p> <p>(<i>P</i> < 0.005 for change between measurements)</p> <p>Mefenamic acid:</p> <p>Baseline = 211 (91 to 491)</p> <p>Cycle 3 = 151 (57 to 280) (<i>P</i> < 0.001 in favour of LNG-IUS)</p> <p>Cycle 6 = 157 (76 to 319) (<i>P</i> < 0.001 in favour of LNG-IUS)</p> <p>(<i>P</i> < 0.005 for change between measurements)</p> <p>PBAC score (median (range)):</p> <p>LNG-IUS:</p> <p>Baseline = 240 (91 to 545)</p> <p>Cycle 3 = 49 (0 to 286)</p> <p>Cycle 6 = 25 (0 to 402)</p> <p>(<i>P</i> < 0.005 for change between measurements)</p> <p>Mefenamic acid:</p> <p>Baseline = 233 (77 to 469)</p> <p>Cycle 3 = 161 (77 to 262) (<i>P</i> < 0.001 in favour of LNG-IUS)</p> <p>Cycle 6 = 159 (50 to 307) (<i>P</i> < 0.001 in favour of LNG-IUS)</p> <p>(<i>P</i> < 0.005 for change between measurements)</p> <p>Adverse events:</p> <p>LNG-IUS:</p> <p>Headache = 10</p> <p>Abdominal pain = 8</p> <p>Ovarian cyst = 6</p> <p>Breast pain = 6</p> <p>Nausea = 2</p> <p>Diarrhoea = 1</p> <p>Upper respiratory infection = 5</p>	<p>Funding source: Schering Oy</p> <p>Study summary: Both treatments reduce MBL, but LNG-IUS does this to a greater degree.</p>

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							<p>Mefenamic acid:</p> <p>Headache = 10</p> <p>Abdominal pain = 2</p> <p>Ovarian cyst = 3</p> <p>Breast pain = 2</p> <p>Nausea = 4</p> <p>Diarrhoea = 4</p> <p>Upper respiratory infection = 5</p>	
Soysal 2002 ²⁷⁰	randomised; blind EL = 1+	72: 36 ablation vs 36 IUD. 1 ablation and 5 IUD not included in analysis due to treatment failure.	<p>Population characteristics: Women; > 40 years; completed family; menorrhagia; no pathology; no cancer.</p> <p>LNG-IUS: 44.1 years. TBA: 43.8 years.</p> <p>Country: Turkey</p>	<p>Thermal balloon ablation after GnRH-a; LNG IUD (20 µg daily)</p> <p>Treatment vs baseline; treatment vs treatment</p>	12 months	<p>MBL – PBAC; QoL; Side effects</p>	<p>MBL: TBA – baseline PBAC = 417 (SD 81.4), 12 month PBAC = 21.8 (SD 14) ($P < 0.0001$). LNG-IUD – baseline PBAC = 408 (SD 101), 12 month PBAC = 55 (SD 11) ($P < 0.001$). TBA vs LNG = 388.2 vs 343 reduction ($P < 0.001$).</p> <p>QoL: SF-36 and HADs no difference between groups, except on role limitation where TBA better. No baseline data shown.</p> <p>Patient satisfaction: would recommend treatment = 70% for TBA vs 96% for LNG-IUD.</p> <p>Side effects: 21 of 36 LNG patients reported 1 or more side effects vs 8 of 36 in TBA group. ($P < 0.05$).</p> <p>Discontinuation: 5 LNG-IUS vs 1 TBA discontinued due to treatment failure.</p>	<p>Funding source: Not stated</p> <p>Study summary: Study shows that LNG-IUS and TBA are equivalent.</p>
Stewart 2001 ²⁵⁹	Systematic review EL = 1+		<p>Population characteristics:</p> <p>Country:</p>	RCT; case series		MBL	<p>10 studies included in review: 5 RCTs, 5 Case series. MBL reduction: RCT 1 ($n = 30$ in arm) = 79%; RCT 2 ($n = 20$) = 94%; RCT 3 ($n = 24$) = 90%; RCT 4 ($n = 16$) = 96%. One RCT did not report change in MBL. Case series ranged from 79% to 97% reduction.</p>	<p>Study summary: LNG-IUS is effective at reducing MBL associated with menorrhagia.</p>

Table 8.2 LNG-IUS for treatment of HMB – non-comparative studies

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Hurskainen 2004 ⁴⁸³	randomised EL = 3	LNG-IUS; hysterectomy	236 – 119 (116 available at 12 months) to LNG-IUS, 117 (112 available at 12 months) to hysterectomy	women; menstruating; subjective menorrhagia; aged 35 to 49; completed families; Excluded if – submucous fibroids, endometrial polyps, urinary or bowel symptoms due to large fibroid, or ovarian pathology. Country: Finland	Predictors of outcome	<p>Presence of fibroids nor age were predictors of outcome at 12 months for LNG-IUS or hysterectomy.</p> <p>Multiple regression analysis showed that MBL was the most significant factor predicting outcome.</p> <p>Comparison of women with and without objective menorrhagia (> 80 ml MBL).</p> <p>For women in LNG-IUS group women without menorrhagia had better QoL outcomes than women with menorrhagia on: anxiety ($P=0.04$), EQ-5D ($P=0.05$). In the hysterectomy group, women without menorrhagia had better outcomes than those with menorrhagia on: anxiety ($P=0.007$), emotional well-being ($P=0.01$) and energy ($P=0.0002$).</p> <p>Women without menorrhagia had better outcomes with LNG-IUS than women with menorrhagia on EQ-5D ($P=0.03$).</p> <p>Women with menorrhagia had better outcomes with hysterectomy than LNG-IUS for: anxiety ($P=0.003$), general health ($P=0.04$), energy ($P=0.05$), and pain relief ($P=0.04$).</p>	<p>Funding source: Not stated</p> <p>Study summary: Success or failure of treatment of menorrhagia is multifactorial, so difficult to predict in individual cases.</p>

Table 8.3 Combined oral contraceptives for treatment of HMB – comparative studies

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Coulter 1995 ²⁷³	Systematic review; meta-analysis EL = 1+		Population characteristics: Searches undertaken on MEDLINE Country:	Review of evidence for treatment of HMB		MBL	Antifibrinolytics: Pooled result from 7 trials was a % reduction in MBL of 46.7 (95% CI 47.9–51.6). Reports on 4 RCT of etamsylate. Meta-analysis identifies a % blood loss reduction of 13.1 (95% CI 10.9–15.3). Norethisterone: 4 RCTs showed a reduction change in MBL of -3.6% (-6.1, 1.1) Danazol: 5 RCTs showed a combined reduction in MBL of 49.7% (47.9, 51.6) IUDs: 4 RCTs showed a combined reduction in MBL of 58.6 (56.7, 60.6) Mefenamic acid: Pooled results for 10 studies = -29% (95% CI 27.9–30.2). Diclofenac: 2 studies = -26.9% (23.3–30.6). Naproxen: 5 studies = -26.4% (24.6–28.3). Ibuprofen: 3 studies = -16.2% (13.6–18.7). OCP: 1 RCT – MBL reduction = 43% Side effects not reported.	Funding source: Not stated Study summary: Studies of this preparation report greater reductions in blood loss but slightly more side effects than mefenamic acid.
Fraser 1991 ²⁷⁴	randomised EL = 1+	45 in total. 7 dropped out. 38 assessed: 19 in mefenamic (across 3 groups); 7 naproxen; 6 OCP; 6 danazol	Population characteristics: Women; menorrhagia – ovulatory DUB; no pathology; no hormonal therapy within 3 months Country: Australia	Mefenamic acid (500 mg × 3); naproxen; low dose monophasic oral contraceptive – ethinyl estradiol 30 µg and levonorelgestrel 150 µg for 21 days; danazol (200 mg) daily Treatment vs baseline	8 consecutive cycles: 2 no treatment; 2 treatment; 2 no treatment; 2 treatment	MBL – alkaline haematin	Mefenamic acid – group 1 – control = 131.1 ml (SD 80.8) treatment = 105.1 (SD 88.6) ($P = 0.198$) (-20%); group 2 – control = 101 (SD 52.5), treatment = 62.9 (SD 27.7) ($P = 0.002$) (-38%); group 3 – control = 90.3 (50.2), treatment = 55.3 (34) ($P < 0.001$) (-39%); Naproxen – control = 131.1 ml vs treatment = 115.6 (SD 113) ml ($P = 0.079$) (-12%); Oral contraceptive – 101 vs 57.8, $P < 0.001$, -43%; Danazol – 90.3 vs 45.5 (av), $P < 0.001$, -49%. Differences between Mefenamic vs naproxen $P = 0.129$; vs oral contraceptive $P = 0.154$; vs danazol $P = 0.079$. Side effects not reported.	Funding source: Commercial funding Study summary: All treatments reduce MBL.
Iyer 2000 ²⁷²	Systematic review EL = 1++	1 study included in review	Population characteristics: Search strategy based on key words and MeSH headings Search on MEDLINE, EMBASE, Cochrane library, CINAHL, PsycINFO. Hand searching of 20 journal and conferences proceedings	RCT – Oral Contraceptive pill		MBL; side effects; QoL	One study included in review (17 rejected). OCP vs Naproxen ($n = 12$) – MBL = 66.77 vs 58.4, difference = 8.37 [95% CI -27.31, 44.05](-12.5%). OCP vs danazol ($n = 12$) – MBL = 66.77 vs 47.5, difference = 19.27 [-24.47, 63.01] (-29%). OCP vs mefenamic acid ($n = 12$) – MBL = 66.77 vs 84.26, difference = -17.49 [-62.77, 27.79]. (+26%). Side effects and QoL not reported.	Funding source: No funding

Table 8.4 Oral progestogens for treatment of HMB – comparative studies

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Bonduelle 1991 ²⁷⁶	randomised; open EL = 1–	30: 15 danazol; 15 norethisterone. 6 excluded (5 danazol and 1 norethisterone) for protocol violations	Population characteristics: women; menorrhagia; no pathology. Average age – danazol = 36.1, norethisterone = 39.2. Duration of menorrhagia – danazol = 4.8 years, norethisterone = 3.8 years. Country: UK	Danazol 200 mg daily for 3 months; norethisterone 5 mg × 3 for days 19–26 of cycle treatment vs treatment; treatment vs baseline	3 months	MBL – bleeding intensity score; number pads used; days bleeding	MBL: danazol (mean ± SD)-baseline ($n = 10$) = 31.9 ± 12.4 , 2nd cycle ($n = 7$) = 14.1 ± 11.3 ($P < 0.02$); 3rd cycle ($n = 6$) = 15.0 ± 9.4 ($P < 0.02$) ($P < 0.05$ vs norethisterone) Norethisterone – baseline ($n = 14$) $32.9 (\pm 15.2)$, 2nd cycle ($n = 11$) = $23.7 (\pm 6.5)$ (NS), 3rd cycle ($n = 10$) = $23.6 (\pm 9.6)$ (NS). ($P < 0.05$). 8 patients withdrew (4 from each group) all due to side effects. Side effects: danazol 10 reported vs 14 norethisterone.	Funding source: Not stated Study summary: danazol is more effective than norethisterone at reducing MBL, with similar side effects
Cameron 1987 ²⁶²	randomised EL = 1–	30 in total: 6 in danazol group; 8 in mefenamic acid group; 8 in norethisterone group; and 8 in coil group	Population characteristics: Women; MBL > 50 ml Age: danazol = 42, mefenamic acid = 40, norethisterone = 39, progesterone coil = 40 Parity: danazol = 2, mefenamic acid = 4, norethisterone = 4, progesterone coil = 2 Country: UK	Danazol (200 mg); mefenamic acid (500 mg × 3); norethisterone (5 mg × 2); progesterone coil treatment vs no treatment period	4 consecutive cycles – 2 with no treatment and 2 with treatment	MBL – alkaline haematin; length of cycle; PGE; PGF; PG concentrations	In the mefenamic acid group MBL changed from 85 (range 68–169) in no treatment period to 47 (39–210) in the treatment periods ($P = 0.05$); a –44.5% change. danazol: pre-treatment = 203 ml, treatment = 51 ml; a –75% change. Progesterone coil: pre-treatment = 64 ml ($P < 0.05$), treatment = 45 ml; a 30% change. Norethisterone: pre-treatment = 131, treatment = 110; a –16% change. Side effects not reported.	Funding source: Not stated Study summary: All treatments except norethisterone reduce MBL.
Coulter 1995 ²⁷³	Systematic review; meta-analysis EL = 1+		Population characteristics: Searches undertaken on MEDLINE Country:	Review of evidence for treatment of HMB		MBL	Antifibrinolytics: Pooled result from 7 trials was a % reduction in MBL of 46.7 (95% CI 47.9–51.6). Reports on 4 RCT of etamsylate. Meta-analysis identifies a % blood loss reduction of 13.1 (95% CI 10.9–15.3). Norethisterone: 4 RCTs showed a reduction change in MBL of –3.6% (–6.1, 1.1) Danazol: 5 RCTs showed a combined reduction in MBL of 49.7% (47.9, 51.6) IUDs: 4 RCTs showed a combined reduction in MBL of 58.6 (56.7, 60.6) Mefenamic acid: Pooled results for 10 studies = –29% (95% CI 27.9–30.2). Diclofenac: 2 studies = –26.9% (23.3–30.6). Naproxen: 5 studies = –26.4% (24.6–28.3). Ibuprofen: 3 studies = –16.2% (13.6–18.7). OCP: 1 RCT – MBL reduction = 43% Side effects not reported.	Funding source: Not stated Study summary: Studies of this preparation report greater reductions in blood loss but slightly more side effects than mefenamic acid.
Dunphy 1998 ²⁷⁷	randomised; double-blind EL = 1–	23: 11 medroxyprogesterone; 12 danazol randomised; 9 medroxy, 9 danazol analysed.	Population characteristics: women; menorrhagia (> 80 ml); > 18 years; not pregnant; no contraindications Country: Canada	Danazol 200 mg daily; medroxyprogesterone acetate 10 mg on 16–25 days of cycle treatment vs baseline; treatment vs treatment	7 months: 1 baseline; 3 treatment; 3 follow-up	MBL – alkaline haematin; side effects	MBL (mean): danazol ($n = 9$) – baseline = 592 (SD 336), 1 month treatment = 201 (SD 140), 3 months treatment = 72 (SD 108). 3 months post-treatment = 353 (SD 243). All differences $P < 0.05$ against baseline. Medroxy ($n = 9$) – baseline = 505 (SD 399), 1 month treatment = 378 (SD 321), 3 month treatment = 568 (SD 710). 3rd post treatment month = 150 (SD 121). No difference from baseline. Body weight: danazol mean increase at 3rd treatment	Funding source: Sanofi Winthrop Ltd

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							month = 7 kg (SD 0.7) ($P = 0.0078$). Medroxy = 2.2 kg (SD 1.7) (NS). Side effects: 8 of 9 danazol vs 2 of 7 medroxy ($P = 0.035$). Drop-out: 3 danazol vs 2 medroxy	
Fraser 1991 ²⁷⁴	randomised EL = 1+	45 in total. 7 dropped out. 38 assessed: 19 in mefenamic (across 3 groups); 7 naproxen; 6 OCP; 6 danazol	Population characteristics: Women; menorrhagia – ovulatory DUB; no pathology; no hormonal therapy within 3 months Country: Australia	Mefenamic acid (500 mg × 3); naproxen; low dose monophasic oral contraceptive – ethinyl estradiol 30 µg and levonorelgestrel 150 µg for 21 days; danazol (200 mg) daily Treatment vs baseline	8 consecutive cycles: 2 no treatment; 2 treatment; 2 no treatment; 2 treatment	MBL – alkaline haematin	Mefenamic acid – group 1 – control = 131.1 ml (SD 80.8) treatment = 105.1 (SD 88.6) ($P = 0.198$) (–20%); group 2 – control = 101 (SD 52.5), treatment = 62.9 (SD 27.7) ($P = 0.002$) (–38%); group 3 – control = 90.3 (50.2), treatment = 55.3 (34) ($P < 0.001$) (–39%); Naproxen – control = 131.1 ml vs treatment = 115.6 (SD 113) ml ($P = 0.079$) (–12%); Oral contraceptive – 101 vs 57.8, $P < 0.001$, –43%; Danazol – 90.3 vs 45.5 (av), $P < 0.001$, –49%. Differences between Mefenamic vs naproxen $P = 0.129$; vs oral contraceptive $P = 0.154$; vs danazol $P = 0.079$. Side effects not reported.	Funding source: Commercial funding Study summary: All treatments reduce MBL.
Higham 1993 ²⁷⁸	randomised; single blind EL = 1+	57: 19 danazol 200 mg; 19 danazol reducing dose; 19 norethisterone	Population characteristics: women; regular cycle; menorrhagia (> 80 ml); no pathology; no concomitant treatment. Danazol 200 mg: 40.5 years, 65.6 kg, cycle 28.2 days. danazol reducing: 36.4 years, 63.1 kg, 27.6 days. Norethisterone: 40.1 years, 67.9 kg, 28 days. Country: UK	Danazol 200 mg daily; danazol 200 mg cycle 1, 100 mg cycle 2, 50 mg cycle 3; Norethisterone 5 mg × 3 day 19–26 of cycle. treatment vs baseline; treatment vs treatment	5 consecutive cycles: 2 pre-treatment; 3 treatment	MBL – alkaline haematin; adverse events; patient assessment	MBL (median ml, $n = 17$): danazol reducing dose – 1st pre-treatment = 145.5, 2nd = 136.1, final on-treatment = 101.2. danazol 200 mg ($n = 19$) – 1st = 136, 2nd = 138, final on-treatment = 82.6. Norethisterone ($n = 18$) – 1st = 129.1, 2nd = 162.5, final on-treatment = 140.3. Difference between danazol reducing dose vs norethisterone $P = 0.043$; danazol 200 mg vs norethisterone $P = 0.017$. Side effects: danazol reducing dose = 15, danazol 200 mg = 17, norethisterone = 11. 10 withdrawals: 5 danazol reducing – lack of efficacy; side effects; 3 danazol 200 mg – side effects; 2 norethisterone – side effects..	Funding source: Sanofi Winthrop Ltd Study summary: danazol more effective than norethisterone.
Irvine 1998 ²⁶⁵	randomised, allocation concealed EL = 1+	44: 22 LNG-IUS, 22 norethisterone. 8 did not complete – 6 norethisterone, 2 IUS.	Population characteristics: women; 18–45 years; no pathology; no hormonal 3 months or injected contraceptives in 12 months. LNG-IUS group: av. 38.5 yr, 158.5 cm height, 69.9 kg weight. Norethisterone: 39 years, 159.5 cm, 71.4 kg. Country: UK	LNG-IUS; norethisterone (5 mg from day 5–26 of cycle) treatment vs baseline; treatment vs treatment	3 consecutive cycles	MBL; satisfaction; adverse events	LNG IUS: median MBL changed from pre-treatment = 105 to 6 a 3rd cycle. ($P < 0.001$) (–94%) Norethisterone: median MBL changed from pre-treatment = 120 to 20 ml at 3rd cycle ($P < 0.001$) (–83%). Difference between groups $P = 0.56$. Satisfaction: 64% of LNG-IUS vs 22% of norethisterone were satisfied with treatment. Continuation of treatment: 77% LNG-IUS vs 22% of norethisterone. Period interfered with daily life: 90% (20/22) reduced to 31% (6/19) at 3 months for LNG-IUS vs 82% (18/22) reduced to 17% (2/12) for norethisterone. Mood swings, intermenstrual bleeding and breast tenderness all reduced more by norethisterone. Side effects: No difference between groups – weight gain	Funding source: Not sated Study summary: LNG-IUS is an alternative to hysterectomy and ablation.

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Lethaby 2004 ²⁷⁵	Systematic review EL = 1++	7 RCTs	Population characteristics: For the update of this review in 2003 we searched the Cochrane Menstrual Disorders and Subfertility Group trials register (searched 11 December 2003) which is submitted as part of the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (1966 to December 2003), and EMBASE (1985 to December 2003). No new trials were identified. In addition for the original review, published in 1998, searches of PsychLIT, Current Contents, Biological Abstracts, Social Sciences Index and CINAHL were also performed.	Oral progestogens			7 RCTS of luteal phase only progestogens vs placebo or treatment. Progestogens vs NSAIDs (2 trials, $n = 48$) MBL = 22.97 [-0.62, 46.57] in favour of NSAIDs. Progestagen vs danazol (2 trials, $n = 51$) MBL = 55.63 [14.73, 96.54] in favour of danazol. Progestagen vs tranexamic acid (1 trial, $n = 46$) MBL 111 [43.54, 178.46] in favour of tranexamic acid. Progestagen vs pregesterone IUS (1 trial, $n = 16$) MBL = 51 [18.38, 83.62] in favour of IUS. Adverse events: Luteal phase vs NSAIDs (1 study) Peto OR = 1.86 [0.44, 7.86]; vs danazol (2 studies) Peto OR = 0.34 [0.13, 0.88]; vs tranexamic acid (1 study) Peto OR = 2.44[0.32, 18.70].	
Preston 1995 ²⁷⁹	Randomised; double-blind; placebo-controlled; concealed; cross-over EL = 1++	46 women randomised: 21 Norethisterone; 25 tranexamic acid. 2 from each group withdrew.	Population characteristics: Women; Age 18+; regular cycle – 28 days \pm 7; no hormone therapy for 3 months; no concomitant treatment; normal renal function; normal pelvic exam; negative cervical cytology. TXA: 40.6 years, 71.2 kg. NET: 39.3 years, 63.5 kg ($P < 0.048$) Setting: university O&G department Country: UK	Tranexamic acid (1 g \times 4) for 4 days or norethisterone (5 mg \times 2) for 8 days or Placebo Treatment vs treatment; treatment vs placebo	4 consecutive cycles: 2 baseline/placebo; 2 treatment	Menstrual blood loss – alkaline haematin; QoL; side effects	Tranexamic acid ($n = 25$): Change from 175 ml to 97 ml (95% CI 62 to 108) ($P < 0.0001$); 45% reduction (+23 to -93; $P < 0.0001$). Norethisterone ($n = 21$): Change from 173 ml to 208 ml (-64 to +2) ($P = 0.26$); 20% increase (+114 to -62; $9 < 0.0001$). Between groups difference was 113 ml (95% CI 71 to 155) ($P < 0.0001$). QoL (limitations on activities): 16 TXA vs 9 NET = better, 13 TXA vs 11 NET = same or worse. No differences between reported adverse events between groups. Placebo = 85%; tranexamic acid = 88%; norethisterone = 95%. Two (8%) drop-out from tranexamic acid group and 2 (9.5%) from the norethisterone group.	Funding source: Commercially funded Study summary: Study shows that tranexamic acid reduces MBL, but that norethisterone does not.
Fraser IS; 1990 ²⁸⁰	cohort; comparative EL = 2-	16: 10 with menorrhagia	Population characteristics: women; confirmed menorrhagia Country: Australia	Norethisterone 5 mg \times 3; Medroxyprogesterone acetate (MPA) 10 mg \times 3 from 5–25 day of cycle treatment vs baseline	4 cycles: 2 baseline; 2 treatment	MBL – alkaline hematin	Change in MBL associated with MPA only ($n = 5$): 1st baseline = 104 ml and 6.4 days duration; 2nd baseline = 107.5 ml and 6.6 days; 1st treatment = 72 ml, 5.4 day; 2nd = 67 ml, 5.2 days. Side effects ($n = 16$) – 2 weight gain; 3 abdominal pain; 2 minor acne; 2 mild nausea; 2 headaches	Funding source: Not stated

Table 8.5 Other pharmaceutical treatment for HMB – comparative studies

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Beaumont 2004 ²⁸¹	Systematic review EL = 1++		Population characteristics: Country:	RCT – danazol			9 RCTs ($n = 353$) included (2 others excluded): No data on change in MBL. danazol cause more side effects than NSAIDs (1 study) (OR 7.0; 95% CI 1.7, 28.2) and progestogens (4 studies) (OR 4.05; 1.6, 10.2). danazol reduce duration of menses compared with NSAIDs (2 studies) (WMD -1; -1.8, -0.3) and Progesterone IUD (4 studies) (WMD -6; -7.3, -4.8). Mean MBL vs progestagens (1 study) WMD = -35.6 ml (95% CI -102, +31).	
Bonduelle 1991 ²⁷⁶	randomised; open EL = 1–	30: 15 danazol; 15 norethisterone. 6 excluded (5 danazol and 1 norethisterone) for protocol violations	Population characteristics: women; menorrhagia; no pathology. Average age – danazol = 36.1, norethisterone = 39.2. Duration of menorrhagia – danazol = 4.8 years, norethisterone = 3.8 years. Country: UK	Danazol 200 mg daily for 3 months; norethisterone 5 mg × 3 for days 19–26 of cycle treatment vs treatment; treatment vs baseline	3 months	MBL – bleeding intensity score; number pads used; days bleeding	MBL: danazol (mean ± SD)-baseline ($n = 10$) = 31.9 ± 12.4, 2nd cycle ($n = 7$) = 14.1 ± 11.3 ($P < 0.02$); 3rd cycle ($n = 6$) = 15.0 ± 9.4 ($P < 0.02$) ($P < 0.05$ vs norethisterone) Norethisterone – baseline ($n = 14$) 32.9 (±15.2), 2nd cycle ($n = 11$) = 23.7 (± 6.5) (NS), 3rd cycle ($n = 10$) = 23.6 (± 9.6) (NS). ($P < 0.05$). 8 patients withdrew (4 from each group) all due to side effects. Side effects: danazol 10 reported vs 14 norethisterone.	Funding source: Not stated Study summary: danazol is more effective than norethisterone at reducing MBL, with similar side effects
Cameron 1987 ²⁶²	randomised EL = 1–	30 in total: 6 in danazol group; 8 in mefenamic acid group; 8 in norethisterone group; and 8 in coil group	Population characteristics: Women; MBL > 50 ml Age: danazol = 42, mefenamic acid = 40, norethisterone = 39, progesterone coil = 40 Parity: danazol = 2, mefenamic acid = 4, norethisterone = 4, progesterone coil = 2 Country: UK	Danazol (200 mg); mefenamic acid (500 mg × 3); norethisterone (5 mg × 2); progesterone coil treatment vs no treatment period	4 consecutive cycles – 2 with no treatment and 2 with treatment	MBL – alkaline haematin; length of cycle; PGE; PGF; PG concentrations	In the mefenamic acid group MBL changed from 85 (range 68–169) in no treatment period to 47 (39–210) in the treatment periods ($P = 0.05$); a – 44.5% change. danazol: pre-treatment = 203 ml, treatment = 51 ml; a –75% change. Progesterone coil: pre-treatment = 64 ml ($P < 0.05$), treatment = 45 ml; a –30% change. Norethisterone: pre-treatment = 131, treatment = 110; a –16% change. Side effects not reported.	Funding source: Not stated Study summary: All treatments except norethisterone reduce MBL.
Chimbira 1980 ²⁸³	randomised EL = 1–	8 in placebo controlled study; 32 in danazol dose study. Drop-outs not reported.	Population characteristics: MBL > 60 ml; no pathology Country: UK	Danazol 100 mg; danazol 200 mg; placebo treatment vs placebo; treatment vs treatment; treatment vs baseline	6 cycles: 2 baseline; 2 placebo; 2 treatment. 12 weeks for dose study	MBL – alkaline haematin; side effects	Placebo trial ($n = 8$): baseline = 137 ml and 100 ml; placebo = 114 ml and 121 ml; danazol = 50 ml and 13 ml. 200 mg danazol ($n = 16$): baseline = 182 ml and 184 ml; danazol = 142 ml; 38 ml; 26 ml. 100 mg danazol ($n = 16$): figures not given for baseline; danazol: 52 ml; 42 ml; 52 ml. (< 0.01). Side effects: 200 mg = 24 side effects, plus 2.3 kg average weight gain; 100 mg = 18 side effects, plus 2.1 kg weight gain. Main side effects: tiredness; muscular pain; skin rash; headache.	Funding source: Sterling Winthrop Labs Study summary: danazol reduces MBL, but is associated with side effects.
Chimbira 1979 ³²²	Case series EL = 2–	22 recruited. 4 excluded. 18 included	Population characteristics: women; MBL > 80 ml Aged 25 to 50 years. Country: UK	Danazol (400 mg for 12 weeks) treatment vs baseline	7 months	MBL – alkaline haematin; peripheral blood measurements – platelets, plasminogen, Quick's test,	MBL: pre-treatment mean = 231 ml (SE 39) vs 135 ml (SE 33) in 1st treatment month and 21 ml (SE 3) in treatments months 2 and 3. Side effects: 33 side effects were reported by 18 patients, including tiredness; muscular pain; skin rash; headaches. Weight gain ($P < 0.01$) by end of danazol	Funding source: Sterling-Winthrop research division acknowledged. Study summary: Study shows danazol reduces MBL but has high levels of

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
						Euglobulin, Fibrinogen, Factor VII, Factor VIII, Factor X	treatment.	side effects
Coulter 1995 ²⁷³	Systematic review; meta-analysis EL = 1+		Population characteristics: Searches undertaken on MEDLINE Country:	Review of evidence for treatment of HMB		MBL	Antifibrinolytics: Pooled result from 7 trials was a % reduction in MBL of 46.7 (95% CI 47.9–51.6). Reports on 4 RCT of etamsylate. Meta-analysis identifies a % blood loss reduction of 13.1 (95% CI 10.9–15.3). Norethisterone: 4 RCTs showed a reduction change in MBL of -3.6% (-6.1, 1.1) Danazol: 5 RCTs showed a combined reduction in MBL of 49.7% (47.9, 51.6) IUDs: 4 RCTs showed a combined reduction in MBL of 58.6 (56.7, 60.6) Mefenamic acid: Pooled results for 10 studies = -29% (95% CI 27.9–30.2). Diclofenac: 2 studies = -26.9% (23.3–30.6). Naproxen: 5 studies = -26.4% (24.6–28.3). Ibuprofen: 3 studies = -16.2% (13.6–18.7). OCP: 1 RCT – MBL reduction = 43% Side effects not reported.	Funding source: Not stated Study summary: Studies of this preparation report greater reductions in blood loss but slightly more side effects than mefenamic acid.
Dockeray 1989 ²⁸⁴	randomised; open EL = 1–	41 in total; 20 in mefenamic acid group; 20 in danazol group. 1 withdrawal, but group not stated	Population characteristics: Menorrhagia > 80 ml; normal pelvic examination and pathology. Mefenamic group: age = 38.2, parity = 3.9, dysmenorrhoea = 13 of 20. Danazol group: age = 37.2, parity = 3.5, dysmenorrhoea = 15 of 20. Country: Ireland	Mefenamic acid (500 mg × 3) for 5 days; danazol (100 mg × 2) for 60 days Treatment vs baseline; treatment vs treatment	4 consecutive cycles: 2 baseline; 2 treatment	MBL – alkaline haematin; dysmenorrhoea; side effects	Mefenamic acid group: MBL in pre-treatment = 159.6 (SD 77.6) and in treatment = 127.3 (75.4). 20% reduction in MBL ($P = 0.004$). danazol: MBL in pre-treatment = 163.1 (SD 77.8) and in treatment = 64.8 (SD 43.8). 60% reduction. mefenamic vs danazol = 20% vs 60% ($P < 0.001$). 6 (30%) mefenamic patients reported side effects vs 15 (75%) with danazol ($P < 0.005$). 9 (45%) women in mefenamic acid group and 10 (50%) in danazol group refused offer to continue with treatment	Funding source: Commercial funding Study summary: Study showed danazol reduced MBL more than mefenamic acid, but was associated with more side effects.
Dunphy 1998 ²⁷⁷	randomised; double-blind EL = 1–	23: 11 medroxyprogesterone; 12 danazol randomised; 9 medroxy, 9 danazol analysed.	Population characteristics: women; menorrhagia (> 80 ml); > 18 years; not pregnant; no contraindications Country: Canada	Danazol 200 mg daily; medroxyprogesterone acetate 10 mg on 16–25 days of cycle treatment vs baseline; treatment vs treatment	7 months: 1 baseline; 3 treatment; 3 follow-up	MBL – alkaline haematin; side effects	MBL (mean): danazol ($n = 9$) – baseline = 592 (SD 336), 1 month treatment = 201 (SD 140), 3 months treatment = 72 (SD 108). 3 months post-treatment = 353 (SD 243). All differences $P < 0.05$ against baseline. Medroxy ($n = 9$) – baseline = 505 (SD 399), 1 month treatment = 378 (SD 321), 3 month treatment = 568 (SD 710). 3rd post treatment month = 150 (SD 121). No difference from baseline. Body weight: danazol mean increase at 3rd treatment month = 7 kg (SD 0.7) ($P = 0.0078$). Medroxy = 2.2 kg (SD 1.7) (NS). Side effects: 8 of 9 danazol vs 2 of 7 medroxy ($P = 0.035$). Drop-out: 3 danazol vs 2 medroxy	Funding source: Sanofi Winthrop Ltd

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Lamb 1987 ²⁸⁵	randomised; double-blind EL = 1+	76 entered. At 1 month 19 danazol, 17 placebo. At 3 months 15 danazol, 9 placebo	Population characteristics: women; > 25 years; menorrhagia; no pathology; between 45–110 kg; no cardiac, hepatic or renal impairment; no sensitivity to hormonal treatment; not pregnant. Country: UK	Danazol (200 mg daily for 1 month only); placebo treatment vs baseline; treatment vs placebo	7 months	MBL – tampon use; duration of bleeding; side effects	MBL: no figures given. Graph shows immediate reduction in danazol group and no change in placebo. Side effects: At 3 months: 79% of danazol vs 24% of placebo had weight gain > 1 kg. danazol mean gain = 2.85%. Reported side effects: weight gain, headache, nausea, amenorrhoea. Withdrawals: 19 danazol vs 27 placebo withdraw. 5 danazol vs 1 placebo withdraw due to side effects. 12 placebo vs 2 danazol withdrew due to lack of effectiveness.	Funding source: Not stated – Winthrop Labs provide drug and undertook analysis Study summary: danazol reduces MBL but with associated side effects.
Turnbull 1990 ²⁸²	non-randomised trial. EL = 2++	37 recruited; 20 had MBL > 80 ml; 19 agreed to study	Population characteristics: women; MBL > 80 ml; 34–46 years Country: UK	gestrinone 2.5 mg twice weekly; placebo treatment vs placebo	8 months: 2 placebo; 3 active treatment; 3 follow-up	MBL – alkaline haematin	Baseline MBL: median 173 ml (range 81–831 ml). MBL reduce in 15 of 19 patients during gestrinone period ($P < 0.01$), but no change in MBL during placebo period. Side effects: dizziness, headaches, giddiness and tiredness. No difference between placebo and treatment periods.	Funding source: Not stated Study summary: Gestrinone has a beneficial effect on menorrhagia, and provides an alternative treatment for those prepared to accept amenorrhoea.

Table 8.6 GnRH-a for treatment of HMB – comparative studies

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Carr 1993 ²⁹²	randomised; double-blind; ITT; cross-over EL = 1+	16 randomised	Population characteristics: Women; menstruating; pre-menopausal; uterine fibroids > 12 weeks Country: USA	GnRH-a; GnRH-a with medroxyprogesterone acetate (simultaneous)	24 weeks	Uterine volume – MRI;	Uterine volume: protocol A: GnRH-a plus MPA = no change in volume. GnRH-a plus placebo = -74% from baseline by end of treatment Protocol B: GnRH-a plus placebo = -73% from baseline by end of treatment GnRH-a plus MPA = further decline in volume Reduction in myoma volume (NS) Reduction in non-myoma volume ($P < 0.05$) Greater reduction in non-myoma tissue than myoma tissue.	Funding source: Not stated
Friedman 1988 ²⁹³	randomised; blinded; concealed EL = 1–	16 randomised; 7 to leuprolide only; 9 to leuprolide and medroxyprogesterone	Population characteristics: Women; pre-menopausal; symptomatic fibroids Country: USA	leuprolide only; leuprolide and medroxyprogesterone	24 weeks	Uterine volume; haemoglobin levels	leuprolide only vs leuprolide and medroxyprogesterone: Uterine volume: Baseline 601 vs 811 24 weeks 294 vs no change haemoglobin levels: increased in both after 24 weeks.	Funding source: No stated
Friedman 1993 ²⁹⁴	randomised EL = 1–	51 randomised; 26 (7 failed to complete) to Estrogen; 25 (12 failed to complete) to progestin 35 women with menorrhagia	Population characteristics: Women; fibroids Aged 27–53 years. Country: USA	GnRH-a plus either estrogen-progestin or progestin 'add-back' treatment vs baseline	12 months	self-reported menorrhagia	35 with reported menorrhagia at baseline. 12 months: 29 resolved; 3 improved; 2 no change; 1 worse. 18 of 18 in estrogen group improved, and 14 of 17 in progestin group improved. Add-back results: Hgb (g/dl) – estrogen-progestin: pre-treatment = 11.9, 12 weeks = 12.7, 52 weeks = 13.3. Progestin: pre-treatment = 12.0, 12 weeks = 13.0, 52 weeks = 13.6 Hct (%) – estrogen-progestin: pre-treatment = 35.7, 12 weeks = 37.3, 52 weeks = 39.3. Progestin: pre-treatment = 35.9, 12 weeks = 38.1, 52 weeks = 40.0 Bone mineral density: estrogen-progestin: pre-treatment = 1.102, 12 weeks = 1.074, 52 weeks = 1.053 ($P < 0.05$) Progestin: pre-treatment = 1.081, 12 weeks = 1.045, 52 weeks = 1.047 ($P < 0.05$) Control: pre-treatment = 1.081, 52 weeks = 1.078 (NS)	Funding source: TAP pharmaceutical and grant from Brigham and Women's Hospital Study summary: Limited results suggest GnRH reduces menorrhagia. Estrogen-progestin superior to progestin add-back. GnRH-a/steroid add-back regimens provide a useful long-term treatment strategy in women with large, symptomatic uterine myomas and may obviate the need for surgical intervention in selected cases. The estrogen-progestin add-back regimen was superior or equal to the progestin add-back regimen in all efficacy and safety parameters assessed.
Friedman 1991 ²⁹⁰	randomised; double-blind EL = 1+	128 – 75 with menorrhagia	Population characteristics: women; uterine fibroids; no malignancy; no previous GnRH-a; no treatment for 3 months; bone-density within 2 SD of normal; not pregnant or lactating. Country: USA	Leuprolide acetate depot 3.75 mg vs placebo for 4 weeks treatment vs placebo	24 weeks	fibroid volume; bloating; menorrhagia; pelvic pain; pelvic pressure; constipation; urinary frequency;	Menorrhagia: leuprolide ($n = 38$) – resolved or improved = 37 vs 1 no change or worse. Placebo ($n = 37$) – resolved or improved = 26 vs 11 no change or worse. Side effects ($n = 128$): hot flushes – leuprolide = 52 (83%) vs 5 (8%) placebo ($P < 0.0001$); vaginitis = 11 vs 0 ($P < 0.0005$); arthralgia = 9 vs 0 ($P < 0.005$); asthenia = 10 vs 3 ($P < 0.05$); peripheral oedema = 7 vs 1 ($P < 0.05$); insomnia = 6 vs 0 ($P < 0.05$); nausea = 6 vs 1 ($P < 0.05$); headaches = 18 vs 13;	Funding source: TAP pharmaceutical Study summary: Treatment reduces MBL compared with placebo but with high levels of adverse effects.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
						dyspareunia; menometrorrhagia	depression = 7 vs 2; emotional liability = 5 vs 1; decreased libido = 2 vs 0.	
Nakayama 1999 ²⁹⁵	randomised; blinded; concealed; ITT EL = 1-	12 randomised; 6 to add-back; 6 to no add-back	Population characteristics: Women; symptomatic fibroids; ovulatory cycles; no condition or medical known to affect bone mineral density Country: Japan	GnRH-a; GnRH-a with estriol add-back	6 months	Fibroid size; bone mineral density	Reduction in mean fibroid size by 53.6% by 2 months and a further 31.3% by 6 months in non-add back group; Reduction in mean fibroid size by 59.1% by 2 months and marginal further reduction by 6 months in add back group. Bone mineral density reduced to 96.5% of original by 2 months, and 92.5% by 6 months in the non-add back group; Bone mineral density did not change significantly in the add-back group.	Funding source: Not stated
Palomba 1998 ²⁹⁶	Randomised; double-blind EL = 1-	50 randomised; 25 to GnRH-a plus placebo; 25 to GnRH-s plus tibolone, 1 did not complete	Population characteristics: Women; symptomatic uterine fibroids; excluded if – liver disease, ischemic heart disease, alterations in lipid metabolism, diabetes, acute or recent vascular thrombosis, carcinoma of breast or endometrium. Country: Italy	GnRH-a plus placebo; GnRH-s plus tibolone	6 months	Fibroid size; fibroid symptoms; lipid profile; bone mineral turnover	GnRH-a plus placebo ($n = 25$) vs GnRH-s plus tibolone ($n = 24$): Uterine volume at baseline: 995.8 (SD 170.4) vs 976.1 (SD 114.9) Uterine volume at 6 months: 386.4 (SD 94.6) vs 414.8 (SD 98.1) Both $P < 0.01$ from baseline. Average menorrhagia scores (0 to 10): Baseline = 8.2 vs 8.0 6 months = 0 vs 2.5 (both $P < 0.01$ from baseline) Bone mineral density (g/cm ³): Baseline: 1056 vs 1044 6 months: 1002 vs 1035 $P < 0.01$ for placebo group vs baseline and vs treatment. Bone mineral levels: Serum alkaline phosphatase, osteocalcin levels, urinary calcium/creatinine, hydroxyproline/creatinine ratios significantly increased in placebo group compared with baseline and treatment group ($P < 0.01$) Lipid profile: Total cholesterol level, HDL-c level, Triglyceride level all increased from baseline and compared with treatment group ($P < 0.01$).	Funding source: Not stated Study summary: Administration of tibolone in association with GnRH-a reduces vasomotor symptoms and prevents bone loss, without compromising the therapeutic efficacy of GnRH-a alone.
Palomba 2002 ²⁹⁷	randomised; single blind; concealed; ITT EL = 1-	100 randomised; 50 to GnRH-a plus raloxifene, 45 completed; 50 to GnRH-a plus placebo, 46 completed.	Population characteristics: Women; Symptomatic uterine fibroids; excluded if – neoplastic, metabolic, endocrine, liver, haematological and infectious diseases; active rheumatoid arthritis; history or current acute vascular thrombosis; one mineral density less than 1; smoke more than 20 per day; hypoechoic or calcified fibroid; contraindicated medications. Baseline (treatment vs placebo):	to GnRH-a plus raloxifene; GnRH-a plus placebo	6 menstrual cycles	BMD	to GnRH-a plus raloxifene; GnRH-a plus placebo BMD level: significant fall compared with baseline and treatment group in placebo group ($P < 0.05$). No difference in treatment group between baseline and follow-up.	Funding source: Not stated

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			Age: 48.8 vs 47.5 BMD – lumbar spine: 1.078 vs 1.080 Country: Italy					
Palomba 2004 ²⁹⁸	RCT EL = 1–	100 randomised; 50 to GnRH-a plus raloxifene, 45 completed; 50 to GnRH-a plus placebo, 46 completed. 50 health pre-menopausal women acted population baseline	Population characteristics: Women; pre-menopausal; Symptomatic uterine fibroids; excluded if – neoplastic, metabolic, endocrine, liver, haematological and infectious diseases; active rheumatoid arthritis; history or current acute vascular thrombosis; bone mineral density less than 1; smoke more than 20 per day; hypochoic or calcified fibroid; contraindicated medications. Baseline (treatment vs placebo): Age: 48.8 vs 47.5 BMD – lumbar spine: 1.078 vs 1.080 Country: Italy	GnRH-a plus raloxifene; GnRH-a plus placebo	6 cycles	QoL – Kupperman index, Wechsler memory scale, mini-mental state examination, Hamilton rating scale for depression, self-rating anxiety scale, SF-36, Women's Health Questionnaire.	GnRH-a plus raloxifene ($n = 45$) vs GnRH-a plus placebo ($n = 46$) vs normal population ($n = 50$): Kupperman index (0 to 51): Baseline = 2.6 (1.2) vs 2.1 (1.1) vs 2.1 (1.2) 6th cycle = 22.8 (3.9) vs 25.6 (4.2) vs 2.5 (1.3) Wechsler memory scale (0 to 143): Baseline = 63.2 (6.9) vs 59.7 (6.2) vs 60.3 (5.8) 6th cycle = 48.2 (5.1) vs 46.2 (4.9) vs 58.8 (5.7) Mini-mental state examination: Baseline = 28.2 (1.5) vs 27.8 (1.5) vs 27.9 (1.8) 6th cycle = 24.3 (1.0) vs 23.4 (1.1) vs 27.5 (1.6) Hamilton rating scale for depression: Baseline = 18.2 (2.2) vs 19.9 (2.3) vs 5.8 (1.6) 6th cycle = 10.0 (1.8) vs 11.2 (1.7) vs 5.9 (1.7) Delf-rating anxiety scale: Baseline = 47.9 (3.2) vs 46.7 (2.9) vs 30.3 (2.4) 6th cycle = 36.8 (2.5) vs 34.1 (2.5) vs 31.2 (2.6) SF-36: Baseline = 50.4 (14.1) vs 52.6 (14.5) vs 84.2 (10.4) 6th cycle = 80.3 (11.5) vs 81.7 (12.6) vs 83.4 (10.2) Women's Health Questionnaire: Baseline = 86.3 (11.5) vs 84.5 (11.5) vs 25.2 (8.6) 6th cycle = 42.5 (8.7) 48.1 (9.9) vs 26.8 (9.4)	Funding source: Not stated Study summary: Study shows that GnRH-a cause reduction in cognitive functioning in women with symptomatic fibroids, but improves QoL to near normal levels.
Schlaff 1989 ²⁹⁹	randomised; double-blind; placebo; concealed; ITT EL = 1–	12 randomised; 5 received GnRH; 6 received placebo	Population characteristics: Women; symptomatic uterine fibroids; aged 29 to 47; fibroids > 3.5 cm; regular menstrual cycles without AUB. Groups balanced at baseline Country: USA	GnRH-a; placebo	6 months	Size of fibroid	placebo vs GnRH-a: Uterine volume: Baseline 457 vs 645 (NS) Post-treatment 656 vs 467 Myoma volume: Baseline 267 vs 402 Post-treatment 417 vs 334	Funding source: Not stated
Takeuchi 2000 ²⁹¹	randomised; prospective EL = 1–	67: 34 buserelin MP; 33 leuprorelin.	Population characteristics: women; pre-menopausal; uterine fibroids; endometriosis. Buserelin: 37 years, 158 cm, 52 kg. Leuprorelin: 33 years, 158 cm, 55 kg. Country: Japan	depot buserelin MP 1.8 mg; depot leuprorelin 1.88 treatment vs treatment	20 weeks	MBL – menstruation, petechia, amenorrhoea; side effects	Buserelin: 8 weeks = 52.9% amenorrhea; 20 weeks = 88.9% amenorrhea. Leuprorelin: 8 weeks = 84.4% amenorrhea; 20 weeks = 87% amenorrhea. Difference at 8 weeks $P < 0.01$, at 20 weeks NS. Hot flushes: at 12 weeks – buserelin = 5.9% vs 24.4% in leuprorelin. 11 of Buserelin and 15 of leuprorelin group were lost to follow-up by 24 weeks.	Funding source: Not stated

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
West 1992 ⁵⁷³	Comparative cohort study EL = 2-	20 in total, 10 to goserelin and MPA combined from strat, 10 to goserelin only then MPA after 3 months	Population characteristics: Women; symptomatic uterine fibroids Country: UK	goserelin and MPA combined from strat, goserelin only then MPA after 3 months	6 months	Fibroid volume; fibroid symptoms; vasomotor side effects	goserelin and MPA combined from strat vs goserelin only then MPA after 3 months: Fibroid volume: 3 months: 18% vs 39% 6 months: 18% vs 39% Fibroid symptoms: menorrhagia improvement: 8 of 9 vs 8 of 9 Endocrine response: Suppression of LH, FSH and estradiol in both groups.	Funding source: Not stated

Table 8.7 Antifibrinolytics for treatment of HMB – comparative studies

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Andersch 1988 ³⁰⁶	randomised; open; cross-over EL = 1+	15	Population characteristics: MBL > 80 ml; IUD or myomas excluded; not used IUD or contraceptives or pregnant within 6 months. Setting not specified, but from University O&G department Country: Sweden	Tranexamic acid 1.5 g × 3 for 3 days then 1 g × 2 for 2 further days. Flurbiprofen (100 mg × 2) for 5 days; Placebo treatment vs treatment; treatment vs placebo	6 consecutive cycles: 2 baseline; 2 group A; 2 group B	MBL – alkaline haematin test; duration of period; side effects	Placebo: mean MBL = 295 ± 52 ml. Tranexamic acid: mean MBL = 155 ± 33 ml (53% reduction [perhaps misprint, should be 47%], $P < 0.01$). Flurbiprofen: mean MBL 223 ± 44 ml (24% reduction, $P < 0.01$). Between group difference: tranexamic reduced MBL more than Flurbiprofen ($P < 0.01$). 7 of 15 (46%) in tranexamic and 4 of 15 (26.5%) in Flurbiprofen complained of side effects. No discontinuation due to adverse events.	Funding source: Non-commercial grants Study summary: Flurbiprofen useful addition to treatment for menorrhagia. Although tranexamic acid was generally more effective in reducing MBL, Flurbiprofen provides an important therapeutic alternative to antifibrinolytic agents, especially in patients with concomitant dysmenorrhoea.
Bonnar 1996 ³⁰⁵	Randomised; intention to treat EL = 1–	81 in total: 29 to etamsylate; 25 mefenamic acid; 27 tranexamic acid. 2 etamsylate, 2 mefenamic acid, 1 tranexamic acid excluded.	Population characteristics: Complaint of HMB; organic causes of menorrhagia excluded; history of renal or hepatic impairment, previous thromboembolic disease, inflammatory bowel disease, ulcers, coagulation or fibrinolytic disorders were excluded. A university O&G department Country: Ireland	Etamsylate (500 mg × 4); mefenamic acid (500 mg × 3); tranexamic acid (1 g × 4); no treatment treatments vs no treatment periods	6 consecutive menstrual cycles: 3 baseline; 3 treatment	MBL – alkaline haematin test; duration of bleeding; sanitary towel use; side effects	Tranexamic acid: MBL reduced by 89 ml (24 to 214 ml; 54% reduction; $P < 0.001$). Mean MBL 164 ($n = 78$) in control and 75m ($n = 72$) (89 ml difference) in treatment. Tranexamic acid vs etamsylate: = –97 ml (95% CI 140 to 154; $P < 0.001$); vs mefenamic acid = –56 ml ((95% CI 90 to 2 ml; $P < 0.05$)) (Perhaps misprint: may be 46 ml based on other figures in paper.) mefenamic acid: 20% reduction in MBL ($P < 0.001$). Etamsylate – no effect on MBL. 77% of patient wanted to continue with tranexamic acid after trial. 11 etamsylate (40%), 3 mefenamic acid (13%), 4 tranexamic acid (15%) withdraw from study. Poor efficacy was main reason. Reported side effects were nausea, headache and dizziness – no statistical assessment provided. Etamsylate = 8 ml increase with etamsylate, but no statistical difference. Mean MBL in pre-treatment = 170 ml ($n = 81$) vs 175 ml ($n = 63$) (+3%) (figures do not match reported figures) during treatment. Difference between treatments: +97 ml (95% CI 140 to 154; $P < 0.001$) against tranexamic acid; +51 ml (95% CI –96 to –6; $P < 0.05$) against mefenamic acid. 33% of patients wanted to continue with etamsylate after trial. 11 etamsylate (40%), 3 mefenamic acid (13%), 4 tranexamic acid (15%) withdraw from study. Poor efficacy was main reason. Mefenamic acid: a 43 ml (82 to 179) (20%) reduction in MBL ($P < 0.001$). Mean MBL in pre-treatment = 186 ml ($n = 69$) and 148 ml ($n = 64$) during treatment (difference of 38 ml). mefenamic acid reduce MBL by 56 ml (Perhaps misprint, should be 46 ml) less than tranexamic acid (95% CI 90 to 2 ml; $P < 0.05$) and 51 ml (95% CI –96 to –6; $P < 0.05$) more than against etamsylate. 74% of women wanted to continue with mefenamic acid after	Funding source: Commercial (Pharmacia) and state (Health Research Board of Ireland) funding Study summary: Tranexamic acid given at start of menstrual cycle would reduce MBL by half.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							the trial. 77% with tranexamic, and 33% with etamsylate. 11 etamsylate (40%), 3 mefenamic acid (13%), 4 tranexamic acid (15%) withdraw from study. Poor efficacy was main reason. Side effects were nausea, dizziness and headaches.	
Callender 1970 ³⁰⁴	Randomised; double-blind; cross-over EL = 1+	20. 16 completed.	Population characteristics: Complain of menorrhagia or referred for anaemia; no significant clinical or histological abnormality. Total: 32 years No setting specified, but study from Radcliffe Infirmary Country: UK	Tranexamic acid (1 g × 4) for 4 days or placebo or no treatment treatment vs placebo vs no treatment	9 consecutive menstrual cycles: 3 baseline; 3 group A; 3 group B	MBL – Oxford total body counter; duration of MBL; number of pads used; side effects	Tranexamic acid vs no treatment ($t = 3.44$, $P < 0.02$); tranexamic acid vs placebo ($t = 2.37$, $P < 0.05$). No difference between placebo and no treatment. MBL (ml) during placebo phase = 185; during no treatment phase = 197; during tranexamic acid phase = 122 Side effects were: nausea, headache for tranexamic acid – not fully reported.	Funding source: Kabi Pharmaceuticals supplied treatments and paid for study. Study summary: Tranexamic acid is safe and effective for treating menorrhagia.
Coulter 1995 ²⁷³	Systematic review; meta-analysis EL = 1+		Population characteristics: Searches undertaken on MEDLINE Country:	Review of evidence for treatment of HMB		MBL	Antifibrinolytics: Pooled result from 7 trials was a % reduction in MBL of 46.7 (95% CI 47.9–51.6). Reports on 4 RCT of etamsylate. Meta-analysis identifies a % blood loss reduction of 13.1 (95% CI 10.9–15.3). Norethisterone: 4 RCTs showed a reduction change in MBL of –3.6% (–6.1, 1.1) Danazol: 5 RCTs showed a combined reduction in MBL of 49.7% (47.9, 51.6) IUDs: 4 RCTs showed a combined reduction in MBL of 58.6 (56.7, 60.6) Mefenamic acid: Pooled results for 10 studies = –29% (95% CI 27.9–30.2). Diclofenac: 2 studies = –26.9% (23.3–30.6). Naproxen: 5 studies = –26.4% (24.6–28.3). Ibuprofen: 3 studies = –16.2% (13.6–18.7). OCP: 1 RCT – MBL reduction = 43% Side effects not reported.	Funding source: Not stated Study summary: Studies of this preparation report greater reductions in blood loss but slightly more side effects than mefenamic acid.
Edlund 1995 ³⁰³	Randomised; double-blind; double-dummy; placebo-controlled EL = 1++	91 randomised. Results on 68 reported. Kabi hi = 26; Kabi lo = 28; placebo = 14. ($n = 67$) 19 excluded to incomplete data or non-compliance. 4 for other reasons.	Population characteristics: Women. Age 18+. Regular menstrual cycles. MBL > 80 ml. Normal sized uterus. Excluded due to: concomitant disease; concomitant medication; previous thromboembolic, haemorrhage, or fibrinolytic disorders; creatinine > 120 $\mu\text{mol/l}$; cancer. O&G departments in 3 medical centres Country: Sweden	Tranexamic acid (1200 mg × 2) or (600 mg × 4) for 5 days or placebo Treatment vs placebo	3 consecutive cycles.	Menstrual blood loss – alkaline haematin; patient assessment of blood loss; number of towels used; side effects	Reduction in menstrual blood loss: placebo ($n = 14$) – pre-treatment = 242.5 (83–251.5 [range]) to treatment = 251.5 (87–566) (NS) (+ 4%); 600 mg × 4 ($n = 28$) – pre-treatment = 235.4 (83–728) to treatment = 162.6 (36–640) ($P < 0.001$) (–31%); 1200 mg × 2 ($n = 26$) – pre-treatment = 267.7 (101–554) to treatment = 163.7 (66–371) ($P < 0.001$) (–39%). No difference with intention-to-treat. Side effects not assessed by group allocation, but reported that no differences between groups. 23 (34%) women did not complete study	Funding source: Not stated Study summary: Tranexamic safe and effective treatment for menorrhagia.
Lethaby 2004 ³⁰⁰	Systematic review; meta-analysis EL = 1++					MBL	Antifibrinolytics vs etamsylate: 1 study – MBL = –97 ml (–134.36 to –59.64) in favour of TXA. Side effects reported. Withdrawals due to adverse events: RR 0.78 [95% CI 0.19, 3.15]. Meta-analysis of 2 RCTs of tranexamic vs placebo ($n = 48$)	Funding source: No funding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							<p>–110.17 [95% CI –146.54, –73.81]; $z=5.94$ ($P=0.001$). Antifibrinolytic vs NSAIDs: 1 study ($n=49$) – MBL = –46 (–76.02 to –15.98). Antifibrinolytic vs etamsylate: 1 study ($n=50$) – MBL = –97 ml (–134.36 to –59.64).</p> <p>Side effects: Withdrawals due to adverse events vs NSAIDs (1 study) RR = 2.65 [0.3, 23.77]. Vs etamsylate (1 study) RR = 0.78 [0.19, 3.15].</p>	
Nilsson 1967 ³⁰²	Randomised; double-blind; placebo-controlled EL = 1–	36 – 3 had fibroids, 2 had suspected fibroids, 1 adenomyosis	Population characteristics: Women; Aged 15 to 49; with suspected menorrhagia; gynaecological examination to determine cause of HMB Setting not specified, but from university O&G department Country: Sweden	Tranexamic acid – 0.25 to 0.5 mg × 6; increased to 0.5 to 1 mg × 6 for 4 days; or placebo treatment dose a vs treatment dose b vs placebo	5 consecutive periods: 2 baseline; 3 treatment	Menstrual blood loss alkaline haematin; duration of period; side effects	<p>MBL for 0 g = 149.1; 12 g dosage = 96.1 (–38% ± 4.47); for 24 g = 71 (–51% ± 5.23) ($n=19$). Results on 5 fibroid patients were 175.2 in control, 111.98 high dose (–36%), 142.98 low dose (–18%)</p> <p>Side effects reported by 15 people in high dose period, 7 in low dose period, 8 in placebo period (for all patients). Side effects were diarrhoea, nausea, headache and abdominal pain.</p> <p>No discontinuation from study</p>	Funding source: Not stated Study summary: Tranexamic acid was safe and effective for menorrhagia.
Preston 1995 ²⁷⁹	Randomised; double-blind; placebo-controlled; concealed; cross-over EL = 1++	46 women randomised: 21 Norethisterone; 25 tranexamic acid. 2 from each group withdrew.	Population characteristics: Women; Age 18+; regular cycle – 28 days ± 7; no hormone therapy for 3 months; no concomitant treatment; normal renal function; normal pelvic exam; negative cervical cytology. TXA: 40.6 years, 71.2 kg. NET: 39.3 years, 63.5 kg ($P<0.048$) Setting: university O&G department Country: UK	Tranexamic acid (1 g × 4) for 4 days or norethisterone (5 mg × 2) for 8 days or Placebo Treatment vs treatment; treatment vs placebo	4 consecutive cycles: 2 baseline/placebo; 2 treatment	Menstrual blood loss – alkaline haematin; QoL; side effects	<p>Tranexamic acid ($n=25$): Change from 175 ml to 97 ml (95% CI 62 to 108) ($P<0.0001$); 45% reduction (+23 to –93; $P<0.0001$). Norethisterone ($n=21$): Change from 173 ml to 208 ml (–64 to +2) ($P=0.26$); 20% increase (+114 to –62; $P<0.0001$). Between groups difference was 113 ml (95% CI 71 to 155) ($P<0.0001$).</p> <p>QoL (limitations on activities): 16 TXA vs 9 NET = better, 13 TXA vs 11 NET = same or worse.</p> <p>No differences between reported adverse events between groups. Placebo = 85%; tranexamic acid = 88%; norethisterone = 95%. Two (8%) drop-out from tranexamic acid group and 2 (9.5%) from the norethisterone group.</p>	Funding source: Commercially funded Study summary: Study shows that Tranexamic acid reduces MBL, but that norethisterone does not.
Vermeylen 1968 ³⁰⁷	Randomised; double-blind EL = 1–	22 entered. 16 used for analysis. 6 not assessed or withdrawn – pregnant, hypertension.	Population characteristics: History of menorrhagia; no gynaecological or coagulation disorder. Setting: not specified Country: Belgium	Tranexamic acid (0.5 g × 6) or placebo treatment vs placebo	6 consecutive menstrual periods	Menstrual blood loss (haemoglobin content) – alkaline haematin; duration of period; side effects	<p>MBL reduced by between 12–60% in active group compared with placebo, mean 35% (t-test $P<0.001$). Figures not given only shown in graph.</p> <p>Side effects: nervousness, anorexia; dizziness; insomnia, vomitus, adnominal cramps, tinnitus, diarrhoea, skin eruption, headache, menstrual pain.</p>	Funding source: Not stated Study summary: 'Oral administration of tranexamic acid (3 g daily) ... significantly decreases menstrual haemoglobin loss in women with so-called essential menorrhagia.'
Wellington 2003 ³⁰¹	Systematic review EL = 1+	5 Studies included in review	Population characteristics: Search strategy: MEDLINE; Embase and Adisbase. Keywords search terms used Country:	Use of tranexamic acid in menorrhagia		MBL; QoL; side effects.	<p>Oral tranexamic acid 2–4.5 g daily for 4–7 days per cycle reduced menstrual blood loss by 34–59% over 2–3 cycles. Based on 5 trials. Tranexamic more effective than NSAIDs, etamsylate, norethisterone, but less than IUD.</p> <p>Changes in MBL (ml) with tranexamic acid from baseline to treatment:</p> <p>164 vs 75 – Bonnar 197 vs 122 – Callender 168 vs 69 – Gleeson 295 vs 155 – Milsom</p>	Funding source: Not stated Study summary: '...oral tranexamic acid is an effective and well tolerated treatment for idiopathic menorrhagia.'

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							175 vs 97 – Preston Only one study reported on QoL, showing improvement, but was non-comparative, non-blind design. Studies reported a variety of side effects. 12% of patients reported adverse events, such nausea, vomiting, diarrhoea, and dyspepsia. No reports of DVT in any study. Review shows that quality of studies was varied.	

Table 8.8 NSAIDs for treatment of HMB – comparative studies

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Andersch 1988 ³⁰⁶	randomised; open; cross-over EL = 1+	15	Population characteristics: MBL > 80 ml; IUD or myomas excluded; not used IUD or contraceptives or pregnant within 6 months. Setting not specified, but from university O&G department Country: Sweden	Tranexamic acid 1.5 g × 3 for 3 days then 1 g × 2 for 2 further days. Flurbiprofen (100 mg × 2) for 5 days; Placebo treatment vs treatment; treatment vs placebo	6 consecutive menstrual cycles: 2 baseline; 2 group A; 2 group B	MBL – alkaline haematin test; duration of period; side effects	Placebo: mean MBL = 295 ± 52 ml. Tranexamic acid: mean MBL = 155 ± 33 ml (53% reduction [perhaps misprint, should be 47%], $P < 0.01$). Flurbiprofen: mean MBL 223 ± 44 ml (24% reduction, $P < 0.01$). Between group difference: tranexamic reduced MBL more than Flurbiprofen ($P < 0.01$). 7 of 15 (46%) in tranexamic and 4 of 15 (26.5%) in Flurbiprofen complained of side effects. No discontinuation due to adverse events.	Funding source: Non-commercial grants Study summary: Flurbiprofen useful addition to treatment for menorrhagia. Although tranexamic acid was generally more effective in reducing MBL, Flurbiprofen provides an important therapeutic alternative to antifibrinolytic agents, especially in patients with concomitant dysmenorrhoea.
Bonnar 1996 ³⁰⁵	Randomised; intention to treat EL = 1–	81 in total: 29 to etamsylate; 25 mefenamic acid; 27 tranexamic acid. 2 etamsylate, 2 mefenamic acid, 1 tranexamic acid excluded.	Population characteristics: Complaint of HMB; organic causes of menorrhagia excluded; history of renal or hepatic impairment, previous thromboembolic disease, inflammatory bowel disease, ulcers, coagulation or fibronolytic disorders were excluded. A university O&G department Country: Ireland	Etamsylate (500 mgx4); mefenamic acid (500 mg × 3); tranexamic acid (1 g × 4); no treatment treatments vs no treatment periods	6 consecutive menstrual cycles: 3 baseline; 3 treatment	MBL – alkaline haematin test; duration of bleeding; sanitary towel use; side effects	Tranexamic acid: MBL reduced by 89 ml (24 to 214 ml; 54% reduction; $P < 0.001$). Mean MBL 164 ($n = 78$) in control and 75m ($n = 72$) (89 ml difference) in treatment. Tranexamic acid vs etamsylate: = –97 ml (95% CI 140 to 154; $P < 0.001$); vs mefenamic acid = –56 ml ((95% CI 90 to 2 ml; $P < 0.05$)) (Perhaps misprint: may be 46 ml based on other figures in paper.) mefenamic acid: 20% reduction in MBL ($P < 0.001$). Etamsylate – no effect on MBL. 77% of patient wanted to continue with tranexamic acid after trial. 11 etamsylate (40%), 3 mefenamic acid (13%), 4 tranexamic acid (15%) withdraw from study. Poor efficacy was main reason. Reported side effects were nausea, headache and dizziness – no statistical assessment provided. Etamsylate – 8 ml increase with etamsylate, but no statistical difference Mean MBL in pre-treatment = 170 ml ($n = 81$) vs 175 ml ($n = 63$) (+3%) (figures do not match reported figures) during treatment. Difference between treatments: +97 ml (95% CI 140 to 154; $P < 0.001$) against Tranexamic acid; +51 ml (95% CI –96 to –6; $P < 0.05$) against mefenamic acid. 33% of patients wanted to continue with etamsylate after trial. 11 etamsylate (40%), 3 mefenamic acid (13%), 4 tranexamic acid (15%) withdraw from study. Poor efficacy was main reason. Mefenamic acid: a 43 ml (82 to 179) (20%) reduction in MBL ($P < 0.001$). Mean MBL in pre-treatment = 186 ml ($n = 69$) and 148 ml ($n = 64$) during treatment (difference of 38 ml). mefenamic acid reduce MBL by 56 ml (Perhaps misprint, should be 46 ml) less than tranexamic acid (95%	Funding source: Commercial (Pharmacia) and state (Health Research Board of Ireland) funding Study summary: Tranexamic acid given at start of menstrual cycle would reduce MBL by half.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							<p>CI 90 to 2 ml; $P < 0.05$) and 51 ml (95% CI -96 to -6; $P < 0.05$) more than against etamsylate.</p> <p>74% of women wanted to continue with mefenamic acid after the trial. 77% with tranexamic, and 33% with etamsylate.</p> <p>11 etamsylate (40%), 3 mefenamic acid (13%), 4 tranexamic acid (15%) withdraw from study. Poor efficacy was main reason.</p> <p>Side effects were nausea, dizziness and headaches.</p>	
Cameron 1990 ³⁰⁹	randomised; blinding not specified EL = 1-	32 in total: 17 mefenamic group; 15 norethisterone group	<p>Population characteristics: MBL > 80 ml; regular cycle; organic cause excluded.</p> <p>Average age: 40 years</p> <p>Setting: O&G department</p> <p>Country: UK</p>	Mefenamic acid 500 mg × 3 for 5 days; norethisterone 5 mg × 2 for 7 days treatment vs baseline	6 consecutive cycles: 2 baseline; 2 treatment A; 2 treatment B	MBL – alkaline haematin; number of days bleeding; interval between periods.	<p>Mefenamic acid: MBL at baseline = 123 ml (86–237) and during treatment = 81 ml (22–193) ($P < 0.001$); a -34% change. Norethisterone: MBL at baseline = 109 ml (81–236) and during treatment = 92 ml (43–189) ($P < 0.002$); a -15.5% change.</p> <p>Side effects: headache (4 mefenamic acid vs 5 norethisterone), abdominal pain (3 vs 3), nausea (2 vs 1).</p>	<p>Funding source: Commercial funding</p> <p>Study summary: We conclude that mefenamic acid and norethisterone were similarly effective in reducing the degree of MBL in women.</p>
Cameron 1987 ²⁶²	randomised EL = 1-	30 in total: 6 in danazol group; 8 in mefenamic acid group; 8 in norethisterone group; and 8 in coil group	<p>Population characteristics: Women; MBL > 50 ml</p> <p>Age: danazol = 42, mefenamic acid = 40, norethisterone = 39, progesterone coil = 40</p> <p>Parity: danazol = 2, mefenamic acid = 4, norethisterone = 4, progesterone coil = 2</p> <p>Country: UK</p>	Danazol (200 mg); mefenamic acid (500 mg × 3); norethisterone (5 mg × 2); progesterone coil treatment vs no treatment period	4 consecutive cycles – 2 with no treatment and 2 with treatment	MBL – alkaline haematin; length of cycle; PGE; PGF; PG concentrations	<p>In the mefenamic acid group MBL changed from 85 (range 68–169) in no treatment period to 47 (39–210) in the treatment periods ($P = 0.05$); a -44.5% change. danazol: pre-treatment = 203 ml, treatment = 51 ml; a -75% change. Progesterone coil: pre-treatment = 64 ml ($P < 0.05$), treatment = 45 ml; a -30% change. Norethisterone: pre-treatment = 131, treatment = 110; a -16% change.</p> <p>Side effects not reported.</p>	<p>Funding source: Not stated</p> <p>Study summary: All treatments except norethisterone reduce MBL.</p>
Chamberlain 1991 ³¹⁰	Minimisation; double-blind; double-dummy. EL = 1+	44 in entered, 34 finished: 22 in each arm. 6 of 22 in etamsylate and 4 of 22 in mefenamic group did not complete study.	<p>Population characteristics: Inclusion: Women 18–55; menorrhagia 80 ml>. Exclusion: malignant disease excluded; taking oral contraceptives excluded; hepatic impairment; want to become pregnant during study period; allergies to prostaglandins; anaemic; fitted with IUD; had fibroids.</p> <p>Setting not specified, but study from district general hospital O&G department.</p> <p>Country: UK</p>	Etamsylate 500 mg × 4; mefenamic 500 mg × 3 treatment vs treatment	4 consecutive cycles: 2 baseline; 2 treatment	MBL – alkaline haematin test; tampon use; side effects.	<p>Etamsylate reduced MBL by 20%. mefenamic acid reduced MBL by 24%. Reduction in MBL for etamsylate in 2 of 3 periods ($P < 0.01$) – 95% do not cross zero; significant for mefenamic acid on all three periods ($P < 0.01$, < 0.05, < 0.01 respectively). No difference between groups. Reduction in MBL in mefenamic acid group = 24%, $P < 0.02$, and regression to mean of $r^2 = 0.765$, $P < 0.01$.</p> <p>10 of 18 in mefenamic acid, and 5 of 16 in etamsylate group reported side effects – nausea, backache, bloated abdomen.</p> <p>No cessation due to side effects</p>	<p>Funding source: Not reported. Delandale Lab acknowledges.</p> <p>Study summary: Both treatments effective and perhaps should be used in combination.</p>
Coulter 1995 ²⁷³	Systematic review; meta-analysis EL = 1+		<p>Population characteristics: Searches undertaken on MEDLINE</p> <p>Country:</p>	Review of evidence for treatment of HMB		MBL	<p>Antifibrinolytics: Pooled result from 7 trials was a % reduction in MBL of 46.7 (95% CI 47.9–51.6).</p> <p>Reports on 4 RCT of etamsylate. Meta-analysis identifies a % blood loss reduction of 13.1 (95% CI 10.9–15.3).</p> <p>Norethisterone: 4 RCTs showed a reduction change in MBL of -3.6% (-6.1, 1.1)</p> <p>Danazol: 5 RCTs showed a combined reduction in MBL of 49.7% (47.9, 51.6)</p>	<p>Funding source: Not stated</p> <p>Study summary: Studies of this preparation report greater reductions in blood loss but slightly more side effects than mefenamic acid.</p>

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							<p>IUDs: 4 RCTS showed a combined reduction in MBL of 58.6 (56.7, 60.6)</p> <p>Mefenamic acid: Pooled results for 10 studies = -29% (95% CI 27.9–30.2). Diclofenac: 2 studies = -26.9% (23.3–30.6). Naproxen: 5 studies = -26.4% (24.6–28.3). Ibuprofen: 3 studies = -16.2% (13.6–18.7).</p> <p>OCP: 1 RCT – MBL reduction = 43%</p> <p>Side effects not reported.</p>	
Creatsas 1998 ³¹¹	randomised EL = 1–	48 in total: 23 in tenoxicam group; 25 in lynestrenol-ethinyl estradiol (L-EE) group	<p>Population characteristics: adolescents; menorrhagia; not pregnant</p> <p>Setting: University O&G department</p> <p>Country: Greece</p>	tenoxicam (20 mg); L-EE (1 tablet) Treatment vs no treatment period; treatment vs treatment	For one episode	Haematological parameters	<p>In tenoxicam group the before treatment Hct and HB levels were 32.6 and 10, respectively, and during the treatment period they were 35.9 and 11.5, respectively ($P < 0.001$). Tenoxicam vs L-EE for HCT = 35.9% vs 32.6% $P = 0.02$ and Hb = 11.5% vs 10.4% $P = 0.05$.</p> <p>3 (13%) patient in tranexamic group reported mild GI disorders ($P = 0.0028$ compared with L-EE)</p>	<p>Funding source: Not stated</p> <p>Study summary: Tenoxicam is considered an effective medication for the management of DUB during adolescence</p>
Dock ray 1989 ²⁸⁴	randomised; open EL = 1–	41 in total; 20 in mefenamic acid group; 20 in danazol group. 1 withdrawal, but group not stated	<p>Population characteristics: Menorrhagia > 80 ml; normal pelvic examination and pathology.</p> <p>Mefenamic group: age = 38.2, parity = 3.9, dysmenorrhoea = 13 of 20.</p> <p>Danazol group: age = 37.2, parity = 3.5, dysmenorrhoea = 15 of 20.</p> <p>Country: Ireland</p>	Mefenamic acid (500 mg × 3) for 5 days; danazol (100 mg × 2) for 60 days Treatment vs baseline; treatment vs treatment	4 consecutive cycles: 2 baseline; 2 treatment	MBL – alkaline haematin; dysmenorrhoea; side effects	<p>Mefenamic acid group: MBL in pre-treatment = 159.6 (SD 77.6) and in treatment = 127.3 (75.4). 20% reduction in MBL ($P = 0.004$). danazol: MBL in pre-treatment = 163.1 (SD 77.8) and in treatment = 64.8 (SD 43.8). 60% reduction. mefenamic vs danazol = 20% vs 60% ($P < 0.001$).</p> <p>6 (30%) Mefanamic patients reported side effects vs 15 (75%) with danazol ($P < 0.005$).</p> <p>9 (45%) women in mefenamic acid group and 10 (50%) in danazol group refused offer to continue with treatment</p>	<p>Funding source: Commercial funding</p> <p>Study summary: Study showed danazol reduced MBL more than mefenamic acid, but was associated with more side effects.</p>
Fraser 1991 ²⁷⁴	randomised EL = 1+	45 in total. 7 dropped out. 38 assessed: 19 in mefenamic (across 3 groups); 7 naproxen; 6 OCP; 6 danazol	<p>Population characteristics: Women; menorrhagia – ovulatory DUB; no pathology; no hormonal therapy within 3 months</p> <p>Country: Australia</p>	Mefenamic acid (500 mg × 3); naproxen; low dose monophasic oral contraceptive – ethinyl estradiol 30 µg and levonorhethrel 150 µg for 21 days; danazol (200 mg) daily Treatment vs baseline	8 consecutive cycles: 2 no treatment; 2 treatment; 2 no treatment; 2 treatment	MBL – alkaline haematin	<p>Mefenamic acid – group 1 – control = 131.1 ml (SD 80.8) treatment = 105.1 (SD 88.6) ($P = 0.198$) (–20%); group 2 – control = 101 (SD 52.5), treatment = 62.9 (SD 27.7) ($P = 0.002$) (–38%); group 3 – control = 90.3 (50.2), treatment = 55.3 (34) ($P < 0.001$) (–39%);</p> <p>Naproxen – control = 131.1 ml vs treatment = 115.6 (SD 113) ml ($P = 0.079$) (–12%);</p> <p>Oral contraceptive – 101 vs 57.8, $P < 0.001$, –43%;</p> <p>Danazol – 90.3 vs 45.5 (av), $P < 0.001$, –49%.</p> <p>Differences between mefenamic vs naproxen $P = 0.129$; vs oral contraceptive $P = 0.154$; vs danazol $P = 0.079$.</p> <p>Side effects not reported.</p>	<p>Funding source: Commercial funding</p> <p>Study summary: All treatments reduce MBL.</p>
Fraser 1981 ³¹²	randomised; cross-over; blinding and concealment not outlined. EL = 1–	85 entered. 69 completed.	<p>Population characteristics: Women; report menorrhagia from any cause (including IUD induced)</p> <p>Setting: patient recruited via advert, treated in University O&G department</p>	Mefenamic acid; placebo treatment vs placebo	4 consecutive cycles – 2 with placebo; 2 with active treatment	MBL – alkaline haematin; pain; nausea; headache; diarrhoea; depression; breast symptoms; sanitary towel	<p>Placebo period MBL = 66.9 ml (SE 4.7); mefenamic acid = 48.1 (SE 4.4). –28.1% difference ($P < 0.001$).</p> <p>Ovulatory DUB ($n = 28$) placebo = 70.7 (± 4.7) mefenamic = 47.3 (± 4.1) ($P < 0.001$). Anovulatory DUB ($n = 6$) 50.3 (± 11.2) vs (39.8 (± 15.4) (NS). IUD ($n = 6$) = 80.2 (± 11.7) vs 63.9 (± 11.2) (NS). Tubal sterilisation ($n = 25$) = 61.0 (± 6.5) vs 45.3 (± 6.1)</p>	<p>Funding source: Commercial (Parke-Davis) and government grants (Australian national health and medical research council)</p> <p>Study summary:</p>

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			Country: Australia			use; haematology	($P < 0.001$). Side effects not reported. Results for 16 (19%) women were not reportedly.	...Mefenamic acid should be of considerable value in Australia...
Grover 1990 ³¹³	randomised; double-blind EL = 1-	80 in total: 40 in mefenamic acid group and 40 in placebo group	Population characteristics: Women; complaint of menorrhagia; normal cervical cytology and secretory endometrium. Mefenamic: 35.8 years. Control: 35 years. Setting: O&G department Country: India	Mefenamic acid (500 mg x 3); placebo Treatment vs placebo	3 consecutive cycles	Relief from menorrhagia; number of days bleeding; number of pads used	Menorrhagia relieved in 86% of mefenamic group and 20% of placebo group ($P < 0.001$).	Funding source: Not stated Study summary: mefenamic acid proved to be a potent and efficacious agent in the control of unexplained menorrhagia.
Hall 1987 ³¹⁴	randomised; double-blind; cross-over; double-dummy EL = 1++	41 entered. 5 MBL < 80 ml. 36 assessed in cross-over design. 1 from group 1 and 2 from group 2 were lost to follow-up.	Population characteristics: MBL > 80 ml; no physical or organic problem; regular cycles; excluded if taking NSAIDs or steroids. Average age: Group 1: 40.5 years. Group 2: 38.1 years. Setting: O&G department Country: UK	Naproxen 550 mg x 1 then 275 x 4 for 4 days; mefenamic acid 500 mg x 3 Treatment vs baseline	6 consecutive cycles: 2 baseline; 2 treatment A; 2 treatment B	MBL – alkaline haematin; sanitary towel use; patient assessment; side effects	Baseline MBL = 118.5 ($n = 19$) and 129.3 ml ($n = 19$) in two groups. Naproxen: MBL reduced by 52 ml (44%) and 62 ml (48%) in each group ($P < 0.001$); mefenamic: MBL reduced by 54 ml (45.5%) and 61 ml (47%) ($P < 0.001$). 18 (50%) naproxen and 15 (42%) mefenamic acid patients report side effects – GI and nervous systems.	Funding source: Not stated Study summary: We believe cyclooxygenase inhibitors are useful for women with menorrhagia and a normal uterus...
Jakubowicz 1978 ³¹⁵	alternate allocation; placebo-controlled; double-blind; cross-over EL = 1-	18 entered. 15 assessed. 3 lost to follow-up	Population characteristics: women; menorrhagia; IUD, small fibroids, minor adenomyosis included; gross pathology excluded Setting: O&G outpatient department Country: Australia	Mefenamic acid 1000 mg x 3 placebo treatment vs baseline; treatment vs placebo	4 cycles: 2 treatment; 2 no treatment	sanitary towel use	Number of towels used: mefenamic acid = 32 (SD 32) (45% reduction), placebo = 43 (SD 44) (26.5% reduction), no treatment = 58.5 (SD 53) No side effects reported	Funding source: Parke Davis supplied NSAID and placebo.
Lethaby 2004 ³⁰⁸	Systematic review EL = 1++						NSAID vs oral progestogens T (2 RCTs, $n = 48$) MBL -22.97 [46.57, 0.62] in favour of NSAIDs. NSAIDs vs Progesterone IUS (1 RCT, $n = 16$) MBL -4 [-31.23, 23.23]. NSAID vs OCP (1 trial, $n = 26$) MBL 25.25 [-22.34, 72.84]. NSAIDs vs etamsylate = -42.88 ml/cycle [95% CI -86.25 to 0.50]	
van Eijkeren 1992 ³¹⁶	randomised; double-blind; placebo-controlled EL = 1++	19 entered. 8 did not complete. 11 assessed: 5 in placebo group; 6 in mefenamic acid group	Population characteristics: Women; MBL > 80 ml; Age ≤ 45 ; regular cycle; no IUD; no NSAIDs; no contraindications Setting: not specified Country: Netherlands	Mefenamic acid (500 mg x 3); placebo Treatment vs placebo; treatment vs no treatment period	Not stated	MBL – alkaline haematin; side effects; morphologic findings	MBL in placebo group 151 (SD 46) before treatment and 189 (SD 69) (+ 25%) during placebo treatment. MBL in mefenamic acid group = 108 (SD 27) before treatment and 65 (SD 19) (- 40%) during active treatment ($P < 0.01$). 1 women discontinued study to skin rash and was taking mefenamic acid. 7 others drop-out – 4 due to planned hysterectomy, 1 due to fibroid, 2 phase of menstruation.	Funding source: Commercially funded (Parke Davis)

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Vargyas 1987 ³¹⁷	randomised; double-blind; placebo controlled EL = 1+	32 in cross-over design	Population characteristics: women; MBL > 60 ml; exclusion criteria: anovulatory cycles, pathology in endometrium, extra-uterine disease or fibroids, senility to test treatments, thyroid dysfunction, hepatic or renal disease, abnormal cervical cytology. 16 to 42 years. Includes 7 women with IUD, 6 sterilised. Setting: O&G department Country: USA	Meclofenamate sodium 100 mg x 3 for 6 days; placebo treatment vs treatment; treatment vs baseline	6 consecutive cycles: 2 baseline; 4 cross-over	MBL – alkaline haematin; duration; sanitary towel use; side effects	MBL: baseline = 141.6 (± 15.9); placebo = 135.6 (± 11.3), meclomen = 69.0 (± 6.3). ($P < 0.0001$). MBL reduced by 49% in meclofenamate group and 4% in placebo group. Meclofenamate caused more dysmenorrhoea ($P < 0.006$), backache ($P < 0.02$), and headache ($P < 0.002$) than placebo. No difference in nausea or vomiting. 3 women did not complete study.	Funding source: Study summary: It appears that many women with unexplained menorrhagia may benefit from this treatment.
Ylikorkala 1986 ³¹⁸	randomised; placebo-controlled; cross-over EL = 1–	25 in total: 11 with fibroids; 14 without fibroids	Population characteristics: Menorrhagia; fibroids or not Country: Finland	Naproxen 500 mg x 2 for 5 days; placebo treatment vs baseline	6 consecutive cycles: 2 baseline; 2 treatment; 2 placebo	MBL – alkaline haematin; side effects	Fibroids group: MBL at baseline = 239.4 ml (SE 38.4); with placebo = 220.6 (47.2) (–8%); with naproxen = 195.6 (32.3) (–20%). Non-fibroids group: MBL at baseline = 135.9 (SE 10.9); with placebo = 150.7 (SE 9.1) (+11%); with naproxen = 96.8 (7.3) ($P < 0.001$) (–29%). No side effects reported. No discontinuations reported.	Funding source: Not reported Study summary: Naproxen reduces MBL in primary menorrhagia but not menorrhagia associated with fibroids.

Table 8.9 Etamsylate for treatment of HMB – comparative studies

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Bonnar 1996 ³⁰⁵	Randomised; intention to treat EL = 1–	81 in total: 29 to etamsylate; 25 mefenamic acid; 27 tranexamic acid. 2 etamsylate, 2 mefenamic acid, 1 tranexamic acid excluded.	Population characteristics: Complaint of HMB; organic causes of menorrhagia excluded; history of renal or hepatic impairment, previous thromboembolic disease, inflammatory bowel disease, ulcers, coagulation or fibrinolytic disorders were excluded. A university O&G department Country: Ireland	Etamsylate (500 mg x 4); mefenamic acid (500 mg x 3); tranexamic acid (1 g x 4); no treatment treatments vs no treatment periods	6 consecutive menstrual cycles: 3 baseline; 3 treatment	MBL – alkaline haematin test; duration of bleeding; sanitary towel use; side effects	<p>Tranexamic acid: MBL reduced by 89 ml (24 to 214 ml; 54% reduction; $P < 0.001$). Mean MBL 164 ($n = 78$) in control and 75m ($n = 72$) (89 ml difference) in treatment. Tranexamic acid vs etamsylate: = -97 ml (95% CI 140 to 154; $P < 0.001$); vs mefenamic acid = - 56 ml (95% CI 90 to 2 ml; $P < 0.05$)) (Perhaps misprint: may be 46 ml based on other figures in paper.) mefenamic acid: 20% reduction in MBL ($P < 0.001$).</p> <p>Etamsylate – no effect on MBL.</p> <p>77% of patient wanted to continue with tranexamic acid after trial.</p> <p>11 etamsylate (40%), 3 mefenamic acid (13%), 4 tranexamic acid (15%) withdraw from study. Poor efficacy was main reason. Reported side effects were nausea, headache and dizziness – no statistical assessment provided.</p> <p>Etamsylate – 8 ml increase with etamsylate, but no statistical difference Mean MBL in pre-treatment = 170 ml ($n = 81$) vs 175 ml ($n = 63$) (+3%) (figures do not match reported figures) during treatment. Difference between treatments: +97 ml (95% CI 140 to 154; $P < 0.001$) against tranexamic acid; +51 ml (95% CI -96 to -6; $P < 0.05$) against mefenamic acid.</p> <p>33% of patients wanted to continue with etamsylate after trial.</p> <p>11 etamsylate (40%), 3 mefenamic acid (13%), 4 tranexamic acid (15%) withdraw from study. Poor efficacy was main reason.</p> <p>Mefenamic acid: a 43 ml (82 to 179) (20%) reduction in MBL ($P < 0.001$). Mean MBL in pre-treatment = 186 ml ($n = 69$) and 148 ml ($n = 64$) during treatment (difference of 38 ml). mefenamic acid reduce MBL by 56 ml (Perhaps misprint, should be 46 ml) less than tranexamic acid (95% CI 90 to 2 ml; $P < 0.05$) and 51 ml (95% CI -96 to -6; $P < 0.05$) more than against etamsylate.</p> <p>74% of women wanted to continue with mefenamic acid after the trial. 77% with tranexamic, and 33% with etamsylate.</p> <p>11 etamsylate (40%), 3 mefenamic acid (13%), 4 tranexamic acid (15%) withdraw from study. Poor efficacy was main reason.</p> <p>Side effects were nausea, dizziness and headaches.</p>	<p>Funding source: Commercial (Pharmacia) and state (Health Research Board of Ireland) funding</p> <p>Study summary: Tranexamic acid given at start of menstrual cycle would reduce MBL by half.</p>

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
k	Randomised; placebo-controlled; crossover; double blind EL = 1+	31 entered. Only 9 primary menorrhagia patients. 9 patients were excluded from analysis.	Population characteristics: Inclusion/exclusion – complaint of HMB, a regular menstrual cycle, no organic disease. IUD HMB patients also included. Women referred to O&G department for HMB Country: UK	Etamsylate; placebo treatment vs treatment	4 consecutive cycles	Menstrual blood loss – alkaline haematin test; tampon use; side effects	For primary HMB menorrhagia only ($n = 9$): Difference between etamsylate and placebo = 59.4 ml ($P < 0.01$); Mean MBL reduction with etamsylate = 49.7 ± 2.3 SE. 95% CI 44.2 to 55.2, –46% MBL. Side effects: 34% (17 of 50) in placebo periods and 34% (18 of 53) in etamsylate. None reported as serious.	Funding source: Not reported Study summary: 'The results of the study suggest that etamsylate is a safe and effective agent in the treatment of primary menorrhagia...'
Lethaby 2004 ³⁰⁰	Systematic review; meta-analysis EL = 1++					MBL	Antifibrinolytics vs etamsylate: 1 study – MBL = –97 ml (–134.36 to –59.64) in favour of TXA. Side effects reported. Withdrawals due to adverse events: RR 0.78 [95% CI 0.19, 3.15]. Meta-analysis of 2 RCTs of tranexamic vs placebo ($n = 48$) –110.17 [95% CI –146.54, –73.81]; $z = 5.94$ ($P = 0.001$). Antifibrinolytic vs NSAIDs: 1 study ($n = 49$) – MBL = –46 (–76.02 to –15.98). Antifibrinolytic vs etamsylate: 1 study ($n = 50$) – MBL = –97 ml (–134.36 to –59.64). Side effects: Withdrawals due to adverse events vs NSAIDs (1 study) RR = 2.65 [0.3, 23.77]. Vs Etamsylate (1 study) RR = 0.78 [0.19, 3.15].	Funding source: No funding
Lethaby 2004 ³⁰⁸	Systematic review EL = 1++						NSAID vs oral progestogens T (2 RCTs, $n = 48$) MBL –22.97 [46.57, 0.62] in favour of NSAIDs. NSAIDs vs progesterone IUS (1 RCT, $n = 16$) MBL –4 [–31.23, 23.23]. NSAID vs OCP (1 trial, $n = 26$) MBL 25.25 [–22.34, 72.84]. NSAIDs vs etamsylate = –42.88 ml/cycle [95% CI –86.25 to 0.50]	
Chamberlain 1991 ³¹⁰	Minimisation; double-blind; double-dummy. EL = 1+	44 in entered, 34 finished: 22 in each arm. 6 of 22 in etamsylate and 4 of 22 in mefenamic group did not complete study.	Population characteristics: Inclusion: Women 18–55; menorrhagia 80 ml>. Exclusion: malignant disease excluded; taking oral contraceptives excluded; hepatic impairment; want to become pregnant during study period; allergies to prostaglandins; anaemic; fitted with IUD; had fibroids. Setting not specified, but study from district general hospital O&G department. Country: UK	etamsylate 500 mg \times 4; mefenamic 500 mg \times 3 treatment vs treatment	4 consecutive cycles: 2 baseline; 2 treatment	MBL – alkaline haematin test; tampon use; side effects.	Etamsylate reduced MBL by 20%. mefenamic acid reduced MBL by 24%. Reduction in MBL for etamsylate in 2 of 3 periods ($P < 0.01$) – 95% do not cross zero; significant for mefenamic acid on all three periods ($P < 0.01$, < 0.05 , < 0.01 respectively). No difference between groups. Reduction in MBL in mefenamic acid group =24%, $P < 0.02$, and regression to mean of $r^2 = 0.765$, $P < 0.01$. 10 of 18 in mefenamic acid, and 5 of 16 in etamsylate group reported side effects – nausea, backache, bloated abdomen. No cessation due to side effects	Funding source: Not reported. Delandale Lab acknowledge. Study summary: Both treatments effective and perhaps should be used in combination.
Coulter 1995 ²⁷³	Systematic review; meta-analysis EL = 1+		Population characteristics: Searches undertaken on MEDLINE Country:	Review of evidence for treatment of HMB		MBL	Antifibrinolytics: Pooled result from 7 trials was a % reduction in MBL of 46.7 (95% CI 47.9–51.6). Reports on 4 RCT of etamsylate. Meta-analysis identifies a % blood loss reduction of 13.1 (95% CI 10.9–15.3). Norethisterone: 4 RCTs showed a reduction change in MBL of –3.6% (–6.1, 1.1) Danazol: 5 RCTs showed a combined reduction in MBL	Funding source: Not stated Study summary: Studies of this preparation report greater reductions in blood loss but slightly more side effects than mefenamic acid.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							<p>of 49.7% (47.9, 51.6)</p> <p>IUDs: 4 RCTS showed a combined reduction in MBL of 58.6 (56.7, 60.6)</p> <p>Mefenamic acid: Pooled results for 10 studies = -29% (95% CI 27.9-30.2). Diclofenac: 2 studies = -26.9% (23.3-30.6). Naproxen: 5 studies = -26.4% (24.6-28.3). Ibuprofen: 3 studies = -16.2% (13.6-18.7).</p> <p>OCP: 1 RCT - MBL reduction = 43%</p> <p>Side effects not reported.</p>	

Table 9.1 Surgery as first-line treatment for HMB – comparative studies

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Barrington 2003 ²⁶⁰	randomised EL = 1+	50: 25 LNG-IUS; 25 Thermal balloon ablation. 2 LNG-IUS discontinued, 2 were lost to follow-up. 2 TBA lost to follow-up.	Population characteristics: women; menorrhagia; no pathology; cervical cavity > 12 cm Country: UK	LNG-IUS; thermal balloon ablation treatment vs baseline	6 months	MBL – PBAC	MBL (mean): IUS pre-treatment = 107 ml vs 31 ml post-insertion (–71%); Ablation pre-treatment = 122 ml vs 61 ml post-surgery (–50%). No difference between groups ($P = 0.689$). MBL (median): IUS pre-treatment = 75 ml vs 19 ml post-insertion; Ablation pre-treatment = 101 ml vs 27 ml post-surgery.	Funding source: not stated Study summary: Study shows LNG-IUS and thermal ablation are equivalent.
Cooper 1999 ²⁴³	Randomised; concealed EL = 1++	272 eligible, 187 recruited, 94 randomised to medical treatment, 93 to TCRE. By 2 years 86 medical and 87 TCRE patients remained in the study.	Population characteristics: Women; referred due to HMB; completed family; < 10 weeks size uterus; normal uterine pathology; referred for surgery. Baseline characteristics (medical vs TCRE): Age = 41.4 vs 41.9 Haemoglobin (g/dl) = 12.79 vs 12.61 Menstrual symptom rating: mild/moderate = 6 vs 4 Severe = 54 vs 52 Very severe = 26 vs 32 Bleeding score = 24.7 vs 24.8 Country: UK	Medical treatment; TCRE	2 years	QoL (SF-36); patient satisfaction; menstrual status; bleeding score	Outcomes for medical vs TCRE. QoL (SF-36): Baseline: Physical functioning = 78.67 vs 82.33 Social functioning = 68.35 vs 70.03 Role: physical = 53.01 vs 56.98 Role: emotional = 57.43 vs 55.03 Mental health = 58.20 vs 59.43 Energy/fatigue = 40.36 vs 41.49 Pain = 53.55 vs 58.14 General health = 68.17 vs 65.90 Change by 2 years: Physical functioning = 3.73 vs 5.00 Social functioning = 3.94 vs 10.59 Role: physical = 12.95 vs 18.60 Role: emotional = 11.25 vs 22.48 Mental health = 7.17 vs 9.98 Energy/fatigue = 10.06 vs 14.58 Pain = 11.38 vs 12.34 General health = –0.67 vs 1.69 No significant difference between groups. Patient satisfaction: Totally or generally satisfied with treatment = 48 (57%) vs 68 (79%), $P = 0.002$ Cure or acceptable improvement = 53 (61%) vs 69 (81%), $P = 0.017$ Treatment acceptable = 65 (77%) vs 79 (93%), $P = 0.004$ Menstrual status: No bleeding or light = 36 (42%) vs 50 (58%), $P = 0.04$ Unchanged or heavier = 16 (18%) vs 5 (6%), $P = 0.02$ Bleeding score = 6.8 (SD 9.9) vs 5.4 (SD 8.1)	Funding source: Scottish Office Department of Health Study summary: The results at 2 years consolidate the findings and conclusions based on the four-month follow up data. A policy of early TCRE is effective and safe and does not result in an increase in hysterectomies. It should not be routinely withheld in an effort to try alternative medical therapies.
Crosignani 1997 ²⁶³	randomised; open; prospective EL = 1+	97 assessed. 27 refused entry. 70 accepted entry to study – 35 in IUD group, 35 in endometrial resection group.	Population characteristics: women; 38 years or older; referred for hysterectomy; confirmed menorrhagia – PBAC > 100; pregnant or breast feeding excluded; using hormonal treatment in last 3 months; serious concomitant condition excluded.	LNG-IUS; endometrial resection	12 months – 6 and 12 months	MBL – PBAC; SF-36	MBL outcome: LNG-IUS ($n = 30$) baseline = 184.8 ml (SD 62.2), 12 months = 38.8 (SD 37.1) ($P < 0.001$). Endometrial resection ($n = 30$) baseline = 203.2 (SD 77.4), 12 months = 23.5 (SD 32.6) ($P < 0.001$). Difference between LNG-IUS and resection $P = 0.015$. Patient satisfaction: LNG-IUS: 29 (85%) satisfied. Endometrial resection: 33 (94%)	Funding source: National Research Council (Rome) Study summary: LNG-IUS produces slightly less satisfactory results than resection at 12 months.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			IUD group – age 43.8, parity = 1.8, BMI = 25.3 Endometrial resection group – age = 45.4, parity = 1.6, BMI = 24.0 Country: Italy				satisfied. Mean SF-36 scores at 12 months (LNG-IUS vs Resection): Physical functioning = 78.0 vs 79.2. Role limitation = 72.5 vs 74.2 Bodily pain = 58.9 vs 70.3 General health = 64.1 vs 70.3 Vitality = 56.3 vs 54.8 Social functioning = 69.8 vs 69.7 Role limitation = 61.3 vs 72.4 Mental health = 60.1 vs 59.6 Side effects reported by 19 of 34 in IUS group and 9 of 35 in resection group. 1 LNG-IUS patient lost to follow-up. 4 LNG and 3 resection patients had persistent menorrhagia after treatment and sought other treatment.	
Halmesmaki 2004 ²⁶⁴	randomised; prospective EL = 1+	119 LNG-IUS vs 117 hysterectomy. 81 IUDs at 12 months – 24 hysterectomy, 10 removed, 5 used ERT. 107 hysterectomies undertaken at 12 months.	Population characteristics: Women; 35–49; menstruating; completed family. No fibroids, endometrial polyps, urinary or bowel symptoms, ovarian pathology. Hysterectomy: age 43.1, parity = 2.1, BMI = 26.6. LNG-IUS: age = 43.0, parity = 2.1, BMI = 25.1 Country: Finland	LNG-IUS; Hysterectomy Treatment vs baseline; treatment vs treatment	12 months	FSH serum levels; Kupperman index – menopausal symptoms- hot flushes etc	FSH levels increased from 8.4 iu/ml at baseline to 13.8 iu/ml at 12 months vs 8.7 to 9.2 in LNG-IUS groups. ($P = 0.005$). No difference between or within groups on Kupperman index at 12 months (based on treatment use not intention-to-treat). Hot flushes increased in hysterectomy ($P = 0.02$) but not IUD; no difference between groups.	Funding source: Not stated Study summary: Hysterectomy may impair ovarian function.
Istre 2001 ²⁶⁶	Randomised EL = 1+	60: 30 LNG-IUS; 30 resection – 6 discontinued treatment by 12 months.	Population characteristics: women; menorrhagia (PBAC > 75); pre-menopausal; 30–49 years; regular uterine cavity < 10 cm; no pregnant or wanting to become so, breast feeding; large fibroid > 40 cm; pelvic disease; DVT; cancer; endometritis; liver disease; hormone therapy in 3 months Country: Norway	LNG-IUS; endometrial resection treatment vs baseline; treatment vs treatment	12 months	MBL = PBAC; duration of menstruation; haematological test; side effects	MBL (mean) – PBAC: LNG-IUS – baseline = 420 (SD 352), 12 months = 42 (SD 99) (–90%). TCRE – baseline = 404 (SD 480), 12 months = 7 (SD 15) (–98%). PBAC < 75 in 67% of LNG-IUS and 90% of TCRE patients at 12 months. ($P = 0.005$) Side effects: LNG-IUS 13 reported events – bleeding, abdominal pain, breast tenderness, headache, mood change. 6 discontinued treatment due to irregular bleeding, pain and acne.	Funding source: Leiras Oy Study summary: Resection reduces MBL more than IUS-LNG but only marginally.
Kupperman 2004 ³²⁶	RCT EL = 1+	63 in total, 31 (2 lost to follow-up) to hysterectomy and 32 (2 lost to follow-up) to medical treatment	Population characteristics: Women; failed medical treatment – medroxyprogesterone; 30 to 50 years of age; minimum of 2 months AUB; no hyperplasia on biopsy; excluded if – wanted future fertility desired, pregnant, or coagulopathy; long-acting treatments within 6 months; COC or IUD within 3 months; pelvic pathology for which surgery was indicated. Average age: hysterectomy = 42,	Hysterectomy; expanded medical treatment treatment vs treatment; treatment vs baseline	24 months	SF-36; Body image and sexual functioning; Mental health; General health	Baseline QoL scores (all on 0 to 100 scale, with 100 being optimal health): SF-36 MCS score: hysterectomy = 45 (SD 11), medicine = 45 (SD 10) SF-36 PCS score: hysterectomy = 43 (SD 8), medicine = 42 (SD 9) Body image score: hysterectomy = 59 (SD 28), medicine = 62 (SD 22) Satisfaction with sex: hysterectomy = 45 (SD 31), medicine = 56 (SD 32) Psychological well-being score: hysterectomy = 73 (SD 17), medicine = 71 (SD 18) Overall health score: hysterectomy = 58 (SD 19), medicine = 59	Funding source: Agency for Healthcare Research and Quality grant Study summary: Hysterectomy was superior to expanded medical treatment at 6 months in study population, at 24 months there was no difference by half of women in medical group had had hysterectomy.

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			<p>medicine = 40</p> <p>Health insurance = 65%, 81%</p> <p>< high school education = 39%, 38%</p> <p><\$25000 income = 42%, 53%</p> <p>Uterine fibroids = 65%, 63%</p> <p>Previous treatment:</p> <p>hysterectomy = COC 39%, Prostaglandin inhibitors 13%, GnRH-a 10%, D&C 19%, myomectomy 6%, endometrial ablation 3%</p> <p>Medicine = COC 50%, Prostaglandin inhibitors 19%, GnRH-a 6%, D&C 38%, myomectomy 0%, endometrial ablation 0%</p> <p>Country: USA</p>				<p>(SD 18)</p> <p>Satisfaction with health: hysterectomy = 38 (SD 22), medicine = 39 (SD 24)</p> <p>Change in QoL scores from baseline to 6 months using intention to treat (hysterectomy, medicine, <i>P</i> value for difference between groups):</p> <p>SF-36 MCS score: hysterectomy = 8, medicine = 2, <i>P</i> = 0.04</p> <p>SF-36 PCS score: hysterectomy = 6, medicine = 3, <i>P</i> = 0.21</p> <p>Body image score: hysterectomy = 15, medicine = 5, <i>P</i> = 0.07</p> <p>Satisfaction with sex: hysterectomy = 20, medicine = 10, <i>P</i> = 0.19</p> <p>Psychological well-being score: hysterectomy = 8, medicine = 0.2, <i>P</i> = 0.07</p> <p>Overall health score: hysterectomy = 12, medicine = 2, <i>P</i> = 0.006</p> <p>Satisfaction with health: hysterectomy = 31, medicine = 14, <i>P</i> = 0.01</p> <p>Symptom resolution: hysterectomy = 75, medicine = 29, <i>P</i> < 0.001</p> <p>Satisfaction with symptom level: hysterectomy = 44, medicine = 7, <i>P</i> < 0.001</p> <p>By 24 months 17 (53%) of medical group had undergone hysterectomy</p> <p>Change in QoL scores from baseline to 24 months using intention to treat (hysterectomy, medicine, <i>P</i> value for difference between groups):</p> <p>SF-36 MCS score: hysterectomy = 7, medicine = 4, <i>P</i> = 0.25</p> <p>SF-36 PCS score: hysterectomy = 7, medicine = 9, <i>P</i> = 0.19</p> <p>Body image score: hysterectomy = 11, medicine = 12, <i>P</i> = 0.97</p> <p>Satisfaction with sex: hysterectomy = 17, medicine = 18, <i>P</i> = 0.89</p> <p>Psychological well-being score: hysterectomy = 7, medicine = 3, <i>P</i> = 0.24</p> <p>Overall health score: hysterectomy = 11, medicine = 9, <i>P</i> = 0.64</p> <p>Satisfaction with health: hysterectomy = 27, medicine = 25, <i>P</i> = 0.68</p> <p>Symptom resolution: hysterectomy = 70, medicine = 256, <i>P</i> = 0.09</p> <p>Satisfaction with symptom level: hysterectomy = 46, medicine = 40, <i>P</i> = 0.36</p> <p>Change in QoL scores from baseline to 24 months using as treated (hysterectomy, medicine, <i>P</i> value for difference between groups):</p> <p>SF-36 MCS score: hysterectomy = 7, medicine = 2</p> <p>SF-36 PCS score: hysterectomy = 7, medicine = 11</p> <p>Body image score: hysterectomy = 12, medicine = 8</p> <p>Satisfaction with sex: hysterectomy = 17, medicine = 13</p> <p>Psychological well-being score: hysterectomy = 7, medicine = 0.6</p> <p>Overall health score: hysterectomy = 11, medicine = 5</p>	

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							Satisfaction with health: hysterectomy = 27, medicine = 20 Symptom resolution: hysterectomy = 71, medicine = 35 Satisfaction with symptom level: hysterectomy = 47, medicine = 31	
Learman 2004 ¹¹⁹	randomised – block; non-blinded; concealment EL = 1+	63 in total, 31 (2 lost to follow-up) to hysterectomy and 32 (2 lost to follow-up) to medical treatment	Population characteristics: Women; failed medical treatment – medroxyprogesterone; 30 to 50 years of age; minimum of 2 months AUB; no hyperplasia on biopsy; excluded if – wanted future fertility desired, pregnant, or coagulopathy; long-acting treatments within 6 months; COC or IUD within 3 months; pelvic pathology for which surgery was indicated. Average age: hysterectomy = 42, medicine = 40 Health insurance = 65%, 81% < high school education = 39%, 38% <\$25000 income = 42%, 53% Uterine fibroids = 65%, 63% Previous treatment: hysterectomy = COC 39%, Prostaglandin inhibitors 13%, GnRH-a 10%, D&C 19%, myomectomy 6%, endometrial ablation 3% Medicine = COC 50%, Prostaglandin inhibitors 19%, GnRH-a 6%, D&C 38%, myomectomy 0%, endometrial ablation 0% Country: USA	medical treatment; hysterectomy treatments vs baseline	2 years	Menstrual bleeding; Pelvic discomfort; urinary symptoms; menopausal symptoms	Baseline symptomology figures: Hysterectomy group = pelvic pain 74%, pelvic or bladder pressure 55%, low back pain 68%, Hot flushes 19%, Urinary symptoms – urgency 26%, frequent urination 26%, stress incontinence 29%. Continued vaginal bleeding at 6 months was 87% for medicine and 11% for hysterectomy ($P < 0.001$). Continued vaginal bleeding at 24 months was 37% for medicine and 7% for hysterectomy ($P < 0.001$). Continued bleeding in hysterectomy group due to cross-over between treatments. Medicine group = pelvic pain 88%, pelvic or bladder pressure 84%, low back pain 72%, Hot flushes 41%, Urinary symptoms – urgency 44%, frequent urination 41%, stress incontinence 25%. Change in symptom frequency from baseline at 6 months (intention-to-treat): Pelvic pain: hysterectomy = -2.3, medicine = -0.7, $P < 0.01$ Urinary urgency: hysterectomy = -0.7, medicine = 0.0, $P = 0.03$ Urinary incomplete emptying: hysterectomy = -0.6, medicine = +0.1, $P = 0.03$ Breast pain: hysterectomy = -1.3, medicine = -0.5, $P = 0.02$ No difference for other pelvic, urinary or menopausal symptoms. Change in symptom frequency from baseline at 2 years (intention-to-treat): Urinary incomplete emptying: hysterectomy = -0.8, medicine = -0.3, $P = 0.04$ Hot flushes: hysterectomy = -0.6, medicine = 0.5, $P < 0.01$ No difference for other pelvic, urinary or menopausal symptoms. Change in symptoms for groups as treated: Hysterectomy only groups produced significant reduction in symptoms, except for stress incontinence ($P = 0.34$) and urge incontinence ($P = 0.74$). Medicine then hysterectomy group produced same results, except hot flushes not significant ($P = 0.13$). Medicine only group produced significant reductions in symptoms for pelvic pain, pelvic pressure, and stress incontinence ($P < 0.05$), all other changes were non-significant.	Funding source: Agency of HealthCare Research and Quality grant Study summary: Hysterectomy was more effective treatment than additional medical treatment in this selected patient group.
Marjoribanks 2004 ³²⁵	Systematic review EL = 1++	8 RCTs including 821 women	Population characteristics: Cochrane Menstrual Disorders and Subfertility Group trial register (September 2005), the Cochrane Central Register of Controlled Trials (CENTRAL/CCTR) on The Cochrane Library (Issue 3, 2005), MEDLINE (1966 to September	Surgical vs medical therapies		MBL – objective and PBAC; QoL; Additional treatment; Adverse events	Two trials comparing oral pharmaceuticals with endometrial ablation. Control of bleeding (cure or improvement): 4 months ($n = 186$) Surgery 77/93 vs medical 29/93; OR = 10.62 (5.3 to 21.27) in favour of surgery. 2 year ($n = 173$) Surgery 69/87 vs medical 53/86; OR = 2.39 (1.21 to 4.70) in favour of surgery.	Funding source: No funding Study summary: Surgery, especially hysterectomy, reduces menstrual bleeding at one year more than medical treatments but

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			2005), EMBASE (1980 to September 2005), Current Contents (1993 to September 2005), Biological Abstracts (1969 to September 2005), PsycINFO (1985 to September 2005), CINAHL (1982 to September 2005), and reference lists of articles Country:				<p>5 years ($n = 140$) Surgery 61/71 vs medical 52/69; OR = 1.99 (0.84 to 4.73) in favour of surgery.</p> <p>Amenorrhoea rates:</p> <p>4 months ($n = 186$) Surgery 34/93 vs medical 3/93; OR = 17.29 (5.08 to 58.87) in favour of surgery</p> <p>2 year ($n = 173$) Surgery 33/87 vs medical 26/86; OR = 1.41 (0.75 to 2.65) in favour of surgery</p> <p>5 years ($n = 140$) Surgery 41/71 vs medical 47/73; OR = 0.76 (0.39 to 1.48) in favour of surgery</p> <p>Bleeding score:</p> <p>4 months ($n = 183$) WMD = 1.12.70 (115.04 to -10.36) in favour of surgery</p> <p>2 years ($n = 173$) WMD = -1.40 (-4.10 to 1.30)</p> <p>Pre-menstrual symptoms (breast discomfort, bloating, irritability, headaches, depression) – At 4 months all less likely in surgery than medical treatment. At 2 years and 5 years no difference between medical and surgical groups.</p> <p>Patient satisfaction:</p> <p>4 months ($n = 183$) – OR = 8.28 (4.29 to 15.97) in favour of surgery</p> <p>2 year ($n = 173$) OR = 2.83 [1.46, 5.50] in favour of surgery</p> <p>5 years ($n = 140$) - OR = 1.69 (0.77 to 3.70) in favour of surgery</p> <p>Extra surgery received:</p> <p>2 year ($n = 236$) OR = 0.12 [0.06, 0.22] in favour of surgery</p> <p>5 years ($n = 140$) - OR = 0.11 (0.06 to 0.22) in favour of surgery</p> <p>Physical function:</p> <p>4 months + 10.16 (SD 16.51) + 4.84 (SD 16.72) $P = < 0.05$</p> <p>2 years + 5.00 (SD 18.97) + 3.73 (SD 17.19) $P = 0.65$</p> <p>5 years + 7.75 (SD 16.39) + 1.06 (SD 23.81) $P = 0.10$</p> <p>Social function:</p> <p>4 months + 17.44 (SD 16.51) + 7.57 (SD 26.26) $P = < 0.05$</p> <p>2 years + 10.59 (SD 26.52) + 3.94 (SD 25.26) $P = 0.10$</p> <p>5 years + 10.24 (SD 24.49) + 2.96 (SD 27.22) $P = 0.10$</p>	LNG-IUS appears equally effective in improving quality of life. The evidence for longer term comparisons is weak and inconsistent. Oral medication suits a minority of women long term.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							Physical role: 4 months + 32.26 (SD 38.23) + 15.32 (SD 46.78) $P = < 0.01$ 2 years + 18.60 (SD 44.58) + 12.95 (SD 44.58) $P = 0.42$ 5 years + 31.62 (SD 33.15) + 15.14 (SD 39.77) $P = 0.06$ Emotional role: 4 months + 31.54 (SD 45.94) + 8.96 (SD 49.93) $P = < 0.01$ 2 years + 22.48 (SD 50.47) + 11.25 (SD 45.17) $P = 0.13$ 5 years + 33.81 (SD 34.11) + 14.35 (SD 40.61) $P = 0.02$ Mental health: 4 months + 15.01 (SD 19.00) + 4.78 (SD 16.69) $P = < 0.01$ 2 years + 9.98 (SD 19.14) + 7.17 (SD 19.20) $P = 0.35$ 5 years + 13.26 (SD 16.94) + 3.62 (SD 18.21) $P = 0.01$ Energy/fatigue: 4 months + 20.53 (SD 20.76) + 7.07 (SD 20.23) $P = < 0.01$ 2 years + 14.58 (SD 21.96) + 10.06 (SD 19.57) $P = 0.17$ 5 years + 17.31 (SD 22.35) + 10.62 (SD 18.79) $P = 0.07$ Pain: 4 months + 21.62 (SD 31.33) + 8.84 (SD 26.39) $P = < 0.01$ 2 years + 12.34 (SD 27.20) + 11.38 (SD 28.51) $P = 0.82$	

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							<p>5 years + 14.81 (SD 25.35) + 11.98 (SD 23.66) $P = 0.6$</p> <p>General health: 4 months + 10.49 (SD 20.85) -0.25 (SD 15.99) $P < 0.01$</p> <p>2 years + 1.69 (SD 18.83) -0.67 (SD 13.90) $P = 0.36$</p> <p>5 years + 6.97 (SD 23.10) -3.88 (SD 20.13) $P = 0.01$</p> <p>Four RCTs included comparing surgery (hysterectomy, ablation) with LNG-IUS.</p> <p>Objective MBL (1 RCT, $n = 223$) OR 25.72 [1.5, 439.98] at 12 months in favour surgery. Subjective MBL (3 RCTs, $n = 189$) – OR = 3.99 [1.53, 10.38] at 12 months in favour of surgery.</p> <p>Amenorrhoea rates: 6 months (1 RCT, $n = 46$) OR 0.63 [0.10, 4.21] 1 year (2 studies, $n = 120$) OR 1.90 (0.76 to 4.73) in favour of surgery 2 years ($n = 43$) OR = 1.60 (0.42 to 6.03) 3 years ($n = 40$) OR 1.63 (0.44 to 5.95)</p> <p>Mean reduction in PBAC: 12 months ($n = 127$) – WMD = 44.07 [33.01, 55.12] in favour of surgery.</p> <p>QoL: SF-36: General health (3 RCTs, $n = 354$) WMD = 1.83 [-2.13, 5.78] physical function ($n = 274$) WMD = 2.91 (-1.36 to 7.19); mental health ($n = 277$) WMD = 2.97 (-1.21 to 7.16); vitality ($n = 275$) WMD = 2.77 (-2.03 to 7.57); physical role limitation ($n = 271$) WMD = 3.64 (-3.58 to 10.86); emotional role ($n = 269$) WMD = 9.67 (1.65 to 17.69) in favour of surgery; social function ($n = 274$) WMD = 3.64 (-1.14 to 8.43); bodily pain ($n = 274$) WMD = 6.98 (1.68 to 12.29) in favour of surgery.</p> <p>Satisfaction at 12 months OR 1.91 [0.82, 4.48] in favour of surgery.</p> <p>Adverse events at 12 months OR 0.24 [0.11, 0.49] in favour of surgery.</p> <p>Additional surgery at 12 months: ($n = 423$) OR = 0.11 (0.04 to 0.30) in favour of surgery.</p> <p>Additional surgery at 24 months (1 RCT, $n = 79$) OR 0.69 [0.20, 2.40]</p>	

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Rauramo 2004 ²⁶⁸	randomised; open; equivalence EL = 1+	60: 30 LNG-IUS; 29 endometrial resection – 1 not randomised. 12 months – 6 LNG IUS vs 1 ablation discontinued or treatment failure. 36 months 5 vs 7 discontinued or treatment failure. 19 vs 22 at 36 months.	Population characteristics: women; menorrhagia; not pregnant or lactating; finished family; normal uterine cavity; abnormal uterine bleeding; pathology. LNG-IUS: 41.4 years, 73.4 kg. TCRE: 42.1 years, 70.4 kg. Country: Norway	LNG-IUS; endometrial resection treatment vs treatment; treatment vs baseline	3 years	MBL = PBAC; duration of menstruation; haematological test; side effects Analysis based on intention-to-treat.	MBL: LNG-IUS (median)- baseline ($n = 30$) = 261.5 (60–1503), 1 year ($n = 24$) = 12, 2 years ($n = 20$) = 8.5, 3 years ($n = 19$) = 7. Resection – baseline ($n = 29$) = 311 (81–2506), 1 year ($n = 28$) = 8.5, 2 years ($n = 24$) = 10, 3 years ($n = 22$) = 4. Difference between groups not significant. Adverse events: 1 oedema from LNG, plus 3 endometritis, 2 PID, 1 expulsion. 1 endometritis, 1 bleeding and pain from resection, plus 1 stroke	Funding source: Schering AG Study summary: Both treatments effectively reduced MBL.
Soysal 2002 ²⁷⁰	randomised; blind EL = 1+	72: 36 ablation vs 36 IUD. 1 ablation and 5 IUD not included in analysis due to treatment failure.	Population characteristics: Women; > 40 years; completed family; menorrhagia; no pathology; no cancer. LNG-IUS: 44.1 years. TBA: 43.8 years. Country: Turkey	Thermal balloon ablation after GnRH-a; LNG IUD (20 µg daily) Treatment vs baseline; treatment vs treatment	12 months	MBL – PBAC; QoL; Side effects	MBL: TBA – baseline PBAC = 417 (SD 81.4), 12 month PBAC = 21.8 (SD 14) ($P < 0.0001$). LNG-IUD – baseline PBAC = 408 (SD 101), 12 month PBAC = 55 (SD 11) ($P < 0.001$). TBA vs LNG = 388.2 vs 343 reduction ($P < 0.001$). QoL: SF-36 and HADs no difference between groups, except on role limitation where TBA better. No baseline data shown. Patient satisfaction: would recommend treatment = 70% for TBA vs 96% for LNG-IUD. Side effects: 21 of 36 LNG patients reported 1 or more side effects vs 8 of 36 in TBA group. ($P < 0.05$). Discontinuation: 5 LNG-IUS vs 1 TBA discontinued due to treatment failure.	Funding source: Not stated Study summary: Study shows that LNG-IUS and TBA are equivalent.

Table 10.1 Indications for non-hysterectomy surgery or interventional radiology – comparative studies

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Vuorma 2003 ⁵⁷⁴	Comparative; cohorts EL = 2–	376 – 184 in hysterectomy group, 192 in conservative treatment group	Population characteristics: Women; Referred due to HMB; aged 35 to 64 Country: Finland	Correlates with treatment plan	N/A	Multiple regression analysis of correlates with treatment plan	Correlates with choosing hysterectomy over conservative treatment: Patient preference for hysterectomy, OR = 95% CI 0.08 to 0.25 Pelvic pain, OR = 95% CI 1.02 to 2.71 Irregular periods, OR = 95% CI 0.33 to 0.96 Unemployment, OR = 95% CI 0.15 to 0.98 Anxiety, OR = 95% CI 0.95 to 0.99 Other factors, such as age, desire for future pregnancies, and inconvenience of HMB were not significant factors in treatment plan.	Funding source: Not stated

Heavy menstrual bleeding

Table 10.2 Indications for surgery (non-hysterectomy) – non-comparative studies

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Bongers 2002 ³²⁹	Prognostic; case series EL = 3	Prognostic factors for treatment failure – age, duration of menstruation, dysmenorrhoea, position of uterus, uterine depth, endometrial thickness > 4 mm	130	Women; undergone thermal balloon ablation due to HMB Country: Netherlands	Multivariate analysis of prognostic factors	Hazard ratios for prognostic factors: age = 0.86 ($P = 0.1$), duration of menstruation = 1.2 ($P = 0.1$), dysmenorrhoea = 1.3 ($P = 0.51$), position of uterus – retroversion = 3.3 ($P = 0.02$), endometrial thickness > 4 mm = 3.6 ($P = 0.02$)	Funding source: Not stated Study summary: Study shows that age, position of uterus and endometrial thickness are prognostic factors for success of ablation.
Bourdrez 2004 ²⁴⁴	Prospective; cohort EL = 3	Patient preferences for treatments	96	Women; DUB; scheduled for either hysterectomy, endometrial ablation and LNG-IUS. No statistical difference between groups for age or symptoms. Country: Netherlands	Importance of symptoms; reasons for treatment choice; patient preference to avoid hysterectomy	HMB was most serious symptom for 74% of IUD group, 77% of ablation group and 84% of hysterectomy group. Main reasons to choose treatment: IUD – Short or no admittance, fast recovery, no general anaesthetics, no hysterectomy, no oral contraceptive. Ablation – No IUD, No hysterectomy, No oral contraceptive, Advice from gynaecologist, Short or no admittance. Hysterectomy – no complaints anymore, no oral contraceptive, No IUD, Advice of gynaecologist. Patient preference: 70% of women undergoing ablation preferred this to hysterectomy when success rate was presumed to be 50%. 95% of LNG-IUS patients preferred this to hysterectomy when success was presumed to be 50%	Funding source: Not stated Study summary: Study shows that the majority of women are willing to take a 50:50 chance of treatment success to avoid hysterectomy.
Hurskainen 2004 ⁴⁸³	randomised EL = 3	LNG-IUS; hysterectomy	236 – 119 (116 available at 12 months) to LNG-IUS, 117 (112 available at 12 months) to hysterectomy	women; menstruating; subjective menorrhagia; aged 35 to 49; completed families; Excluded if – submucous fibroids, endometrial polyps, urinary or bowel symptoms due to large fibroid, or ovarian pathology. Country: Finland	Predictors of outcome	Neither presence of fibroids nor age were predictors of outcome at 12 months for LNG-IUS or hysterectomy. Multiple regression analysis showed that MBL was the most significant factor predicting outcome. Comparison of women with and without objective menorrhagia (> 80 ml MBL). For women in LNG-IUS group women without menorrhagia had better QoL outcomes than women with menorrhagia on: anxiety ($P = 0.04$), EQ-5D ($P = 0.05$). In the hysterectomy group, women without menorrhagia had better outcomes than those with menorrhagia on: anxiety ($P = 0.007$), emotional well-being ($P = 0.01$) and energy ($P = 0.0002$). Women without menorrhagia had better outcomes with LNG-IUS than women with menorrhagia on EQ-5D ($P = 0.03$). Women with menorrhagia had better outcomes with hysterectomy than LNG-IUS for: anxiety ($P = 0.003$), general health ($P = 0.04$), energy ($P = 0.05$), and pain relief ($P = 0.04$).	Funding source: Not stated Study summary: Success or failure of treatment of menorrhagia is multi-factorial, so difficult to predict in individual cases.
Sculpher 1998 ²⁴⁵	Cohort EL = 3	Patient preferences for surgery	221	Women; referred to specialist care with menorrhagia. Average age: 40.94 Duration of menorrhagia = 18 months Country: UK	Importance scores for patient outcomes	Mean importance scores: Stops periods for good = 1.18 Not removing womb = 0.71 Back to usual activities as soon as possible = 1.07 Removing womb = 0.47 Least pain and discomfort = 0.68 Hospital stay as short as possible = 0.59 Reduce periods = 0.42 Resume sex life as soon as possible = 0.59	Funding source: Not stated Study summary: Many women referred for surgery for menorrhagia have conflicting objectives from treatment.

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
						No worry about contraception = 0.14 Not leaving scar = 0.14 Patient preferences based on descriptions of surgery: abdominal hysterectomy = 43% endometrial resection = 41% Neither = 4% Unable to choose = 11%	

Table 10.3 Endometrial ablation for treating HMB – comparative studies

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Aberdeen Endometrial Ablation Trials Group 1999 ³³¹	randomised; concealment; intention-to-treat EL = 1+	204 – 105 (76 at 4 years) to ablation, 99 (72 at 4 years) to hysterectomy	Population characteristics: Women; menorrhagia; uterine size = 10 weeks; aged < 50; < 100 kg Country: UK	Hysterectomy; endometrial ablation – laser or TCRE; GnRH pre-treatment Hysterectomy vs ablation	4 years	Menstrual bleeding pattern; patient satisfaction	Gynaecological outcomes at 4 years: Amenorrhoea rates: ablation = 33 (45%), hysterectomy = 65 (98%) Brown discharge: ablation = 9 (12%) Hypomenorrhoea: ablation = 29 (40%), hysterectomy = 1 (2%) Patient satisfaction at 4 years: Totally satisfied: ablation = 33 (43%), hysterectomy = 41 (57%) Generally satisfied: ablation = 28 (37%), hysterectomy = 23 (32%) Fairly satisfied: ablation = 8 (11%), hysterectomy = 3 (4%) Neutral or dissatisfied: ablation = 7 ((%), hysterectomy = 5 (7%)	Funding source: Scottish Office grant Study summary: High percentage of women who have ablation will require further surgery, and this has associated costs.
Abbott 2003 ³³⁷	Randomised – 2:1 ratio, computer generated; concealment – opaque envelopes; double-blind EL = 1+	57 randomised. 38 Novasure, and 19 Cavaterm	Population characteristics: Women; referred for AUB; PBAC > 150; no intrauterine pathology; normal endometrial biopsy; uterine length < 12 cm; pre-menopausal gonadotrophin level; excluded if – hyperplasia or malignancy found, pelvic inflammatory disease; endometriosis found; had had a caesarean section. Average age: Cavaterm = 40.5, NovaSure = 40.5 Parity: Cavaterm = 2, Novasure = 2 Country: Australia	Cavaterm – balloon ablation; Novasure – bipolar radiofrequency ablation; pre-treatment of D&C in Cavaterm group	6 and 12 months	Menstrual category; MBL – PBAC; QoL – EQ-5D	Change in menstrual status from baseline to 6 and 12 month follow-up (normal or no bleeding): Cavaterm: 0%, 18 of 18 (100%), 17 of 17 (100%). Novasure: 0%, 30 of 35 (85%), 26 of 37 (70%). No difference between groups. Patient satisfaction at 12 months: Cavaterm = 83% (15/18) Novasure = 92% (34/37) No major complications in either group Change in MBL (PBAC) from baseline to 12 months: Cavaterm: 334 to 21 Novasure: 482 to 3 Difference between groups, $P = 0.2$. QoL – EQ-5D and SF-12: Cavaterm produced change on EQ-5D VAS scale ($P = 0.48$), but not on EQ-5D index, SF-12 PCS or SF-12 MCS. Novasure produced significant change on all indexes: EQ-5D VAS scale ($P = 0.006$), EQ-5D index ($P = 0.001$), SF-12 PCS ($P < 0.001$) or SF-12 MCS ($P = 0.016$). No difference between techniques, except for SF-12 MCS ($P = 0.04$)	Funding source: Not stated Study summary: Both techniques are effective and safe, but Novasure produced better quality of life outcomes.
Abbott 2003 ¹⁰¹	Cohort EL = 2+	139: 55 Cavaterm, 34 ELA, 13 ELITT, 37 NovaSure	Population characteristics: Women; menorrhagia; PBAC > 150; No intrauterine pathology; normal biopsy; Uterine length < 12 cm; pre-menopausal gonadotrophin level; Normal smear test; no plans for future childbearing. Country: UK and Australia	ELA, Cavaterm, ELITT, Novasure	12 months	QoL: EQ-5D, SF-12	Endometrial ablation vs general population at baseline: EQ-5D index: ablation = 0.72 (SD 0.28) vs general population = 0.89 (SD 0.17), $P < 0.0001$. EQ-5D VAS: 75.79 (SD 17.21) vs 85.19 (SD 15.51), $P < 0.0001$. SF-12 PCS: 46.31 (SD 8.80) vs 52.8, $P < 0.0001$. SF-12 MCS: 43.28 (SD 4.55) vs 51.9, $P < 0.0001$ Endometrial ablation baseline vs 12 month: EQ-5D index: ablation = 0.72 (SD 0.28) vs general population = 0.83 (SD 0.25), $P = 0.005$. EQ-5D VAS: 75.79 (SD 17.21) vs 82.49 (SD 15.28), $P < 0.0001$. SF-12 PCS: 46.31 (SD 8.80) vs 51.24 (SD 7.54), $P < 0.0001$. SF-12 MCS: 43.28 (SD 4.55) vs 49.31 (SD 10.07), $P < 0.0001$ Endometrial ablation 12 months results vs general population: EQ-5D index: ablation = 0.83 (SD 0.25 vs general population = 0.89 (SD 0.17), $P = 0.03$.	Funding source: Unclear? Grants for research on ELITT and NovaSure Study summary: Quality of life in women who have undergone ablation is improved to normal level, equivalent to the general population.

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							EQ-5D VAS: 82.49 (SD 15.28) vs 85.19 (SD 15.51), NS. SF-12 PCS: 51.24 (SD 7.54) vs 52.8, NS. SF-12 MCS: 49.31 (SD 10.07) vs 51.9, NS	
Alborzi 2002 ⁴⁰¹	randomised; blinding and concealment not mentioned EL = 1-	90: 45 pre-treatment group, 45 control group	Population characteristics: Women; menorrhagia – subjective; excluded if – active pelvic inflammatory disease, hyperplasia, malignancy; extensive uterine cavities; large fibroids; wish for future fertility Country: Iran	Pre-treatment – danazol 600 mg daily for 4 to 6 weeks or Decapeptyl one ampule monthly for 2 months; control group	3 months	Menstrual bleeding patterns; Duration of procedure; adverse events.	Operative time: Pre-treatment = 25 min (SD 4), control = 40 min (SD 5) Distending medium used during procedure: Pre-treatment = 3.5 litres, Control = 4.5 litres Menstrual bleeding pattern (normal or no bleeding): Pre-treatment = 42 (93%), control = 42 (93%)	Funding source: Not stated Study summary: Ablation is an effective treatment, but pre-treatment has no effect on patient outcome, though does reduce operating time.
Barrington 2003 ²⁶⁰	randomised EL = 1+	50: 25 LNG-IUS; 25 Thermal balloon ablation. 2 LNG-IUS discontinued, 2 were lost to follow-up. 2 TBA lost to follow-up.	Population characteristics: women; menorrhagia; no pathology; cervical cavity > 12 cm Country: UK	LNG-IUS; thermal balloon ablation treatment vs baseline	6 months	MBL – PBAC	MBL (mean): IUS pre-treatment = 107 ml vs 31 ml post-insertion (~71%); Ablation pre-treatment = 122 ml vs 61 ml post-surgery (~50%). No difference between groups ($P = 0.689$). MBL (median): IUS pre-treatment = 75 ml vs 19 ml post-insertion; Ablation pre-treatment = 101 ml vs 27 ml post-surgery.	Funding source: not stated Study summary: Study shows LNG-IUS and thermal ablation are equivalent.
Bhattacharya 1997 ³³⁸	randomised – computer-generated; concealment – sealed envelopes EL = 1-	372 (phase 1 = 105, phase 2 = 267) randomised. 188 to ELA, 184 to TCRE. 157 of ELA received treatment, 180 of TCRE received treatment.	Population characteristics: Women; 50 years or younger; < 100 kg; DUB diagnosis; uterus less than 10 weeks Average age: ELA = 40.4, TCRE = 40.9 Bleeding score (accumulated 1 to 5 scale scores for duration of period): ELA = 23, TCRE = 24 Country: UK	Endometrial Laser Ablation (ELA); Transcervical Resection of the Endometrium (TCRE)	12 months	Duration of procedure; Equipment failure; Complications; menstrual bleeding patterns; Acceptability of treatment; Patient satisfaction	Duration of procedure: ELA = 30min (SD 10), TCRE = 21 min (SD 9) Equipment/instrument failure: ELA = 17, TCRE = 5 Complications: ELA = 7, TCRE = 10 Menstrual bleeding pattern at 12 months: Normal or no bleeding – ELA = 106 (72%); TCRE = 100 (68%) Patient assessment of outcome – cured or acceptability reduction in MBL: ELA = 109 (67%), TCRE = 99 (64%) Patient satisfaction – satisfied or very satisfied: ELA = 144 (90%), TCRE = 140 (91%)	Funding source: Not stated Study summary: No difference between ELA and TCRE in terms of outcome for DUB.
Bhattacharya 1996 ³⁶⁰	Groups based on RCT EL = 2+	204 – 99 (21 non-responders) in hysterectomy, 105 (23 non-responders) in ablation	Population characteristics: Women; part of previous RCT for ablation vs hysterectomy for HMB Country: UK	Hysterectomy; Endometrial ablation – ELA or TCRE	2 years	Bladder function; ovarian function	Cystometry findings: Total bladder dysfunction – hysterectomy = 14 (31%), Ablation = 17 (35%) Bladder symptoms: Stress incontinence – hysterectomy = 32 (44%), ablation = 35 (44%) Urge incontinence – hysterectomy = 15 (21%), ablation = 15 (19%) Ovarian function: FSH level > 40 – hysterectomy = 3 (6%), ablation = 5 (10%) Patients on HRT – hysterectomy = 8 (16%), ablation = 5 (10%) Hot flushes – hysterectomy = 25 (35%), ablation = 35 (44%) Worsening of symptoms from baseline to 2 years:	Funding source: Not stated Study summary: Bladder and ovarian symptoms do not differ between hysterectomy and ablation at 2 years follow-up.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Bongers 2005 ³³⁶	randomised; concealment EL = 1+	126 randomised. 83 to bipolar ablation, 43 to balloon ablation. No loss to follow-up	Population characteristics: women; PBAC > 150; uterine cavity was 6 to 11 cm; normal smear test; negative Chlamydia test; FSH level < 40 iu/l; excluded if: desire to retain fertility, coagulation disorders, prior uterine surgery. Average age: bipolar = 42.2, balloon = 43.3 PBAC Score: 570 (150 to 3401, 620 (188 to 3220) Country: Netherlands	bipolar radiofrequency endometrial ablation; thermal balloon ablation	12 months	Quality of life – SF-36, depression scale, Rotterdam symptom checklist, State-Trait Anxiety Inventory	Stress incontinence – hysterectomy = 11 (15%), ablation = 13 (16%) Urge incontinence – hysterectomy = 10 (14%), ablation = 12 (15%) Hot flushes – hysterectomy = 5 (7%), ablation = 14 (18%) SF-36 scores (at baseline (SD) and at 12 months (SD) for bipolar then balloon, with <i>P</i> values for change since baseline, and comparison of treatments): Physical function: 82 (SD 19) to 91 (SD 18), 83 (SD 16) to 88 (SD 21), <i>P</i> < 0.001, <i>P</i> = 0.54 Role physical: 79 (SD 30) to 94 (SD 28), 73 (SD 27) to 89 (SD 24), <i>P</i> < 0.001, <i>P</i> = 0.56 Role emotional: 85 (SD 26) to 99 (SD 5), 80 (SD 26) to 95 (SD 15), <i>P</i> < 0.001, <i>P</i> = 0.97 Social functioning: 76 (SD 19) to 89 (SD 16), 76 (SD 21) to 86 (SD 21), <i>P</i> < 0.001, <i>P</i> = 0.86 Mental health: 72 (SD 18) to 80 (SD 15), 72 (SD 18) to 80 (SD 18), <i>P</i> < 0.001, <i>P</i> = 0.74 Energy/vitality: 56 (SD 19) to 73 (SD 18), 54 (SD 20) to 64 (SD 21), <i>P</i> < 0.001, <i>P</i> = 0.88 Pain: 62 (SD 20) to 76 (SD 24), 63 (SD 22) to 77 (SD 25), <i>P</i> < 0.001, <i>P</i> = 0.59 General health: 73 (SD 19) to 81 (SD 18), 76 (SD 21) to 75 (SD 23), <i>P</i> = 0.18, <i>P</i> = 0.84 On differences between groups on Rotterdam symptom checklist or state-trait anxiety score.	Funding source: Not stated Study summary: Both methods of ablation significantly improve QoL
Bongers 2004 ³³⁶	randomised – 2:1 ratio; double-blind; intention-to-treat; allocation concealment – opaque envelopes EL = 1+	126 randomised. 83 to bipolar ablation, 43 to balloon ablation. No loss to follow-up	Population characteristics: women; PBAC > 150; uterine cavity was 6 to 11 cm; normal smear test; negative Chlamydia test; FSH level < 40 iu/l; excluded if: desire to retain fertility, coagulation disorders, prior uterine surgery. Country: Netherlands	bipolar radiofrequency endometrial ablation; thermal balloon ablation	3, 6, and 12 months follow-up	Amenorrhoea rates; MBL – PBAC; duration of menstruation; dysmenorrhoea; presence of clots.	Amenorrhoea rates at 3, 6, and 12 months: Bipolar = 51%, 55%, 56% Balloon = 8%, 8%, 8% Relative risk = 6.6, 7.1, 7.1 (1.8 to 27) Change in MBL – PBAC. Figures only shown graphically. However, reduction significant from baseline in both group (<i>P</i> = 0.001), and bipolar reduce MBL more than balloon (<i>P</i> = 0.02). Dissatisfaction with treatment at 3, 6, and 12 months: Bipolar = 4%, 7%, 6% Balloon = 27%, 27%, 23%	Funding source: Equipment provided by companies Study summary: Bipolar ablation is more effective than balloon ablation for treating menorrhagia.
Bongers 2000 ³⁶¹	Cohort; comparative; prospective EL = 2–	152 of which 75 TCRE, 77 TBEA	Population characteristics: Women; menorrhagia; failed medical treatment; uterus < 12 cm; no submucous fibroids or intra-uterine adhesions Country: Netherlands	TCRE; TBEA TCRE vs TBEA	24 months	Patient satisfaction; Subsequent surgery; complications	Patient satisfaction: Satisfied or better with TCRE: 3 months = 68 (91%), 6 months = 44 (64%), 12 months = 31 (54%), 24 months = 23 (49%) Satisfied or better with TBEA: 3 months = 66 (86%), 6 months = 45 (73%), 12 months = 48 (76%), 24 months = 30 (64%) Cumulative re-intervention rate at 3 years: TCRE = 26%, TBEA = 13%, NS Complications: 13 (17%) of TCRE had to be abandoned. 8 (10%) of TBEA had to be converted to TCRE	Funding source: Not stated Study summary: TBEA is as effective as TCRE but with lower complications rates.
Boujida 2002 ³³⁹	randomised; concealed EL = 1–	120: 61 (4 lost to follow-up by 5 years) rollerball ablation, 59 (3 lost to follow-up by 5 years)	Population characteristics: Women; uterine bleeding disorders requiring hysterectomy; Exclude if uterine size twice normal; wanted future fertility; had pain as major symptom. Mean age: REA = 42.6,	Rollerball Endometrial Ablation; Transcervical Resection of the Endometrium	5 years	Bleeding index; Additional surgery; complications	Bleeding index, based on numbers of days bleeding in 3 month period (Pre-opt <i>n</i> = 120, 2 years = 60, 5 years = 40): REA: Pre-operatively = 36, 2 years = 13, 5 years = 16 TCRE: Pre-operatively = 34, 2 years = 13, 5 years = 18 Additional surgery at 5 years: REA = 20, TCRE = 16	Funding source: West Zealand Health Authority

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
		5 years) TCRE	TCRE = 44.8 Number with menorrhagia = 31, 30 Number with submucous fibroids = 13, 12 Country: Denmark				Recommend to a friend: 49 in REA and 46 in TCRE would recommend ($P > 0.05$) Complications: 1	
Cooper 2002 ³⁴¹	Randomised – 2:1 ratio; multicentre EL = 1+	265 randomised. 175 (153 available at 12 months) to Novasure, 90 (82 available at 12 months) to Rollerball	Population characteristics: Women; pre-menopausal; Aged between 25 and 50; No STD; FSH < 40 iu/l; Excluded if: active infection; pelvic inflammatory disease; previous uterine surgery that would interfere; previous endometrial ablation; abnormal smear test; taking hormonal treatment; desire for future fertility; abnormal or obstructed uterus (myomas, polyps > 2 cm); If uterus was < 6 cm or > 10 cm. Average age: Novasure = 39.7, Rollerball = 39.9. Parity: Novasure = 2.2, Rollerball = 2.2 PBAC: Novasure = 562, Rollerball = 562 Country: USA	NovaSure – Electrode ablation; rollerball ablation;	3, 6, and 12 months	MBL – PBAC; Adverse events; QoL	Change in PBAC score from baseline, 6 months, and 12 months: Novasure: 562 (SD 381), 28.1 (SD 58.2), 26.8 (SD 57.4) Rollerball: 562 (SD 487), 41.9 (SD 57.4), 36.4 (SD 66.3). Adverse events: Novasure = 23 (13%), Rollerball = 23 (25.3%) Patient satisfaction at 12 months: Novasure = 92.8%, Rollerball = 93.9% QoL – un-validated measure: Improvements shown in patients physical and mental well being for both Novasure and rollerball.	Funding source: Novacept Inc Study summary: Novasure is a safe and effective technique for ablation of endometrium for menorrhagia.
Cooper 2004 ³⁴²	Prospective; multicentre; randomised – 2:1 ratio; blinding not mentioned; concealment not mentioned EL = 1++	322: 215 (194 evaluable) in MEA group, 107 (96 evaluable) in REA group	Population characteristics: Women; Pre-menopausal; Aged > 30 years; no plans to become pregnant; failed or refused medical treatment; PBAC score > 185; Submucosal myomas < 3 cm; No hyperplasia or carcinoma; no active pelvic inflammation; no previous ablation surgery; no caesarean section scar; No IUD devices. Average age: MEA = 40.5, REA = 40.9 PBAC = 451.8 (SD 356.6), 524.6 (SD 429.5) Country: USA	Microwave ablation (MEA); Rollerball Ablation (REA); pre-treatment of leuprolide acetate 3.75 mg Surgery vs baseline; surgery vs surgery	3-, 6-, 12 month follow-up	MBL – PBAC; amenorrhoea rates; complications; adverse events; QoL – SF-36; Patient satisfaction; treatment acceptability.	PBAC scores at 12 months: 87.0% of MEA group had PBAC < 75 based on intention-to-treat compared with 83.2% for REA ($P = 0.4$). Figures were 96.4% and 92.7% ($P = 0.24$) for all evaluable patients. Actual PBAC scores changed from 450 to 10 in MEA group, and 501 to 24 in REA group (both $P < 0.0005$). No difference between techniques with or without presence of myomas ($P = 0.59$ with myomas vs $P = 0.18$ without myomas). No difference between success (PBAC < 75) with or without presence on myomas.(no figures shown). No adverse events reported. SF-36 scores change from baseline to 12 months: MEA – physical component = 47.1 (SD 9.22) to 54.1 (SD 6.6), mental component from 46.5 (SD 8.1) to 52.2 (SD 9.1). REA – physical component change from 46.5 (SD 8.1) to 53.6 (SD 6.9), mental component from 46.6 (SD 11.4) to 51.5 (SD 9.7).	Funding source: Not stated Study summary: Microwave ablation is safe and efficacious treatment for menorrhagia

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Cooper 2005 ³⁴⁰	randomised – 1:1 ratio, balanced blocks; concealment – opaque envelopes EL = 1++	279 screened. 263 randomised. 129 to MEA, 143 to TCRE. At 5 years, 116 MEA and 120 TCRE available.	Population characteristics: Women; HMB – subjective; completed families; no endometrial atypia; uterus no greater than 10 weeks size. Country: UK	Microwave Endometrial Ablation (MEA); Transcervical Resection of the Endometrium (TCRE); Pre-treatment of depot goserelin 3.6 mg	5 years	Menstrual bleeding pattern; QoL – SF-36; additional treatment	Change in menstrual bleeding pattern from baseline: normal or no bleeding: MEA = 111 (96%), TCRE = 115 (96%) Additional surgical treatment: MEA = 31 of 129 (25%), TCRE = 40 of 134 (29.5%) Change in SF-36 scores for MEA and TCRE, respectively, between baseline and 5 years (MEA baseline, TCREA baseline, MEA change, MEA <i>P</i> value of change since baseline, TCRE change, MEA <i>P</i> value of change since baseline): Physical functioning: 84.6 (SD 19.2), 82.2 (SD 23.3), 0.2 (SD 24), NS, -1.2 (SD 21), NS. Social functioning: 60.1 (23.0), 60.1 (22.9), 7.7 (30), <i>P</i> < 0.01, 9.7 (25), <i>P</i> < 0.001. Role – physical: 56.5 (42.2), 62.9 (41.7), 17 (54), <i>P</i> < 0.01, 11 (43), <i>P</i> < 0.01. Role – emotional: 61.8 (42.5), 62.6 (43.2), 19 (48), <i>P</i> < 0.001, 20 (41), <i>P</i> < 0.001. Mental health: 63.6 (18.8), 63.8 (21.7), 1.4 (21), NS, 1.2 (21), NS. Energy/fatigue: 44.3(22.6), 43.3 (24.3), 9.3 (25), <i>P</i> < 0.001, 12 (23), <i>P</i> < 0.001. Pain: 55.4 (28.2), 63.7 (26.1), 9.3 (35.0), <i>P</i> < 0.01, 6.4 (31), <i>P</i> < 0.05. General Health: 69.7 (21.7), 73.0 (19.4), -3.3 (26), NS, -2.4 (19), NS. Patient satisfaction: MEA = 100 (86%), TCRE = 87 (74%) Cure or acceptable improvement: MEA = 95 (83%), TCRE = 88 (75%)	Funding source: Not stated Study summary: Both treatments are safe and effective treatments for HMB, however, MEA is associated with greater patient satisfaction.
Cooper 1999 ²⁴³	Randomised; concealed EL = 1++	272 eligible, 187 recruited, 94 randomised to medical treatment, 93 to TCRE. By 2 years 86 medical and 87 TCRE patients remained in the study.	Population characteristics: Women; referred due to HMB; completed family; < 10 weeks size uterus; normal uterine pathology; referred for surgery. Baseline characteristics (medical vs TCRE): Age = 41.4 vs 41.9 Haemoglobin (g/dl) = 12.79 vs 12.61 Menstrual symptom rating: mild/moderate = 6 vs 4 Severe = 54 vs 52 Very severe = 26 vs 32 Bleeding score = 24.7 vs 24.8 Country: UK	Medical treatment; TCRE	2 years	QoL (SF-36); patient satisfaction; menstrual status; bleeding score	Outcomes for medical vs TCRE. QoL (SF-36): Baseline: Physical functioning = 78.67 vs 82.33 Social functioning = 68.35 vs 70.03 Role: physical = 53.01 vs 56.98 Role: emotional = 57.43 vs 55.03 Mental health = 58.20 vs 59.43 Energy/fatigue = 40.36 vs 41.49 Pain = 53.55 vs 58.14 General health = 68.17 vs 65.90 Change by 2 years: Physical functioning = 3.73 vs 5.00 Social functioning = 3.94 vs 10.59 Role: physical = 12.95 vs 18.60 Role: emotional = 11.25 vs 22.48 Mental health = 7.17 vs 9.98 Energy/fatigue = 10.06 vs 14.58 Pain = 11.38 vs 12.34 General health = -0.67 vs 1.69 No significant difference between groups. Patient satisfaction: Totally or generally satisfied with treatment = 48 (57%) vs 68 (79%), <i>P</i> = 0.002 Cure or acceptable improvement = 53 (61%) vs 69 (81%), <i>P</i> = 0.017 Treatment acceptable = 65 (77%) vs 79 (93%), <i>P</i> = 0.004 Menstrual status:	Funding source: Scottish Office Department of Health Study summary: The results at 2 years consolidate the findings and conclusions based on the four-month follow up data. A policy of early TCRE is effective and safe and does not result in an increase in hysterectomies. It should not be routinely withheld in an effort to try alternative medical therapies.

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							No bleeding or light = 36 (42%) vs 50 (58%), $P = 0.04$ Unchanged or heavier = 16 (18%) vs 5 (6%), $P = 0.02$ Bleeding score = 6.8 (SD 9.9) vs 5.4 (SD 8.1)	
Corson 2001 ³⁴⁴	randomised – 1:2 ratio; intention-to-treat (ITT) EL = 1+	276 randomised. 187 (184 by ITT, 177 by protocol, 167 at 12 months) to Hydro Thermablator, 89 (85 by ITT, 85 by protocol, 83 at 12 months) to rollerball ablation.	Population characteristics: Women; Aged between 30 and 50; family planning complete; uterine cavity = 10.5 cm; history of HMB; failed medical treatment; no active pelvic inflammatory disease; intramural myoma < 4 cm; no submucous fibroids or polyps; no hyperplasia or malignancy Mean age: HTA = 40.7, RB = 40.6 Parity: HTA = 2.2, RB = 2.2 PBAC: HTA = 596.6, RB = 585.5 Country: USA	Hydro Thermablator (HTA); Rollerball ablation (RB)	12 months	MBL – PBAC	Change in MBL (PBAC) from baseline to 12 months: HTA = 596.6 (SD 787.6) to 95 (SD 350) RB = 585.5 (SD 565.2) to 87 (SD 359) Successful treatment (PBAC < 75): HTA = 77%, RB = 82% Adverse events: 12 in HTA, 10 in RB.	Funding source: Author holds stock in device company Study summary: HTA is a safe and effective method of endometrial ablation. :
Corson 2000 ³⁴³	randomised – block EL = 1–	637 screened. 276 randomised. 150 (132 treated, 122 at 12 months) to Vesta group, 126 (123 treated, 112 at 12 months) to resection group	Population characteristics: Women; aged 30 to 49 years; PBAC > 150; failed medical treatment or intolerance to medical treatment; no systemic disease; active pelvic inflammation; Clotting defects; IUD within 3 months; Prior endometrial ablation. Average age: Vesta = 41.0, resection = 40.1 Parity: Vesta = 2.2, resection = 11.2 (?1.2?) PBAC score: Vesta = 535, resection = 445. Country: USA	Vesta – electrode ablation; transcervical resection of the endometrium (TCRE) or Rollerball	12 months	MBL – PBAC; Treatment failure; Treatment complications	Change in MBL (PBAC) from baseline to 12 months: Vesta: 520 (SD 600) to 18 (SD 37). TCRE: 447 (SD 316) to 28 (SD 70). No significant difference between groups. Treatment failure: Vesta = 6, TCRE = 11 Complications: Vesta = 6, TCRE = 7	Funding source: Vesta and Valleylab inc Study summary: Vesta system equivalent in effectiveness and safety to standard resection techniques.
Croignani 1997 ²⁶³	randomised; open; prospective EL = 1+	97 assessed. 27 refused entry. 70 accepted entry to study – 35 in IUD group, 35 in endometrial resection group.	Population characteristics: women; 38 years or older; referred for hysterectomy; confirmed menorrhagia – PBAC > 100; pregnant or breast feeding excluded; using hormonal treatment in last 3 months; serious concomitant condition excluded. IUD group – age 43.8, parity = 1.8, BMI = 25.3 Endometrial resection group –	LNG-IUS; endometrial resection	12 months – 6 and 12 months	MBL – PBAC; SF-36	MBL outcome: LNG-IUS ($n = 30$) baseline = 184.8 ml (SD 62.2), 12 months = 38.8 (SD 37.1) ($P < 0.001$). Endometrial resection ($n = 30$) baseline = 203.2 (SD 77.4), 12 months = 23.5 (SD 32.6) ($P < 0.001$). Difference between LNG-IUS and resection $P = 0.015$. Patient satisfaction: LNG-IUS: 29 (85%) satisfied. Endometrial resection: 33 (94%) satisfied. Mean SF-36 scores at 12 months (LNG-IUS vs Resection): Physical functioning = 78.0 vs 79.2. Role limitation = 72.5 vs 74.2 Bodily pain = 58.9 vs 70.3 General health = 64.1 vs 70.3	Funding source: National Research Council (Rome) Study summary: LNG-IUS produces slightly less satisfactory results than resection at 12 months.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			age = 45.4, parity = 1.6, BMI = 24.0 Country: Italy				Vitality = 56.3 vs 54.8 Social functioning = 69.8 vs 69.7 Role limitation = 61.3 vs 72.4 Mental health = 60.1 vs 59.6 Side effects reported by 19 of 34 in IUS group and 9 of 35 in resection group. 1 LNG-IUS patient lost to follow-up. 4 LNG and 3 resection patients had persistent menorrhagia after treatment and sought other treatment.	
Duleba 2003 ³⁴⁵	Randomised – 2:1 ratio; concealment – sealed envelopes EL = 1+	279 randomised. 193 (156 available at 12 months) to cryoablation, and 86 (72 available at 12 months) to rollerball ablation.	Population characteristics: Women; pre-menopausal; Aged 30 to 50 years; documented history of HMB for 3 months; failed medical therapy; no desire to retained fertility; excluded if: uterine volume > 300 ml, coagulation disorders, pelvic inflammatory disease, abnormal cervical cytology, intramural myoma > 2 cm, submucous myoma or polyps, previous ablation, pregnant, hyperplasia or malignancy. Average age: cryoablation = 41.2, electroablation = 41.1 Parity: cryo = 2.5, electro = 2.2 PBAC score: cryo = 576, Electro = 466 ($P = 0.02$) Uterine myomas: cryo = 20.1%, electro = 25.6% Country: USA	Cryoablation; electroablation; pre-treatment with leuprolide acetate 3.75 mg	12 months	treatment success (PBAC < 75); patient satisfaction; QoL; adverse events	Success of treatment (PBAC < 75): Cryoablation = 84.9%, Electro = 88.9% Adverse events: cryoablation = 5, Electro = 2 QoL and satisfaction results only presented in graphical form – showed that both treatments improved QoL and were satisfactory to majority of patients.	Funding source: Cryogen Inc Study summary: Cryoablation if a safe and effective procedure for treatment of HMB.
English 1998 ³⁹⁷	randomised; concealed; blinded – but method not mentioned EL = 1+	39 – 11 in decapeptyl SR group, 12 in danazol group, 13 in placebo group	Population characteristics: women; DUB; schedule for TCRE Country: Ireland	Pre-treatment – danazol, decapeptyl SR, placebo; TCRE	6 months	Duration of surgery; fluid absorption;	No statistical difference between groups for duration of surgery or fluid absorption. No difference in QoL scores at 4, 5, and 6 months follow up ($P = 0.1486$).	Funding source: Not stated Study summary: No difference in patient outcome or surgery with the use of pre-treatment.
Erian 1998 ³⁹⁸	randomised; blinded assessment EL = 1+	163 screened for inclusion, 43 not randomised, 40 (32 at 12 months) in 200 mg danazol group, 40 (32	Population characteristics: Women; menorrhagia; scheduled for TCRE; failed medical treatment; uterine size < 10 weeks; no uterine scars Country: Australia	Pre-treatment with danazol 200 mg for 6 weeks; TCRE; post-surgery – danazol 200 mg, danazol 600 mg, placebo	12 months	menstrual blood loss; adenomyosis prevalence	12 month menstrual bleeding: Placebo ($n = 30$) 100% had reduced bleeding Danazol 600 mg ($n = 32$) 100% had reduced bleeding Danazol 200 mg ($n = 28$) 100% had reduced bleeding Amenorrhoea rates higher in danazol groups than placebo ($P = 0.011$)	Funding source: Winthrop

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
		at 12 months) in 600 mg danazol group, and 40 (30 at 12 months) in placebo group						
Garside 2004 ³³⁴	systematic review; meta-analysis; economic analysis EL = 1+	2 systematic reviews and 10 primary RCTs	Population characteristics: Searches undertaken on MEDLINE, EMBASE, Cochrane library; DARE; NHS EED and HTA databases; Web of Science; Bibliographies of existing studies Country:	Microwave ablation; thermal balloon ablation MEA vs TBEA, MEA vs TCRE, MEA vs TCRE and RB, MEA vs RB, MEA vs hysterectomy, TBEA vs TCRE, TBEA vs TCRE and RB, TBEA vs RB, TBEA vs hysterectomy		Patient outcomes – amenorrhoea rates; patient satisfaction; patient QoL; Change in MBL. Study quality and characteristics – randomisation, blinding, concealment, intention-to-treat, study size, etc.	Quality assessment of RCTs: Internal validity – sample size: calculations were reported in 3 of 10 studies, selection bias: 2 trials were not randomised, 3 trials did not report on method of randomisation. Performance bias: all studies undertaken by experienced surgeons. Detection bias: not possible to blind patients or surgeons to treatment. Attrition rates: limited use of intention-to-treat and loss to follow-up rates. External validity: most studies appeared generalisable due to clear inclusion and exclusion criteria. Assessment of effectiveness: Amenorrhoea rates reported by 7 trials. Range for MEA was 36% to 40%, and for TBEA was 10% to 40% at 12 months. Bleeding patterns: trials reported significant reductions in levels of MBL or reclassification of bleeding patterns for both MEA and TBEA. Satisfaction with treatment: trials show high level of satisfaction (> 75%) with both MEA and TBEA. QoL: trials report improvement in QoL with both MEA and TBEA. Duration of procedure: trials show that MEA and TBEA both took less time to complete than first generation ablation techniques. Adverse effects: trial report that MEA was associated with greater equipment failure than first-generation ablation. No figures were available for TBEA.	Funding source: HTA programme grant Study summary: First-generation ablation techniques are equivalent to hysterectomy in effectiveness. Second-generation techniques are equivalent to first-generation techniques.
Gervaise 1999 ³⁶²	Prospective; cohort; matched EL = 2–	147: 73 in TBEA, 74 in TCRE	Population characteristics: Women; > 40 years of age; Menorrhagia; failed medical treatment; Uterine pathology excluded; Uterus > 12 weeks equivalent excluded; Normal histopathology. Average age: TBEA = 46.3, TCRE = 47.4 Menopause: TBEA = 5, TCRE = 20 Parity: TBEA = 2.4, TCRE = 1.9 Country: France	TCRE; TBEA	Up to 44 months	Menstrual bleeding pattern; Complications; predictors of failure	Menstrual bleeding pattern postoperatively: TBEA: amenorrhoea = 18 (24.7%), Hypomenorrhoea = 16 (21.9%) Eumenorrhoea = 28 (38.4%) Menorrhagia = 8 Metrorrhagia = 3 TCRE: amenorrhoea = 28 (37.8%), Hypomenorrhoea = 23 (31.1%) Eumenorrhoea = 10 (13.5%) Menorrhagia = 9 Metrorrhagia = 4 Complications: TCRE = 2; TBEA = 1. Factors associated with failure: TCRE = age < 43 years TBEA = Retroverted uterus	Funding source: Not stated Study summary: TBEA appears to be as efficacious as TCRE.
Goldrath 2003 ³⁵⁷	Randomised – 2:1 ratio; multicentre EL = 1+	276 randomised, 269 received treatment. 177 (18 lost to follow-up,	Population characteristics: Women; aged 30 to 50 years; completed families; menorrhagia – PBAC; uterine cavity between 4 and 10.5 cm; failed or refused medical	Hydrothermal ablation (HTA); rollerball ablation (REA); pre-treatment of depot leuprolide acetate	12, 24, 36 months	Change in MBL (PBAC); Patient satisfaction; Additional treatment;	Change in menstrual classification from baseline to 12, 24 and 36 months: HTA baseline = 596.6 (SD 787.6) Amenorrhoea = 66 (40%), 70 (46%), 72 (53%) Normal = 137 (82%), 139 (92%), 127 (94%) Rollerball baseline = 585.5 (SD 565.2)	Funding source: BEI medical systems Study summary: HTA was a safe and effective method of treating HMB.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
		24 had additional treatments) in HTA group, and 85 (14 lost to follow-up, 8 had additional treatments) in rollerball group	treatment; excluded if – pelvic inflammatory disease, intramural myomas > 4 cm, submucous myomas, polyps or septate uterus. Country: USA	7.5 mg.		Change in QoL	Amenorrhoea = 41 (51%), 34 (46%), 31 (46%) Normal = 71 (85%), 68 (92%), 62 (91%) Patient satisfaction at 36 months: HTA = 97%, Rollerball = 97% Adverse events: HTA = 11, Rollerball = 10 Overall success (normal bleeding and no additional treatments) was 81.4% for HTA and 81.6% for rollerball at 36 months.	
Grainger 2000 ³⁵⁴	randomised – 1:1; non-blinded; concealment not mentioned; ITT not mentioned; Sample size given EL = 1–	275 enrolled; 239 at 12 months; 227 at 2 years	Population characteristics: Women; > 30 years of age; minimum of 3 month history of HMB; normal uterine pathology; normal cavity shape between 6 and 10 cm; no desire for future fertility and willing to use contraceptives for 3 years after surgery; submucous fibroids, genital tract infection or malignancy excluded. Country: USA	TBEA; REA	2 years	MBL (PBAC); QoL	Outcomes for TBEA vs REA. MBL (PBAC) % change: 12 months = –85.5 vs –91.7 Amenorrhoea rates at 2 years: 109 (89.1%) vs 95 (90.4%) Satisfaction rates at 24 months: 105 (86.1%) vs 91 (86.7%) Hysterectomy rates by 24 months: 4 vs 11 Operative details and complications not stated.	Funding source: Gynecare Inc. Study summary: Endometrial ablation by both procedures was highly successful in avoiding hysterectomy and relieving symptoms of menorrhagia. Additional benefits were reduction in dysmenorrhoea and premenstrual syndrome.
Istre 2001 ²⁶⁶	Randomised EL = 1+	60: 30 LNG-IUS; 30 resection – 6 discontinued treatment by 12 months.	Population characteristics: women; menorrhagia (PBAC > 75); pre-menopausal; 30–49 years; regular uterine cavity < 10 cm; no pregnant or wanting to become so, breast feeding; large fibroid > 40 cm; pelvic disease; DVT; cancer; endometritis; liver disease; hormone therapy in 3 months Country: Norway	LNG-IUS; endometrial resection treatment vs baseline; treatment vs treatment	12 months	MBL = PBAC; duration of menstruation; haematological test; side effects	MBL (mean) – PBAC: LNG-IUS – baseline = 420 (SD 352), 12 months = 42 (SD 99) (–90%). TCRE – baseline = 404 (SD 480), 12 months = 7 (SD 15) (–98%). PBAC < 75 in 67% of LNG-IUS and 90% of TCRE patients at 12 months. (<i>P</i> = 0.005) Side effects: LNG-IUS 13 reported events – bleeding, abdominal pain, breast tenderness, headache, mood change. 6 discontinued treatment due to irregular bleeding, pain and acne.	Funding source: Leiras Oy Study summary: Resection reduces MBL more than IUS-LNG but only marginally.
Jack 2005 ⁴⁰⁰	Randomised – 1:1 ratio using block randomisation; concealment – opaque letters via telephone; EL = 1++	210 – 97 (4 drop-outs by 12 months) received immediate post-menstrual phase ablation, 100 (3 drop-outs by 12 months) had hormonal pre-treatment then ablation.	Population characteristics: Women; complaining of HMB; normal endometrial pathology; family completed; uterine size 12 weeks or less; Submucous fibroids < 3 cm Average age: non-drug = 42.36, drug = 42.41 Median bleeding score (IQR): non-drug = 23, drug = 24 Regular cavity: non-drug = 83.5%, drug = 86% Country: UK	Surgery in post-menstrual phase; hormonal pre-treatment (Danazol 200 mg bd, depot Goserelin 3.6 mg 5 weeks prior to surgery); endometrial ablation	12 months	Procedure time; Endometrial thickness; patient satisfaction; Amenorrhoea rates; periods no longer heavy; Median bleeding score – IQR	Intention to treat analysis – 3 people in post-menses group received hormonal preparation Procedure time: Post-menses = 21.30 minutes (SD 5.08), Drug group = 20.94 (4.13) Endometrial thickness: Post-menses = 4.47 mm (SD 2.67), Drug group = 2.6 mm (1.83) Differences groups for Midazolam use (in favour of hormonal group), acceptable – 2 weeks (in favour of post-menses group), post-op opiates (in favour of hormonal group) Patient satisfaction at 12 months: Post-menses = 92.5%, Drug group = 88.4%. No statistical difference Bleeding score at 12 months: Post-menses = 5, Drug group = 3 Periods no longer a problem: Post-menses = 87.8%, Drug group = 89.2% Amenorrhoea rates: Post-menses = 55.9%, Drug group = 61.9%	Funding source: Scottish Executive Health Office Study summary: MEA undertaken in post-menses period has high levels of patient satisfaction and reduced costs. Important menstrual outcomes are not affected by omission of drug preparation.

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
		13 not randomised						
Kriplani 2001 ⁴⁰³	randomised – computer generated EL = 1–	50: 25 in MPA pre-treatment group, 25 controls	Population characteristics: Women; menorrhagia or metrorrhagia – PBAC Average age: 33.9 Parity = 3.1 Country: India	Medroxy Progesterone Acetate (DMPA) pre-treatment; endometrial resection	4 years	Menstrual bleeding pattern; Duration of procedure; fluid deficit	Menstrual bleeding patterns (normal or no bleeding): DMPA = 22 (88%), Control = 24 (96%) Additional treatment: DMPA = 3, Control = 1 Duration of procedure: DMPA = 37.1 min, Control = 31.6 min Fluid deficit: DMPA = 690.2 ml, Control = 476 ml, ($P < 0.005$)	Funding source: Not stated Study summary: DMPA pre-treatment appears to have no effect on treatment outcome.
Kriplani 2002 ³⁹⁹	randomised – computer generated; no concealment; no blinding EL = 1–	132: danazol = 67, Untreated = 65	Population characteristics: Women; menorrhagia or metrorrhagia (PBAC showing menorrhagia); uterus < 12 weeks equivalent; no desire for further children. Mean age – danazol = 37.23, no treatment = 38.6 Mean parity – danazol = 3.38, no treatment = 3.2 Duration of symptoms – danazol = 4 years, no treatment = 3.8 years Country: India	Danazol (as pre-treatment) 400–600 mg a day for 4–6 weeks prior to surgery; TCRE – all patients Pre-treatment vs no pre-treatment group	Up to 6 years	Bleeding pattern; procedure differences	Changes in bleeding patterns: All patients had menorrhagia at baseline. Danazol group at 6 months ($n = 67$): 31 had amenorrhoea, 16 had spotting and 17 had significant improvement No pre-treatment at 6 months ($n = 64$): 31 had amenorrhoea, 12 had spotting and 19 had significant improvement. Danazol group at 6 years ($n = 30$): 15 had amenorrhoea, 7 had spotting, 8 had significant improvement. No pre-treatment at 6 years ($n = 31$): 15 had amenorrhoea, 8 had spotting, and 8 had significant improvement. Later groups had smaller numbers as not all patients had reached that length of follow-up. Procedure differences (Danazol vs no pre-treatment): endometrial thickness – 3.43 (SD 1.02) vs 11.45 (SD 1.89), $P < 0.001$ Mean fluid used – 3630.30 ml (SD 1378) vs 5013.67 (SD 1779), $P < 0.005$ Mean fluid deficit – 512.5 (SD 268.8) vs 632.4 (SD 264.7), $P < 0.05$ Mean duration of surgery – 25.7 min (as 3.4) vs 33.6 min (SD 3.8), $P < 0.001$. Repeat resection – 1 vs 1 Hysterectomy = 1 vs 1	Funding source: Not stated Study summary: Study shows that TCRE is an effective treatment for menorrhagia, with or without pre-treatment.
Lethaby 2005 ³³⁵	Systematic review; meta-analysis EL = 1++	19 studies included. 3285 pre-menopausal women included.	Population characteristics: Search on MEDLINE; EMBASE; Cochrane Library; PsycLit; CINAHL. Article reference lists, hand-searching of journals and pharmaceutical companies contacted. Inclusion criteria: RCT only; Comparison of endometrial techniques only; HMB; no pathology – fibroids Country:	Any endometrial destruction technique: transcervical resection of the endometrium (TCRE); vaporising electrode; rollerball; thermal laser ablation; hydro-thermablator; cryoablation; electrode ablation; microwave ablation; balloon; bipolar electrode	N/A	Patient outcome – amenorrhoea rates; satisfaction; QoL. Operative time; re-operation rates; complications.	Laser vs TCRE: Laser ablation took longer – 9 min (WMD: 9.15) – and equipment more likely to fail – (OR = 6 [CI 1.7 to 20.9]. No difference between methods for patient outcomes – amenorrhoea rates, satisfaction, QoL or complications. Vaporising electrode vs TCRE: TCRE was more likely to be difficult – OR = 0.25 [CI 0.09 to 0.73] – and greater fluid deficit – WMD = 258 ml [CI 173.9 to 342.1] – and take longer to perform – WMD = 1.5 min [CI 0.35 to 2.65]. No difference between methods for patient outcomes – amenorrhoea rates, satisfaction, QoL. Rollerball vs TCRE: No difference between techniques on future hysterectomy or re-surgery at 2 and 5 years follow-up. Thermal laser vs TCRE: Amenorrhoea rates were higher at 1 and 3 years follow-up in thermal group (OR = 4.9 [CI 2.2 to 11.0], OR = 4.6 [CI 2.04 to 10.5]. Mean length of surgery was shorter in thermal group (WMD = 9.3 [CI 11.4 to 7.2]). Women experienced more pain in thermal group (OR = 0.7 units [CI 0.02 to 1.4]). No difference between groups for menorrhagia, re-surgery, complications or satisfaction. Hydrothermablator vs rollerball: Hydro patients more likely to have local than general anaesthesia (OR = 2.85 [CI 1.6 to 5.1]). Hydro patients less likely to experience haematomata (OR = 0.18 [CI 0.03 to 0.93]), but more likely to have abdominal pain (OR = 1.85 [CI 1.1 to 3.1]) and nausea (OR = 3.7 [CI 1.5 to 9.0]). Cryoablation vs rollerball: Cryo group less likely to have amenorrhoea at 1 year	Funding source: No stated Study summary: Newer ablation techniques have success and complications rates comparable with 'gold standard' method of TCRE.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							<p>(OR = 0.3 [CI 0.2 to 0.6]), but more likely to have local than general anaesthesia (OR 13.2 [CI 5.8 to 30.0]). No difference in satisfaction rates, success rates (PBAC < 75), menorrhagia rates, hysterectomy rates.</p> <p>Electrode ablation (balloon or mesh) vs TCRE: Operative time with TCRE was longer (WMD = 18.7 min [CI 16.8 to 20.7]). Electrode group more likely to have local than general anaesthesia (OR = 15.9 [CI 10.1 to 25.1], and less likely to have cervical tears or lacerations (OR = 0.11 [CI 0.01 to 0.9]). No difference between groups in: amenorrhoea rates, complications rates, 12 month PBAC, satisfaction rates, and need for hysterectomy.</p> <p>Microwave vs TCRE plus rollerball: At 2 years follow-up, microwave was more satisfactory and acceptable than TCRE (OR = 1.9 [CI 1.1 to 3.3], OR = 2.7 [1.1 to 6.8]). At five-years follow-up the difference was maintained (OR = 2.3 [CI 1.22 to 4.3], OR = 3.7 [CI 1.3 to 10.1]). In addition, odds of haemorrhage were lower in the microwave group (OR = 0.14 [CI 0.02 to 0.8]). However, equipment failure rates (OR 4.07 [CI 1.1 to 15]), vomiting (OR = 4 [CI 1.4 to 11.7]), and uterine cramping (OR = 1.7 [1.1 to 2.8]) were greater in the microwave group. No difference in other outcomes or same outcomes at different time periods.</p> <p>Balloon vs rollerball: Amenorrhoea was less likely with balloon at 12 and 36 months (OR 0.6 [CI 0.33 to 0.96], OR = 0.5 [0.25 to 0.97]), but no difference at 24 months and 5 years. At 5 years odds of satisfaction with treatment lower in balloon group (OR = 0.13 [CI 0.02 to 0.94]). Complications more likely with balloon than rollerball. Duration of surgery was lower in balloon group (WMD = 20.8 min [CI 19.2 to 22.5]). Other outcomes showed no differences at 12, 24 and 36 months.</p> <p>Balloon vs laser: Balloon caused more pain (WMD 32.7 [CI 23.7 to 41.7]). Balloon had higher EUROQoL score at 12 months (WMD = 5.3 [CI 0.11 to 10.6]).</p> <p>Balloon vs TCRE: Balloon surgery quicker (WMD 13 min [CI 10.8 to 15.2]). Mean intra-operative blood loss lower with balloon (WMD – 81.8 [CI –70.3 to –93.3]). Satisfaction greater with balloon group at 24 months (OR = 7.2 [CI 1.4 to 35.9]).</p> <p>Bipolar electrode ablation vs balloon: Amenorrhoea was more likely in electrode group (OR = 7.4 [CI 3.8 to 14.4]). Women in electrode group more likely to be satisfied at 12 months (OR = 3.0 [CI 1.3 to 7.0]). No difference between groups on other outcomes: menorrhagia rates, satisfaction at 6 months, complication rates.</p> <p>Second generation vs first generation: First-generation procedures take longer (WMD –14.9 [CI –10.1 to –19.7]). Second generation equipment more likely to fail (OR 4.2 [CI 1.3 to 13.8]). Second generation groups less likely to have complications than first. However, no difference in satisfaction rates, except at 24 months. No difference in amenorrhoea rates or need for additional surgery.</p>	
Lissak 1999 ⁴⁰²	randomised; blinding and concealment not mentioned EL = 1–	30 – 17 control, 13 pre-treatment	Population characteristics: Women; aged 30 to 50 years; excessive menstrual bleeding, PBAC > 150; failed medical treatment; Normal endometrial biopsy; normal pap smear; uterine cavity between 4 and 12 cm; excluded if – pelvic inflammatory disease, endometrial hyperplasia, endometrial polyps, history of drug or alcohol abuse, pregnant, wish for future	Pre-treatment – intramuscular injection of decapeptyl 3.75 mg at 4–6 weeks prior to treatment; control group – no pre-treatment; both groups received balloon ablation	1, 3, and 6 months	Menstrual bleeding pattern; duration of procedure; adverse events; additional treatment; patient satisfaction	<p>Duration of procedure: pre-treatment = 8.44 min, control = 8.44 min</p> <p>Menstrual bleeding pattern (normal or no bleeding): pre-treatment = 17 (100%), control = 13 (100%)</p> <p>Patient satisfaction: Pre-treatment = 15 (88%), control = 11 ((2%)</p> <p>No major adverse events reported in either group.</p>	<p>Funding source: Not stated</p> <p>Reviewer comments: Small study size, plus lack of information on concealment and blinding, are likely causes of bias.</p>

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			fertility. Average age: pre-treatment = 48.7, control = 45.6 Gravidity: 4.9, 3.9 Country: Israel					
Loffer 2001 ³⁵²	Randomised – 1:1; EL = 1–	Sample size set at 108 per arm. 255 randomised. 131(17 dropped out) to UBT, 124 (24 dropped out) to RB	Population characteristics: Women; Aged 30 >; pre-menopausal; normal smear and biopsies; Documented history of HMB; normal uterus between 4 cm and 10 cm; Patient had no desire for future fertility; willing to use same contraception for 3 years; minimum MBL score – PBAC Country: USA and Canada	Thermal uterine balloon ablation (UBT); Hydroscopic rollerball ablation (RB);	3 years	MBL – PBAC and questionnaire; Additional treatment; QoL; adverse events	Overall success rate (normal or no bleeding, no repeat surgery or hysterectomy) at 3 years was: UBT = 106 of 123 (86.2%), RB = 93 of 113 (82.3%). Bleeding pattern change from baseline, at 12, 24, and 36 months (normal or no bleeding): UBT: 0 of 131 (0%), 101 of 126 (80%), 109 of 122 (89%), 106 of 114 (93%). RB: 0 of 124 (0%), 97 of 115 (84.3%), 95 of 105 (90%), 93 of 99 (94%). Adverse events: UBT = 4, RB = 4	Funding source: Gynecare Inc Study summary: Both methods of ablation were safe and effective treatments for HMB at 3 years follow-up
Loffer 2002 ³⁵³	randomised – 1:1 ratio; non-blinded; concealment not mentioned; ITT not mentioned EL = 1–	255 enrolled; 147 at 5 years, 76 TBEA, 71 REA.	Population characteristics: Women; > 30 years of age; minimum of 3 month history of HMB; normal uterine pathology; normal cavity shape between 6 and 10 cm; no desire for future fertility and willing to use contraceptives for 3 years after surgery; submucous fibroids, genital tract infection or malignancy excluded. Country: USA	TBEA; REA	5 years	Menstrual status; additional surgery	Outcomes for TBEA vs REA: Menstrual status: Amenorrhoea = 14 vs 20 Spotting = 6 vs 7 Hypomenorrhoea = 23 vs 15 Eumenorrhoea = 15 vs 17 Menorrhagia = 3 vs 2 Additional surgery: Hysterectomies = 21 vs 21 Ablation = 3 vs 2 D&C = 0 vs 1	Funding source: Gynecare Study summary: UBT continues to be an effective, simple treatment of menorrhagia, with clinical outcomes similar to those of rollerball ablation at 5 year follow-up.
McClure 1992 ³⁴⁶	randomised EL = 1–	38 women assessed. 22 randomised. 12 to laser ablation, and 10 to electrocautery.	Population characteristics: Women; Menorrhagia (> 80 ml); uterine pathology excluded; normal cervical cytology Average age: argon = 42.58, electro = 42.5 Parity = 2.83, 2.1 MBL (ml) = 170.8, 153.4 Country: Australia	Argon laser ablation; electrocautery ablation	24 weeks	Change in MBL; change in bleeding classification; additional treatment; duration of procedure	Change in MBL (ml) from baseline to 3-, and 6 months: Argon = 170.8 to 51.2 and 50.6 Electro = 153.4 to 30.2 and 27.0 2 patients in laser group underwent second procedure due to persistent menorrhagia. Duration of procedure (min): Laser = 114 min, electro = 80 min ($P < 0.001$).	Funding source: Not stated
Meyer 1998 ³⁵⁵	randomised – 1:1 ratio; concealment not mentioned; non-blinded EL = 1–	275 randomised, 255 included in study, 250 treated as per protocol. Numbers	Population characteristics: Women; menorrhagia; ≥ 30 years of age; failed medical treatment for HMB; normal biopsy and pap smear; normal uterine cavity; excluded if – suspected	TBEA; REA	12 months	Satisfaction; MBL (menstrual diaries); Amenorrhoea rate; Procedure duration (minutes);	Outcomes for TBEA vs REA: Satisfaction at 12 months (%): Very satisfied = 85.6 vs 86.7 Satisfied = 10.4 vs 12.4 Not satisfied = 4.0 vs 0.9 MBL at 12 months (menstrual diaries):	Funding source: Gynecare Inc. Study summary: In the treatment of dysfunctional uterine bleeding, uterine balloon therapy is as efficacious

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
		randomised to each group not stated. Demographic data available on 128 in TBEA and 117 in REA.	submucous myomas, malignancy, genital tract infection, previous endometrial ablation. Baseline characteristics (TBEA vs REA): Age = 40.2 vs 40.9 BMI = 24.0 vs 22.9 Years with menorrhagia = 9.9 vs 10.0 Country: Canada			Complications	-85.5% vs -91.7% Amenorrhoea rate (%) at 12 months: 15.2 vs 27.2 ($P < 0.05$) Complications: Intra-operatively = 0 vs 4 Post-operatively = 4 vs 3	as hysteroscopic rollerball ablation and may be safer.
Mousa 2001 ³⁶³	Matched case-control EL = 2+	169: 91 rollerball ablation, 78 abdominal hysterectomy	Population characteristics: Women; surgery for menorrhagia Average age: ablation = 43, hysterectomy = 41 Duration of problem = 20 months, 24 months Menorrhagia = 25%, 25% Menorrhagia and dysmenorrhoea = 75%, 75% Country: UK	Rollerball ablation; hysterectomy	At least 18 months	Procedure outcomes; Patient outcomes	Operative complications: ablation = 4, hysterectomy = 0 Post-operative complications: ablation = 0, hysterectomy = 5 Bleeding pattern: ablation – 35 amenorrhoea, 32 improved, 6 same, 7 had hysterectomy. Hysterectomy – all amenorrhoea. Patient satisfaction: ablation: 63 (79%) satisfied, hysterectomy: 40 (100%) satisfied Would recommend to friend: ablation: 73 (91%), hysterectomy: 40 (100%).	Funding source: Not stated Study summary: Both treatments are effective, but hysterectomy is associated with better patient outcomes.
Pellicano 2002 ³⁵⁸	randomised; non-blinded; concealment not mentioned EL = 1–	105 eligible and randomised, 23 withdraw prior to treatment (13 in HTER and 10 in TD group). 42 had HTER and 40 had TD. With 38 and 37 followed for 1 years, and 33 and 35 followed for 2 years.	Population characteristics: Women; aged < 50; Weighed < 100 kg; menorrhagia; failed medical treatment; normal endometrial histology; uterine < 12 weeks; absence of submucosal fibroids, adnexal masses, or endometriosis; absence of severe concurrent disease. Baseline characteristics (HTER vs TD): Age = 43.2 vs 42.6 BMI = 28.3 vs 29.8 Parity = 1.8 vs 1.9 Country: Italy	Hysteroscopic transcervical endometrial ablation (HTER) + pre-treatment with GnRH; Thermal Destruction (TD using Cavaterm)+ no pre-treatment	2 years	Operative data; Patient satisfaction; Return to work; return to normal domestic activities; Complications; re-operation rate; bleeding recurrence	Outcomes for HTER vs TD Operative data: Duration of operation = 37 vs 24 Intra-operative blood loss (ml) = 89 vs 7.2 Postoperative pain (VAS): 3.8 vs 3.2 Intra-operative complications: Fluid overload = 5 vs 0 Cervical tear = 1 vs 0 Conversion to hysterectomy = 2 vs 0 Discharge time (days): 1.3 vs 1.0 Patient satisfaction: at 3 months: Excellent = 21 vs 27 ($P < 0.001$); Good = 12 vs 13; Moderate = 9 vs 0; No change = 0 vs 0 At 1 year: Excellent = 12 vs 20 ($P < 0.001$); Good = 12 vs 10; Moderate = 10 vs 5; No change = 4 vs 2 At 2 years: Excellent = 2 vs 16 ($P < 0.001$); Good = 18 vs 12; Moderate = 3 vs 5; No change = 10 vs 2 Return to work (weeks): 0.9 vs 0.7 Return to normal domestic activities (days): 6.2 vs 4.1 Complications: Fever = 2 vs 1	Funding source: Not stated Study summary: Thermal destruction of the endometrium for the treatment of menorrhagia should be considered an effective therapeutic option because of its acceptability among patients, shorter operative time, and lower blood loss.

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							UTI = 1 vs 0 Haemorrhage = 4 vs 5 Blood transfusions = 0 vs 2 Re-operation rate: 9 vs 4 Bleeding recurrence: 17 vs 6	
Perino 2004 ³⁴⁷	randomised – computer generated; EL = 1+	116 enrolled. 58 to ELITT, 58 to TCRE.	Population characteristics: Women; DUB; no uterine pathology; no coagulation disorders; Menorrhagia – PBAC. Average age: ELITT = 41.4, TCRE = 41.9 Parity: 1.9, 1.8 PBAC: 167.2, 162.5 Country: Italy	Endometrial Laser Intrauterine Thermal Therapy (ELITT); TCRE; Pre-treatment of depot GnRH 3.75 mg	36 months	Bleeding category; Patient satisfaction; duration of procedure; Adverse events;	Change in bleeding category (normal or no bleeding) from baseline to 12 and 36 month follow-up: ELITT = 0%, 54 of 56 (96%), 53 of 56 (95%) TCRE = 0%, 51 of 55 (93%), 50 of 55 (95%). Patient satisfaction at 12 and 36 months ELITT = 94.5%, 93% TCRE = 91%, 91% Re-treatment: ELITT = 3, TCRE = 5 No difference between groups.	Funding source: Not stated Study summary: Both procedure are equally safe and effective for treating HMB.
Rauramo 2004 ²⁶⁸	randomised; open; equivalence EL = 1+	60: 30 LNG-IUS; 29 endometrial resection – 1 not randomised. 12 months – 6 LNG IUS vs 1 ablation discontinued or treatment failure. 36 months 5 vs 7 discontinued or treatment failure. 19 vs 22 at 36 months.	Population characteristics: women; menorrhagia; not pregnant or lactating; finished family; normal uterine cavity; abnormal uterine bleeding; pathology. LNG-IUS: 41.4 years, 73.4 kg. TCRE: 42.1 years, 70.4 kg. Country: Norway	LNG-IUS; endometrial resection treatment vs treatment; treatment vs baseline	3 years	MBL = PBAC; duration of menstruation; haematological test; side effects Analysis based on intention-to-treat.	MBL: LNG-IUS (median)- baseline ($n = 30$) = 261.5 (60–1503), 1 year ($n = 24$) = 12, 2 years ($n = 20$) = 8.5, 3 years ($n = 19$) = 7. Resection – baseline ($n = 29$) = 311 (81–2506), 1 year ($n = 28$) = 8.5, 2 years ($n = 24$) = 10, 3 years ($n = 22$) = 4. Difference between groups not significant. Adverse events: 1 oedema from LNG, plus 3 endometritis, 2 PID, 1 expulsion. 1 endometritis, 1 bleeding and pain from resection, plus 1 stroke	Funding source: Schering AG Study summary: Both treatments effectively reduced MBL.
Shawki 2000 ³³²	RCT EL = 1–	131 randomised (D&C = 39, goserelin 3.6 mg SC for 1 months = 2, 3, goserelin 3.6 mg SC for 3 months, danazol 400–600 mg PO per day for 3 months = 2, 6	Population characteristics: Women; failed medical treatment; AUB; endometrial biopsy confirming no neoplasia; no desire for future fertility; AUB at level for hysterectomy to be considered; uterine size < 12 weeks; patient refusal to consider further medical treatment. Average age = 45.7 Country: Egypt	D&C, goserelin 3.6 mg SC for 1 months goserelin 3.6 mg SC, danazol 400–600 mg PO per day for 3 months, MPA 15 mg PO per day before procedure. All prior to endometrial ablation or resection	1 year	Change in bleeding pattern; change in bleeding pattern by surgical technique; operative time (minutes)	Change in bleeding patterns (improvement, amenorrhoea): D&C ($n = 39$): 39, 7 goserelin for 1 month ($n = 23$): 21, 9 goserelin for 3 months ($n = 26$): 24, 10 danazol ($n = 26$): 24, 9 MPA 1 ($n = 23$): 23, 7 No difference between any of the pre-treatment groups Operative time (minutes): D&C ($n = 39$): 68 (SD 7) goserelin for 1 month ($n = 23$): 39 (SD 7) goserelin for 3 months ($n = 26$): 37 (SD 5) danazol ($n = 26$): 43 (SD 3) MPA 1 ($n = 23$): 54 (SD 9) D&C and MPA groups took significantly longer ($P < 0.05$)	Funding source: Not stated

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
		MPA 15 mg PO per day before procedure = 23)					Change in bleeding pattern by surgical technique: no difference between groups (THIS ANALYSIS IS NOT BASED ON RANDOMISED GROUPS)	
Sowter 2002 ³⁹⁶	Systematic review; meta-analysis EL = 1+	12 studies	Population characteristics: Search on MEDLINE, EMBASE, current contents, Cochrane Library, MDSG trials register. Pharmaceutical companies contact about unpublished studies. Used Menstrual Disorders and Subfertility Group strategy – including pre-treatment terms (GnRH etc) Only RCTs included in review Country:	Pre-surgical endometrial thinning agents – GnRH, goserelin, leuprolide acetate, danazol, progestins, progestogens. Treatment vs treatment; treatment vs placebo		Endometrial thickness; endometrial atrophy; cavity length; duration of surgery; operative difficulty; Distension medium absorption; blood loss during procedure; complications; amenorrhoea rates; patient satisfaction; need for further surgery; post-operative blood loss.	Review compared treatments vs placebo, and against one another. Only statistically significant differences reported here. GnRH vs placebo ($n = 8$): Endometrial thickness – WMD = -2.70 [-3.49 to -1.91] Endometrial atrophy – RR = 6.02 [4.11 to 8.81] Duration of operation – WMD = -4.79 [-6.54 to -3.04] Operative difficulty – RR = 0.32 [0.22 to 0.46] Distension medium absorption – WMD = -161.56 [-220.07 to -103.04] Post-operative amenorrhoea rate at 12 months – RR = 1.62 [1.04 to 2.52] No difference for other patient outcomes. GnRH vs danazol ($n = 4$): Endometrial atrophy – RR = 1.84 [1.23 to 2.75] No difference on other measures. GnRH vs progestogens ($n = 2$): Endometrial thickness – WMD = -2.80 [-3.59 to -2.01] No other differences. Danazol vs no pre-treatment ($n = 2$): Endometrial atrophy – RR = 3.15 [1.46 to 6.80] No other differences. Progestogens vs no pre-treatment ($n = 2$) No differences Proportion with atrophic endometrial glands RR (fixed) 2.50 (95% CI 1.27 to 4.92) and proportion with post-operative amenorrhoea at 12 months or less RR (fixed) 2.43 (95% CI 1.23 to 4.81) in favour of danazol.	Funding source: No funding Study summary: Endometrial thinning prior to endometrial destruction improves operating conditions for surgeon and short-term post-operative outcomes. GnRHs are more consistent than danazol. Long-term effects are reduced with time, such amenorrhoea rates.
Soysal 2002 ²⁷⁰	randomised; blind EL = 1+	72: 36 ablation vs 36 IUD. 1 ablation and 5 IUD not included in analysis due to treatment failure.	Population characteristics: Women; > 40 years; completed family; menorrhagia; no pathology; no cancer. LNG-IUS: 44.1 years. TBA: 43.8 years. Country: Turkey	Thermal balloon ablation after GnRH-a; LNG IUD (20 µg daily) Treatment vs baseline; treatment vs treatment	12 months	MBL – PBAC; QoL; Side effects	MBL: TBA – baseline PBAC = 417 (SD 81.4), 12 month PBAC = 21.8 (SD 14) ($P < 0.0001$). LNG-IUD – baseline PBAC = 408 (SD 101), 12 month PBAC = 55 (SD 11) ($P < 0.001$). TBA vs LNG = 388.2 vs 343 reduction ($P < 0.001$). QoL: SF-36 and HADs no difference between groups, except on role limitation where TBA better. No baseline data shown. Patient satisfaction: would recommend treatment = 70% for TBA vs 96% for LNG-IUD. Side effects: 21 of 36 LNG patients reported 1 or more side effects vs 8 of 36 in TBA group. ($P < 0.05$). Discontinuation: 5 LNG-IUS vs 1 TBA discontinued due to treatment failure.	Funding source: Not stated Study summary: Study shows that LNG-IUS and TBA are equivalent.
Soysal 2001 ³⁴⁸	Prospective; randomised – computer generated; concealment – opaque	96: thermal balloon ablation = 45, rollerball ablation = 48	Population characteristics: Women; menorrhagia – PBAC > 150; aged > 40 years; completed childbearing; myomatous uterus – < 12 weeks pregnancy in size or < 5 cm; active pelvic	Thermal balloon ablation (TBA); Rollerball ablation (RBA); Pre-treatment in both groups of GnRH	3, 6, 12 months follow-up	MBL – PBAC; Duration of procedure; complications; pain score of surgery; Amenorrhoea	Change in MBL (PBAC) from baseline to 12 months: TBA = 384.3 (SD 101) and 41.1 (SD 29) ($P < 0.0001$); RBA = 385.6 (SD 103), 40.2 (SD 45) ($P < 0.0001$). Mean decrease in MBL (PBAC) was 343.2 for TBA and 345.5 for RBA (No statistical difference between groups). Mean operating time: TBA = 11.5 min vs RBA = 37.3 min ($P < 0.0001$)	Funding source: Not stated

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
	envelopes EL = 1+		inflammatory disease; Submucous fibroids > 3 cm or < 50% intramural extension. Average age: TBA = 43.6, RBA = 44.3 Parity: TBA = 2.9, RBA = 3.1 PBAC: TBA = 383.1, RBA = 387.1 Country: Turkey	Surgery vs surgery		rates	Intra-operative complication rates: TBA = 0 vs RBA = 3 ($P < 0.05$) No difference on other outcome measures. No loss to follow-up	
Van Zon-Rabelink 2004 ³⁵¹	random; blinded; concealment not outlined in detail EL = 1+	139 randomised, 2 excluded due to test results, 60 in REA and 77 in TBEA at baseline, 58 and 76 at 6 months, 55 and 74 at 12 months, 55 and 66 at 24 months.	Population characteristics: Women; Included if – DUB, failed medical treatment for DUB; pre-menopausal; no wish for hysterectomy; no wish for future fertility. Excluded if – malignancy or other abnormal test results Baseline characteristics (TBEA vs REA): Age = 43.1 vs 43.1 Nulliparous = 2 vs 3 Cavity length (cm) = 7.6 vs 7.9 Country: Netherlands	TBEA; REA; Goserelin acetate pre-treatment given to all patients	24 months	MBL (menstrual scoring system); Patient satisfaction; additional treatment	Outcomes for TBEA vs REA. Change in MBL (Menstrual scoring system); median (Range): Pre-operatively = 425.5 (160 to 2055) vs 412 (137 to 1850) 6 months = 76.5 (3 to 635) vs 99.5 (0 to 1000) 12 months = 73.0 (0 to 535) vs 70.0 (0 to 2265) 24 months = 73.0 (0 to 585) vs 33.5 (0 to 905) ($P < 0.01$) Success rate (score < 185): 12 months = 79% vs 79% 24 months = 78% vs 76%: Patient satisfaction at 24 months: 80% vs 75%) Additional surgery: Hysterectomy = 8 vs 6; Ablation = 1 vs 1; LNG-IUS = 2 vs 0; Other = 2 vs 1 Change in Hb level from baseline = $P < 0.001$ in both groups Procedure details and complications not stated.	Funding source: Not stated Study summary: Endometrial ablation by uterine balloon thermal ablation (Thermachoice trade mark) is equally effective as hysteroscopic RBE of the endometrium.
Van Zon-Rabelink 2003 ³⁵⁰	Randomised; blinded EL = 1+	139 randomised, 2 excluded due to test results, 60 in REA and 77 in TBEA at baseline, 58 and 76 at 6 months, 55 and 74 at 12 months, 55 and 66 at 24 months.	Population characteristics: Women; Included if – DUB, failed medical treatment for DUB; pre-menopausal; no wish for hysterectomy; no wish for future fertility. Excluded if – malignancy or other abnormal test results Baseline characteristics (TBEA vs REA): Age = 43.1 vs 43.1 Nulliparous = 2 vs 3 Cavity length (cm) = 7.6 vs 7.9 Country: Netherlands	TBEA; REA	24 months	Complications	Outcomes for TBEA vs REA Complications: Perforation of uterus = 0 vs 3 Laceration of cervix = 0 vs 3 Electrolyte dysbalance = 0 vs 1 Suspicion of perforation = 0 vs 1 Other complications = 0 vs 0 $P < 0.001$ for difference between complication rates. Technical complications: 13 vs 10 Post-operative complaints: Pain = 3 vs 0 Nausea = 0 vs 1 Infection = 0 vs 1 Pain, Nausea and headache = 1 vs 0	Funding source: Not stated Study summary: Endometrial ablation by uterine balloon thermal ablation (Thermachoice) is a safe and simple non-hysteroscopic procedure.
Vercellini 1999 ³⁴⁹	randomised – 1:1; blinded; concealment – opaque envelopes EL = 1+	134 eligible, 34 refused randomisation, 47 randomised to REA, 44 to TCRE	Population characteristics: Women; > 35 years of age; referred for hysterectomy due to menorrhagia (PBAC > 100); uterine volume < 12 weeks; normal pathology results; no future fertility wanted; no use of hormonal treatments that may impact on treatments;	vaporising electrode; TCRE; pre-treatment with GnRH	12 months	Duration of operation (minutes); complications with operation; fluid deficit; MBL (PBAC); Menstrual pattern; Patient	Outcomes for vaporising vs TCRE. Duration of operation (minutes): 9.2 vs 10.7 Complications with operation: Minimal = 11 vs 14; Moderate = 4 vs 7; Severe = 0 vs 6 Fluid deficit (ml): 109 (SD 126) vs 367 (SD 257) MBL (PBAC): 15 (SD 24) vs 20 (SD 42) Menstrual pattern: Amenorrhoea = 17 vs 21	Funding source: Not stated Study summary: Endometrial ablation with the vaporizing electrode limited fluid absorption compared with resection by the standard cutting loop.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			intramural or submucous fibroids > 3 cm were excluded. Baseline characteristics (Electrode vs TCRE): Age = 45.5 vs 46.2 Parity = 1.9 vs 1.8 BMI = 24.3 vs 23.7 PBAC score = 282 vs 270 Haemoglobin (g/dl) = 11.4 vs 11.1 Country: Italy			satisfaction; Haemoglobin levels (g/dl)	Hypomenorrhoea = 20 vs 14 Eumenorrhoea = 10 vs 7 Menorrhagia = 0 vs 2 Patient satisfaction: Satisfied = 45 vs 41 Uncertain = 2 vs 1 Dissatisfied = 0 vs 2 Haemoglobin levels (g/dl): 13.5 vs 13.6	Long-term effects on uterine bleeding were similar.
Vihko 2003 ³⁵⁹	Randomised; blinding not mentioned; concealment not mentioned EL = 1-	31: 16 in menotreat group, 16 in Cavaterm group	Population characteristics: women; menorrhagia requiring surgery; no endometrial pathology or abnormality; normal cervical cytology; not pregnant or wishing to become pregnant; Polyps or fibroids > 2 cm excluded; urinary tract or genital infection; IUDs; Caesarean section scar; Participating in another trial. Average age: Menotreat = 39.3 vs 40.5 in Cavaterm Parity = 2.7 in Menotreat Vs 2.9 in Cavatherm. Country: Finland	Menotreat and Cavaterm – thermo balloon ablation techniques Surgery vs Surgery; Surgery vs Baseline	3 and 6 months	Change in bleeding classification; length of menstrual bleeding (days); Pad or tampon use; Patient assessment of outcome (poor, good, excellent)	Change in bleeding classification: all patients in both groups experienced reduction in bleeding at both 3 and 6 months. Length of menstrual bleeding time was significantly ($P < 0.01$) reduced in both groups at both 3 and 6 months compared with baseline. There was no difference between groups. Number of pads or tampons used was significantly ($P < 0.01$) reduced in both groups at both 3 and 6 months compared with baseline. There was no difference between groups. Patient satisfaction at 6 months was: for menotreat – 12 excellent, 4 good, 0 poor; for Cavaterm – 9 excellent, 5 good, 1 poor.	Funding source: Not stated
Zupi 2003 ³³³	Randomised; concealment and blinding not mentioned EL = 1+	203 entered study. 13 from HER and 9 from LSH withdraw from study prior to treatment. 89 had HER and 92 had LSH. No difference between those that withdraw and those that underwent treatment.	Population characteristics: Women; referred with menometrorrhagia; younger than 50 years; less than 100 kg; finished families; clear pap test; uterus size < 12 weeks equivalent; no adnexal masses or endometriosis. Average age: HER = 43.2, LSH = 42.6 Parity: = HER = 1.8, LSH = 1.9 Irregular bleeding: HER = 62.9%, LSH = 59.7% Country: Italy	Hysteroscopic endometrial resection (HER), Laparoscopic supra-cervical hysterectomy (LSH) and GnRH-a (3.75 mg) 1 month prior to surgery. Ablation vs hysterectomy	2 year	Peri-operative outcomes; complications; QoL – SF-36; Additional treatment; Haemoglobin levels	Operating times: HER = 41.7 min, LSH = 71.5 min, $P < 0.01$ Operative complications: HER = 13, LSH = 9 Long-term complications: HER = 3, LSH = 6 Additional surgery by 2 years: HER = 12, LSH = 1 SF-36 outcome (HER pre-operatively scores, HER post-operative score, LSH pre-operative score, LSH post-operative score): General health – 51.9 (SD 12.7), 59.6 (SD 13.7), 52.1 (SD 12.2), 69.4 (SD 14.2) Physical function – 62.6 (SD 14.4), 66.4 (SD 15.1), 62.8 (SD 10.9), 67.6 (SD 13.2) Role (physical) – 58.3 (SD 13.0), 61.3 (14.8), 59.2 (SD 15.4), 62.1 (SD 13.9) Role (emotional) – 60.8 (SD 12.0), 64.2 (SD 14.4), 60.3 (SD 11.9), 68.1 (SD 15.2) Mental Health – 58.1 (SD 12.3), 60.5 (SD 14.8), 59.8 (SD 12.9), 63.2 (SD 13.6) Social function – 56.4 (SD 11.0), 67.3 (SD 12.7), 53.6 (SD 9.7), 88.5 (SD 11.5) Vitality 56.7 (SD 11.0), 61.0 (SD 12.8), 55.4 (SD 10.3), 72.3 (SD 11.3) Pain – 57.1 (SD 19.2), 58.6 (SD 17.0), 56.4 (SD 18.5), 60.1 (SD 14.0). $P < 0.01$ for change in general health score for both treatments, and for difference after treatment between groups in favour of hysterectomy. $P < 0.01$ for change in emotional role in hysterectomy group. $P < 0.01$ for change in social function score for both treatments, and for difference after treatment between groups in favour of hysterectomy.	Funding source: Not stated Study summary: Laparoscopic hysterectomy may offer curative advantages of hysterectomy with operative advantages of ablation.

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							$P < 0.01$ for change in vitality score for hysterectomy treatments, and for difference after treatment between groups in favour of hysterectomy.	

Table 10.4 Endometrial ablation for treatment of HMB – additional non-comparative studies

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Clarke 2005 ³⁶⁴	Cohort EL = 3	Hysterectomy; TCRE	5294 of 15280 in hysterectomy group and 4032 of 11478 in the TCR group responded to 5 year follow-up	Women; underwent hysterectomy or TCRE; Surgery for DUB Part of VALUE/MISTLETOE cohorts Country: UK	Readmission rates to hospital	Readmission rates by 5 years: Any type of readmission – 2754 (44.6%) of TCRE, 3477 (41.7%) of hysterectomy. Hazard ratio = 0.87 [CI 0.80 to 0.95], $P = 0.038$ Gynaecological readmission – TCRE = 837, hysterectomy = 440. Hazard ratio = 0.40 [CI 0.33 to 0.48], $P < 0.0001$ Operation related readmission – TCRE = 1026, Hysterectomy = 721. Hazard ratio = 0.53 [CI 0.45 to 0.61], $P < 0.001$.	Funding source: Department of Health, UK Study summary: Differences in readmission patterns for hysterectomy and ablation. Women undergoing hysterectomy are less likely to be readmitted to hospital.
Dequesne; 1997 ³⁶⁵	Case series EL = 3	Vesta – thermoregulated endometrial ablation	187	Women; menorrhagia; failed medical treatment; normal pathology and histopathology; uterus size < 10 cm Country: Europe and Mexico	Complications; Subsequent surgery (failures); Bleeding patterns	Bleeding patterns after surgery: Of 187, 71 had amenorrhoea, 81 had hypomenorrhoea, 18 had eumenorrhoea, and 17 failed Complications: 8 device failures, and 1 complication Survival analysis of freedom from HMB, dissatisfaction or additional surgery by 24 months = 88%	Funding source: Vesta Medical Inc., Valleylab Inc., Pfizer Inc.
Donnez 2000 ³⁶⁶	Case series EL = 3	Endometrial Laser Intrauterine Thermal Therapy (ELITT)	100	Women; PBAC > 150; not pregnant; No desire for future fertility; 30 to 49 years; Non-menopausal; Uterus cavity between 5 and 10 cm; Normal cavity pathology; Absence of fibroids or polyps. Country: Belgium	Menstrual bleeding patterns; Complications; patient satisfaction	Menstrual bleeding patterns at 12 months: Amenorrhoea = 69% Spotting = 21% Hypomenorrhoea = 5% Eumenorrhoea = 4 Menorrhagia = 1 Complications: 4 Patient satisfaction at 12 months: 91 were most satisfied, 7 were satisfied, 2 were not satisfied.	Funding source: Not stated
Dutton 2001 ³⁶⁷	Case series EL = 3	Rollerball endometrial ablation	275	Women; menstrual bleeding problems; 265 for menorrhagia Country: USA	Subsequent hysterectomy rate	Subsequent hysterectomy in 46 – 34 for persistent menorrhagia.	Funding source: Not stated
El-Toukhy 2004 ³⁶⁸	Case series EL = 3	Cavaterm – balloon thermal ablation	220 at 6 months, 108 at 24 months.	Women; menorrhagia; failed medical treatment; no significant uterine pathology; excluded if – uterine cavity > 12 cm, endometrial hyperplasia. Average age = 41 Parity = 2.1 Country: UK	Menstrual bleeding pattern	Menstrual pattern at 18 months ($n = 153$) 72% had reduced MBL, at 24 months ($n = 108$) 74% had reduced MBL.	Funding source: Not stated
Erian 1994 ³⁶⁹	Prospective; case series EL = 3	Endoscopic laser ablation; danazol 200 mg <i>t.i.d.</i> for 6 weeks prior to surgery	2342	women; menorrhagia; failed medical treatment; suitably for hysterectomy; excluded if – endometrial pathology found. Country: UK	Menstrual bleeding patterns; complications; additional treatment	Menstrual bleeding patterns: No data on baseline bleeding patterns, but all included had refractory menorrhagia. At follow up ($n = 1866$): Amenorrhoea = 1043 (56%) Reduced menses = 353 (19%) Normal period = 348 (19%) No change = 122 (7%) Additional treatment: Of 122 with no improvement – 33 had hysterectomy, 84 had re-treatment, 5 do not respond. Complications: 57 complications reported in 2342 patients (2.4%).	Funding source: Not stated Study summary: Laser ablation is an acceptable alternative to hysterectomy.

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Erian 1996 ³⁷⁰	Case series EL = 3	TCRE; Pre-treatment with danazol 200 mg <i>t.i.d.</i> for 6 weeks	126	Women; menorrhagia; no malignancy; uterus < 12 weeks equivalent; failed or refused medical treatment Country: Australia	Menstrual bleeding pattern; complications; Additional surgery	Bleeding patterns (<i>n</i> = 126): Amenorrhoea = 55 Scanty blood loss = 46 Reduced loss = 14 No change = 8 Lost to follow-up = 3 Additional surgery: 6 women requested repeat procedures, 8 underwent hysterectomy Complications: 2 perforations, 3 women required tamponade due to heavy bleeding	Funding source: Not stated
Feitoza 2003 ³⁷¹	Case series EL = 3	Thermal Balloon ablation (TBA)	141: 53 had completed 24 month follow-up	Women; referred due to heavy or prolonged menses; uterus size < 10 cm; Women with AUB associated with pathology were excluded. 47 women had ablation as first-line treatment. Country: USA	Bleeding pattern; patient satisfaction; additional therapy	Bleeding patterns: Baseline – all had menorrhagia. At 6-months: 32 had amenorrhoea, 63 had hypomenorrhoea, 27 had eumenorrhoea, 7 had menorrhagia, 11 had undergone hysterectomy. At 12 months: 25 had amenorrhoea, 47 had hypomenorrhoea, 22 had eumenorrhoea, 2 had menorrhagia, 15 had undergone hysterectomy. At 24 months: 15 had amenorrhoea, 19 had hypomenorrhoea, 14 had eumenorrhoea, 5 had menorrhagia, 19 had undergone hysterectomy. Patient satisfaction: 95% of patients were satisfied with TBA result. Subsequent treatment: 28 of 141 women underwent additional treatment: 1 myomectomy, 6 hormonal treatments, 21 hysterectomies (14 for menorrhagia).	Funding source: Not stated Study summary: TBA is safe and efficient method to treat menorrhagia.
Ferry 1994 ³⁷²	Case series EL = 3	TCRE	278	Women; menstrual disorders; malignancy excluded; uterine size < 12 weeks Country: UK	Patient satisfaction; complications	Patient satisfaction at 4 months: 90% Complications: 13 procedures not completed, 13 patient required overnight stay due to complications	Funding source: Not stated
Friberg 2000 ³⁷³	Case series EL = 3	Thermal balloon endometrial destruction	117: 116 followed up	Women; menorrhagia; failed medical treatment; no desire for future fertility Average age = 43.4 Parity = 2 Country: Sweden	Menstrual bleeding pattern; subsequent hysterectomy	Change in bleeding pattern in pre-menopausal women at follow-up, excluding those who had hysterectomy (<i>n</i> = 70): Amenorrhoea = 10 Minimal MBL = 32 Normal = 23 Profuse = 5 Patient satisfaction: 91.5% excellent, 5.7% good, 1.9% moderate, 0.9% did not improve. Endometrial thickness was less in women with amenorrhoea than those who had bleeding (<i>P</i> < 0.001) Subsequent hysterectomy: 10 women had hysterectomy – 7 for menorrhagia	Funding source: Not stated
Gallinat 2001 ³⁷⁴	Case series EL = 3	Electroballoon ablation	124: 122 had 24 month follow-up	Women; menorrhagia; failed medical treatment Country: Germany	Menstrual bleeding pattern; additional surgery	Bleeding pattern at 24 months (assumed all had menorrhagia at baseline) (<i>n</i> = 122): amenorrhoea = 42%, hypomenorrhoea = 44%, Eumenorrhoea = 4% Subsequent hysterectomies = 5	Funding source: Not stated
Gallinat 2004 ³⁷⁵	Case series; prospective EL = 3	NovaSure – bipolar ablation	107	Women; menorrhagia (PBAC > 150); failed medical treatment; uterine cavity < 10 cm. Average age: 42 years Average PBAC = 563 Parity = 2.62 Country: Germany	Bleeding pattern; additional treatment	Change in bleeding patterns: Baseline – all women had menorrhagia (PBAC > 150) At 26 months (<i>n</i> = 103): 65% had amenorrhoea 26% had spotting 3% had hypomenorrhoea 3% had eumenorrhoea	Funding source: Not stated Study summary: NovaSure is a safe and effective treatment for menorrhagia.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
						3% had menorrhagia Additional treatment: 3 hysterectomies and 1 re-ablation	
Gandhi 1999 ³⁷⁶	Case series EL = 3	TCRE	301 women – 329 procedures	Women; menstrual disorders; no desire for future fertility Average age = 42 years 71% had regular cycle Country: UK	Prognostic factors for subsequent hysterectomy	A total of 51 women have undergone hysterectomy from group of 301. Prognostic factors associated with failed treatment: Aged < 40, $P = 0.01$ Moderate or greater dysmenorrhoea, $P = 0.0001$ Fibroids, $P > 0.05$ Surgery completed, $P > 0.05$ Complications, $P = 0.04$ Histology not normal, $P = 0.02$ Number of procedures > 1, $P = 0.04$ Operator experience, $P = 0.009$	Funding source: Not stated Study summary: Prognostic factors should be taken into account when advising about surgery.
Garry 1991 ³⁷⁷	Case series EL = 3	Endometrial ablation – Nd:YAG laser ablation	859	Women; distressing or debilitating menorrhagia; completed family; No major pathology – malignancy, large fibroids; no severe medical problems – liver and renal disease; gross obesity Country: USA and UK	Operating outcome; Patient outcomes – bleeding patterns	Mean operating time: 24 minutes Complications: 11 Bleeding pattern: Amenorrhoea = 288 (60%) Reduced menses = 152 (32%) First failure = 39 (8%) Subsequent success = 26 (5%) Hysterectomy = 13 (3%)	Funding source: Not stated Study summary: Endometrial ablation is safe and effective methods for treating menorrhagia.
Garry 1995 ³⁷⁸	Case series EL = 3	Endometrial ablation and resection – laser ablation	524 women – 600 operations	Women; severe menorrhagia; no desire for further children; excluded if – malignancy, uterus > 12 weeks in size; Fibroids > 2 cm; suspected adenomyosis; endometriosis. Mean age = 43 years Country: UK	Menstrual bleeding patterns; additional surgery; complications	Change in bleeding patterns: Assumed all women had menorrhagia prior to surgery. Amenorrhoea = 135 (28.9%) Reduced menses = 309 (66.2%) Same menses = 21 (4.5%) Increased = 1 (0.2%) No response = 1 (0.2%) Success of surgery: Successful = 418 (83.4%) Failure = 83 (16.6%) Hysterectomy = 34 (6.8%) Mean fluid absorption = 603 ml Mean operating time = 25 minutes	Funding source: Not stated Study summary: Laser ablation is safe and effective method for treating menorrhagia
Lefler 2003 ³⁷⁹	Case series EL = 3	Rollerbar-loop-rollerbar endometrial ablation	117	women; menorrhagia; completed family Country: USA	Bleeding patterns; patient satisfaction; complications	Change in bleeding pattern (assumed all had menorrhagia at baseline): Amenorrhoea = 60 (55%) – 25 were menopausal Spotting = 21 (19%) – 1 was menopausal Light flow = 5 (5%) Normal flow = 4 (4%) Heavy flow = 2 (2%) 17 patients had hysterectomy. Patient satisfaction: Satisfied or better: 90 (85%) Neutral: 6 (6%) Dissatisfied 11 (10%) Fluid absorption: Median absorption was 100 ml, mean was 154 ml (SD 289)	Funding source: Not stated Study summary: RLR was associated with good long-term outcomes.

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
McPherson 2005 ³⁸⁰	Cohort EL = 3	TCRE; hysterectomy with or without BSO	Numbers responding at 5 year follow-up: TCRE = 3845, hysterectomy = 3397, hysterectomy and BSO = 2305	Women; undergone TCRE or hysterectomy. Average age at 5 year follow-up: TCRE = 47.9, hysterectomy = 54.1, BSO = 50.6 Country: UK	Libido loss, difficult sexual arousal; vaginal dryness.	Adjusted OR for loss of libido against TCRE (adjusted for age and HRT use): Some – Hysterectomy = 1.25 (1.13 to 1.39), BSO = 1.32 (1.16 to 1.51), $P = 0.254$ Severe – Hysterectomy = 1.29 (1.16 to 1.44), BSO = 1.68 (1.48 to 1.92), $P < 0.001$ Extreme – hysterectomy = 1.42 (1.22 to 1.65), BSO = 1.80 (1.51 to 2.14), $P < 0.001$ Adjusted OR for difficulty of sexual arousal against TCRE (adjusted for age and HRT use): Some – Hysterectomy = 1.16 (1.05 to 1.29), BSO = 1.27 (1.11 to 1.44), $P = 0.068$ Severe – Hysterectomy = 1.28 (1.15 to 1.44), BSO = 1.79 (1.56 to 2.05), $P < 0.001$ Extreme – hysterectomy = 1.35 (1.15 to 1.58), BSO = 1.82 (1.52 to 2.19), $P < 0.001$. Adjusted OR for vaginal dryness against TCRE (adjusted for age and HRT use): Some – Hysterectomy = 1.28 (1.15 to 1.41), BSO = 1.17 (1.03 to 1.33), $P = 0.057$ Severe – Hysterectomy = 1.55 (1.36 to 1.78), BSO = 1.43 (1.22 to 1.69), $P = 0.170$ Extreme – hysterectomy = 1.50 (1.19 to 1.88), BSO = 1.69 (1.29 to 2.22), $P = 0.195$.	Funding source: Department of Health and BUPA foundation Study summary: At 5 years follow up women who had undergone hysterectomy reported increase psychosexual problems than those who had undergone TCRE, and these figures were higher for women who had had BSO at the time of hysterectomy.
McPherson 2005 ³⁸¹	Prospective cohort EL = 3	TCRE; Hysterectomy	11323 (5592 with TCRE, 5731 with hysterectomy – 1240 vaginal, 4227 abdominal, 251 LAVH)	Women; undergone hysterectomy or TCRE for DUB. Mean average age: TCRE = 42.17, Hysterectomy = 42.21 Presence of fibroids: TCRE = 924 of 3740 (24.71%), hysterectomy = 424 (7.44%) of 5701 Country: UK	Risk of urinary incontinence	OR of Urinary symptoms for hysterectomy compared with TCRE (adjusted for age, BMI, number of pregnancies, caesarean sections, fibroids, co-morbidities, age of first pregnancy): Urinary incontinence – mild: OR = 1.28 (1.12 to 1.45) Urinary incontinence – severe: OR = 1.54 (1.29 to 1.85) Urinary frequency – mild: OR = 1.17 (1.04 to 1.33) Urinary frequency – severe: OR = 1.36 (1.14 to 1.62) Nocturia – mild: OR 1.23 (1.04 to 1.46) Nocturia – severe: OR 1.28 (1.09 to 1.50) Vaginal: Urinary incontinence – mild: OR = 1.19 (1.00 to 1.41) Urinary incontinence – severe: OR = 1.52 (1.20 to 1.93) Urinary frequency – mild: OR = 1.28 (1.08 to 1.52) Urinary frequency – severe: OR = 1.51 (1.20 to 1.90) Nocturia – mild: OR 1.34 (1.06 to 1.69) Nocturia – severe: OR 1.33 (1.08 to 1.64) Abdominal: Urinary incontinence – mild: OR = 1.30 (1.15 to 1.46) Urinary incontinence – severe: OR = 1.59 (1.34 to 1.89) Urinary frequency – mild: OR = 1.10 (0.97 to 1.23) Urinary frequency – severe: OR = 1.15 (.96 to 1.37) Nocturia – mild: OR 1.19 (1.01 to 1.39) Nocturia – severe: OR 1.17 (1.00 to 1.36) LAVH: Urinary incontinence – mild: OR = 1.82 (1.28 to 2.59) Urinary incontinence – severe: OR = 2.02 (1.32 to 3.07) Urinary frequency – mild: OR = 1.03 (0.74 to 1.43) Urinary frequency – severe: OR = 1.33 (0.85 to 2.07) Nocturia – mild: OR 1.03 (0.68 to 1.57) Nocturia – severe: OR 0.90 (0.57 to 1.41)	Funding source: DoH and BUPA

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
O'Connor 1996 ³⁸²	Case series EL = 3	Endometrial resection; pre-treatment with danazol or GnRH in some cases	525 primary resection, 50 subsequent resections	Women; menorrhagia; eligible to hysterectomy; failed medical treatment or refused treatment; 30 to 50 years old; no desire for further children; normal cervical smear and endometrial biopsy; major uterine pathology excluded – fibroids > 5 cm. Average age = 42 Prior medical treatment = 84% Menstrual symptoms: 93% had HMB, 11% had irregular periods, 44% had painful periods. Country: UK	Operative findings; averting subsequent surgery or hysterectomy	Operative findings ($n = 525$): Fluid balance (Mean) = 585 ml Surgery not completed = 25 (5%) Complications = 34 (6%) Operating time = 33 minutes Hospital stay (Mean) = 0.94 Late post-operative complications = 14 (3%) 17 women required further medical treatment, and 84 required further surgery. 79% to 87% of women expressed satisfaction with the surgery during each of the 5 years of follow-up	Funding source: Not stated Study summary: Endometrial resection is an effective alternative to hysterectomy
Parkin 2000 ³⁸³	Case series EL = 3	Microwave endometrial ablation (MEA)	1433	Women; undergone microwave endometrial ablation for excessive menstrual blood loss Country: UK	Complications	Complication: 1 major complication – small bowel burn. Incidence of 0.7/1000 for series. 4 blunt perforations (1 cause by MEA probe) – incidence = 2.6/1000 for series. 2 women had post-operative pain and 14 cases of endometritis were detected. Total complication rate = 14.6/1000	Funding source: Not stated
Perez-Medina 2002 ³⁸⁴	Case series EL = 3	Loop endometrial resection	286	Women; no major pathology; failed medical treatment. Menorrhagia = 134 (46.4%) Metrorrhagia = 152 (53.1%) Average age = 41.6 years Heavy periods = 95% Country: USA	Menstrual bleeding pattern; subsequent hysterectomy; risk-factors for failed surgery.	Menstrual bleeding patterns by follow up: 3 to 4 years ($n = 286$): amenorrhoea = 46%, improved = 89% Failed treatment: 48 required hysterectomy. Risk factors for hysterectomy in multivariate analysis: Age (< 45 or > 45): RR = 2.93 (CI 1.59 to 5.40), $P = 0.0002$ Adenomyosis: RR = 11.21 (CI 2.70 to 46.46), $P = 0.0009$ Survival analysis for not having hysterectomy at 5 years: 76% (CI 72 to 80)	Funding source: Not stated Study summary: Length of follow-up, patient age, and presence of adenomyosis are risk factors for women requiring hysterectomy after ablation
Pooley 1998 ³⁸⁵	Case series EL = 3	TCRE; GnRH pre-treatment	380	Women; menorrhagia; normal histopathology; completed families Average age = 42.3 years 222 NHS, 158 private 181 had failed medical treatment 10 were post-menopausal and no HRT Country: UK	Complications; subsequent hysterectomy	Complications: 26 complications were registered – 12 perforations. Survival analysis for avoiding hysterectomy by follow-up time: 1 years = 42 hysterectomies, 87.6% survival 2 years = 25 hysterectomies, 77.7% 3 years = 5 hysterectomies, 75.1% 4 years = 3 hysterectomies, 72.6% 5 years = 0 hysterectomies, 72.6%	Funding source: Not stated Study summary: Although TCRE does not avoid hysterectomy in all, it does have low morbidity and a high success rate.
Quenby 1997 ³⁸⁶	Case series EL = 3	TCRE; no pre-treatment	293 women offered surgery, 273 available for follow-up	Women; Offered TCRE as alternative to hysterectomy Country: UK	Menstrual bleeding; patient satisfaction; reason for choosing TCRE; Expected outcome; Influences on satisfaction	Menstrual bleeding patterns: 1 year ($n = 273$): amenorrhoea = 30%, light = 41%, moderate = 6%, heavy = 10%, 13% not followed up. 4 years ($n = 52$): amenorrhoea = 29%, light = 42%, moderate = 2%, heavy = 0%, 27% not followed up Patient satisfaction: 1 year ($n = 249$): further surgery = 13%, satisfied = 67%, advise friend = 70%, prefer hysterectomy = 18%. 4 years ($n = 38$): further surgery = 24%, satisfied = 68%, advise friend = 68%, prefer hysterectomy = 13% Why chose TCRE: Advised by gynaecologist = 74% Shorter recovery time = 46%	Funding source: Not stated

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
						<p>Early recovery of normal activity = 33%</p> <p>Less time off work = 30%</p> <p>Retain uterus = 18%</p> <p>Avoid scar = 16%</p> <p>Advised by GP = 8%</p> <p>Early resumption of sexual activity = 8%</p> <p>What did you expect of surgery:</p> <p>Lighter = 92%</p> <p>No period = 6%</p> <p>Shorter periods = 79%</p> <p>Same length = 6%</p> <p>Less painful = 46%</p> <p>Same degree of pain = 12%</p> <p>No pain = 18%</p> <p>Regression analysis of factors associated with satisfaction:</p> <p>Age (< 40 or > 45) OR 6.66, $P < 0.001$</p> <p>Histology OR 2.11, $P < 0.05$</p> <p>Menstrual cycle (regular vs irregular) OR 2.05, $P < 0.05$.</p>	
Roushdy 1996 ³⁸⁷	prospective cohort EL = 3	Endometrial resection	124	Women; functional menorrhagia; 35 to 47 years old Country: Egypt	Persistent or recurring menorrhagia by risk factor	<p>Bleeding pattern at follow-up:</p> <p>108 had amenorrhoea and mean average uterine volume of 78.9 ml. 8 had improved bleeding and mean average uterine volume of 98.7 ml. 8 had persistent/recurring menorrhagia and mean average uterine volume of 112.8.</p> <p>No patient with uterine volume < 110 ml had recurring or persistent menorrhagia.</p>	Funding source: Not stated
Seidman 2000 ³⁸⁸	Case series EL = 3	Transcervical endometrial resection (TCRE)	162	Women; symptomatic menorrhagia sufficient for hysterectomy. Mean age = 46.2 years Parity = 3.3 Country: Israel	Bleeding pattern; satisfaction; additional surgery; procedure outcome. All against age.	<p>Change in bleeding pattern with age:</p> <p>Decreased or amenorrhoea – < 44 ($n = 59$) = 84.8%, 45 to 49 ($n = 72$) = 95.5%, > 50 ($n = 31$) = 92.6%</p> <p>Patient satisfaction:</p> <p>Satisfied or very satisfied – < 44 = 81.4%, 45 to 49 = 92.5%, > 50 = 92.6%</p> <p>Fluid overload requiring diuretics: < 44 = 20.5%, 45 to 49 = 15.3%, > 50 = 25.8%</p> <p>Blood transfusion: < 44 = 6.8%, 45 to 49 = 5.6%, > 50 = 3.2%</p>	Funding source: Not stated
Sharma 2004 ³⁸⁹	Cohort; prospective EL = 3	Microwave ablation	115 at baseline, 89 at 2 years	Women; menorrhagia – subjective; failed medical treatment; completed families; excluded if – uterine fibroid > 4 cm; hyperplasia or malignancy; uterine cavity > 14 cm Average age: 40.2 Country: UK	Menstrual bleeding pattern	<p>At 24 months: 70% had reduced menstrual blood loss pattern.</p> <p>30 of original 115 had undergone hysterectomy due to recurrence of menorrhagia.</p>	Funding source: Not stated
Steffensen 1997 ³⁹⁰	Retrospective case series, with follow-up EL = 3	TCRE	250	Women; menstrual symptoms requiring surgery; uterus no larger than 10 weeks. 51% had menorrhagia Country: Norway	Patient satisfaction; bleeding pattern; additional surgery	<p>Amenorrhoea rates:</p> <p>3 months ($n = 250$) = 64%</p> <p>12 months ($n = 232$) = 55%</p> <p>48 months ($n = 25$) = 81%</p> <p>Hypomenorrhoea rates:</p> <p>3 months ($n = 250$) = 33%</p> <p>12 months ($n = 232$) = 35%</p> <p>48 months ($n = 25$) = 11%</p>	Funding source: Not stated

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
						<p>Additional surgery: 3 months ($n = 250$) = 0 12 months ($n = 232$) = 2 48 months ($n = 25$) = 13</p> <p>Patient satisfaction: 3 months = 97%</p>	
Thijssen 1997 ³⁹¹	Multicentre; multi-national; case series; prospective EL = 3	Radiofrequency endometrial ablation (with and without pre-treatment)	1280	<p>Women; subjective menorrhagia; aged 30 to 55 years; completed families; wish to retain uterus; no hypergonadotrophic; normal uterus size; normal cervical cytology; normal adnexa; no prolapse; no intrauterine abnormality; no history of bleeding disorders.</p> <p>Recruited between 1990 and 1994.</p> <p>Country: Worldwide: UK, Netherlands, South Africa, Australia, Spain, Denmark</p>	Amenorrhoea rates, Hypomenorrhoea rates, Dissatisfaction rates.	<p>Amenorrhoea rate = 184 of 1280 (14%)</p> <p>Hypomenorrhoea rate = 557 of 1280 (43.5%)</p> <p>Amenorrhoea/greatly reduced MBL/hypomenorrhoea = 78.5%</p> <p>Dissatisfied = 203 of 1280 (16%)</p> <p>Complications: 19</p>	Funding source: Not stated
Tsaltas 1998 ³⁹²	Case series; retrospective EL = 3	Endometrial ablation – exact method not defined	232 questionnaires sent and 149 returned.	<p>Women; undergone endometrial ablation</p> <p>Country: Australia</p>	Bleeding pattern; patient satisfaction	<p>Bleeding patterns at follow-up: No data for baseline</p> <p>At follow-up – 41 (28%) had amenorrhoea, 55 (37%) had very much lighter menses, 29 (19%) had lighter menses, 16 (11%) had the same menses, 6 (4%) had heavier bleeding, and 2 (1%) did not respond.</p> <p>Patient satisfaction: 113 of 145 (78%) stated that they were satisfied with treatment. 19 of 149 (13%) had repeat ablation 26 of 149 (17%) had hysterectomy.</p>	Funding source: Not stated
Vilos 1997 ³⁹³	Prospective case series EL = 3	Thermal balloon ablation (thermacheoic e); varies forms of pre-treatment used	121 – 13 women had insufficient balloon pressure	<p>Women; menorrhagia; major uterine pathology exclude; excluded if wanted future fertility.</p> <p>Average age = 39 years</p> <p>Country: USA</p>	Menstrual bleeding pattern; additional surgical treatment	<p>Change in bleeding patterns: Baseline – all classified as having menorrhagia 3 months: Reduced menstrual bleeding – 88, menorrhagia – 13, no data – 20 6 months: Reduced menstrual bleeding – 95, menorrhagia – 14, no data – 12 12 months: Reduced menstrual bleeding – 56, menorrhagia – 12, no data – 53</p> <p>Additional surgery: 23 patients required additional surgery</p>	Funding source: Not stated
Vilos 1996 ³⁹⁴	Case series EL = 3	hysteroscopic endometrial ablation; pre-treatment with danazol in 70% of cases	800 in 54 hospitals	<p>women; menstrual symptoms requiring surgery.</p> <p>618 (77.2%) had menorrhagia</p> <p>Country: Canada</p>	Complications	<p>Peri-operative complications: 29 in total. 6 false passage, 7 uterine perforation, 8 excess fluid loss, 5 bleeding requiring tamponade, 3 incomplete surgery.</p> <p>Long-term complications: 56 in total. 32 repeat ablation, 18 hysterectomies, 5 infections, 1 pregnancy.</p>	Funding source: Not stated
Wright 2003 ³⁹⁵	Case-control; after screening EL = 3	Endometrial ablation – electrosurgical endometrial	120 offered entry, 12 declined, 9 did not meet entry requirements (urgent)	<p>Women; referred for menorrhagia (subjective); fibroids < 5 cm included, excluded if – endometrial neoplasia, FSH in menopausal range, hypothyroidism, or serious learning</p>	Present State Examination	<p>63 of 108 women achieved 'caseness' with a Present State score ≤ 5</p> <p>Change in psychiatric scores from baseline to follow-up: Clinical Anxiety Scale – 4.14 to 2.70 = 1.44 (0.88 to 2.00), RR of case vs control = 11.6 (3.3 to 40.2)</p>	<p>Funding source: Not stated</p> <p>Study summary: Psychiatric outcome from endometrial ablation were linked to pre-</p>

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
		ablation	hysterectomy required), 5 lost to follow-up, 7 withdraw after learning of normal MBL level. 87 were evaluable.	difficulties. Average age: 42 years, Parity = 2 Country: UK		<p>Monthemery Asberg Depression Scale – 10.72 to 6.02 = 4.70 (3.27 to 6.13. HADs – Anxiety – 7.17 to 6.09 = 1.08 (0.39 to 1.78), RR at 8 cut-off = 18.9 HADs – depression – 5.01 to 2.85 = 2.16 (1.37 to 2.97, RR at 8 cut-off = 4.4 Irritability Depression and Anxiety Scale – Irritability – 7.16 to 4.76 = 2.41 (0.18 to 4.64), RR of case vs control 22.4. Patient satisfaction = 73% of women were satisfied with outcome of procedure at 12 months. Women with low pre-operative MBL and high pre-surgical psychiatric scores were more likely to have high post-operative psychiatric scores (39% vs 6%).</p>	surgical MBL levels and pre-surgical psychiatric scores.

Heavy menstrual bleeding

Table 10.5 Dilatation and curettage for treatment of HMB – comparative studies

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Haynes 1977 ⁴⁰⁹	Non-comparative cohort EL = 2-	22	Population characteristics: women; MBL > 80 ml Country: UK	D&C	2 consecutive cycles	MBL – alkaline haematin	No figures given for change in MBL. Graphs show a reduction in MBL in first month after D&C, but a return to heavy menstrual bleeding by the second month.	

Table 11.1 UAE for treatment of uterine fibroids – comparative RCT and observational studies

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Edwards 2006 ⁴¹⁷	Randomised; open EL = 1+	546 eligible, 157 randomised, 106 to UAE, 51 to surgery. 101 received UAE, and 48 received surgery. 95 UAE analysed, 45 surgery patients analysed.	Population characteristics: Women; referred for surgery due to uterine fibroids Baseline characteristics (UAE vs surgery): Age = 43.8 (SD 5.4) vs 43.3 (SD 7.1) Largest fibroid diameter (cm) = 7.5 (SD 3.0) vs 8.2 (SD 3.1) Uterine volume (ml) = 589.2 (SD 445.3) vs 636.0 (SD 443.3) Main symptom: Bleeding = 52 vs 29 Pain = 19 vs 7 Pressure = 23 vs 12 Other = 4 vs 2 Country: UK	UAE; surgery (myomectomy or hysterectomy)	21 months	SF-36; EuroQoL; pain score; symptom score; recommend to a friend; complications; treatment failure; subsequent treatment	Outcomes for UAE vs surgery: SF-36 at baseline (SD): Physical function = 81.4 (18.9) vs 77.1 (19.6) Role – physical = 50.3 (40.9) vs 44.7 (42.3) Bodily pain = 51.3 (21.3) vs 49.9 (22.3) General health = 61.0 (18.8) vs 60.5 (22.9) Vitality = 40.3 (22.0) vs 41.6 (23.4) Social function = 62.0 (27.1) vs 58.0 (29.6) Role – emotional = 58.5 (43.4) vs 57.3 (43.1) Mental health = 62.0 (18.1) vs 63.0 (21.7) SF-36 at 12 months: Physical function = 92 (14) vs 89 (20), $P = 0.85$ Role – physical = 76 (40) vs 81 (34), $P = 0.33$ Bodily pain = 76 (23) vs 80 (26), $P = 0.28$ General health = 74 (20) vs 79 (17), $P = 0.07$ Vitality = 62 (21) vs 67 (22), $P = 0.26$ Social function = 84 (23) vs 87 (26), $P = 0.35$ Role – emotional = 81 (35) vs 87 (30), $P = 0.22$ Mental health = 76 (17) vs 76 (21), $P = 0.80$ EuroQoL at baseline: 69.8 (15.8) vs 62.9 (20.3) EuroQoL at 12 months: 82 (16) vs 83 (14), $P = 0.18$ pain score at 24 hours (0 to 10 scale, 10 is worst): 3.0 (2.1) vs 4.6 (2.3), $P < 0.001$ Symptom score at 12 months (–5 = worse to +5 score = better): 3.6 (2.0) vs 4.3 (1.7), $P = 0.03$ Recommend to a friend at 12 months: 88% vs 93%, $P = 0.32$ Complications: Minor = 29 (27%) vs 12 (23%) Major = 8 (7%) vs 3 (6%) Adverse events: 11 vs 9 Treatment failure: UAE = 14 Subsequent treatment: 14 (13%) vs 2 (4%)	Funding source: Scottish Office
Broder 2002 ⁴²⁵	Comparative cohort study EL = 2+	81 women undergoing abdominal myomectomy (AH) ($n = 30$) and	Population characteristics: Mean age: UAE: 43.5 years AH: 37.6 years ($P < 0.001$)	abdominal myomectomy vs uterine artery embolisation	AH: mean 49 months UAE: mean 46 months	Further invasive treatment overall symptoms improvement	Further invasive treatment UAE: 15 (29%) (12% hysterectomy, 16% myomectomy, 2% UAE) AM: 1 (3%) (0=0.04) (3% hysterectomy, 0 myomectomy, 0 UAE) Overall symptoms improvement:	Funding source: not stated Study summary: UAE more likely than AM to need further invasive therapy 3–5 years

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
		uterine artery embolisation (UAE) (<i>n</i> = 51) for symptomatic fibroids	More likely to have previous myomectomy (<i>P</i> < 0.001) Country: Germany	abdominal myomectomy vs uterine artery embolisation		patient satisfaction	UAE: 92% AM: 90% (NS) Patient satisfaction: Dissatisfied: UAE: 6%; AM: 21% (<i>P</i> = 0.06) Clinical failure: UAE: 39% AM: 30% (NS) Using logistic regression: UAE more likely to have further invasive therapy (OR 12.5, 95%CI 1.4 to 110.1)	after index procedures
Goodwin 2006 ⁴²⁹	ITT; comparative cohorts; non-matched; multicentre EL = 2+	209 in total (149 UAE (120 at 12 months) and 60 myomectomy)	Population characteristics: Included if – Women scheduled for either UAE or myomectomy; aged > 30 years; regular menses; normal pap smear; confirmed uterine fibroids. Excluded if – hysteroscopically resectable fibroids, pelvic infection, gynaecological malignancy, unexplained AUB, history of pelvic irradiation, coagulopathy, involved in another study, FSH > 40 iu/l, score ≥ 90 of UFQoL outcome measure. Baseline characteristics (UAE (<i>n</i> = 149) vs myomectomy (<i>n</i> = 60)): Mean age = 43.9 vs 38.2 (<i>P</i> < 0.0001) Dominant symptom: AUB = 77 vs 20 (<i>P</i> = 0.02) Bulk/pressure = 38 vs 16 Pelvic pain = 29 vs 18 Infertility = 0 vs 2 Other = 5 vs 4 Duration of dominant symptom (months) = 145 vs 60 Number of fibroids (<i>P</i> = 0.0001 for difference between groups). < 5 = 47 vs 27 6 to 10 = 27 vs 14 > 10 = 75 vs 13 Location of dominant fibroid (<i>P</i> < 0.0001 for difference between groups) Size of dominant fibroid (cm ³) =	UAE; myomectomy	1 year	QoL; MBL; Adverse events	UAE vs myomectomy: 28 of 149 UAE patients either lost to follow, had poor outcome or had additional treatment by 6 months follow-up. 15 of 60 myomectomy patients either lost to follow, had poor outcome or had additional treatment by 6 months follow-up. Change in QoL from baseline (UFQoL – high score better, low score worse; outcome (SD)): UAE at 3 and 6 months (outcome (SD)): General health perception = 4.1 (12.7), 4.3 (15.6) Comprehensive health perception = 44.6 (27.5), 44.4 (27.6) Physical functioning = 16.0 (28.2), 17.8 (25.3) Difficulty with activity = 22.1 (27.4), 26.8 (25.7) Sleep = 18.1 (19.6), 20.8 (21.2) Mental health = 12.7 (17.1), 14.9 (18.3) Energy/vitality = 24.9 (20.8), 26.9 (22.7) Self image = 29.0 (22.9), 30.2 (24.4) Sexual functioning = 8.0 (22.7), 11.3 (24.7) Myomectomy at 3 and 6 months (outcome (SD)): General health perception = 6.0 (26.5), 12.2 (25.2) Comprehensive health perception = 46.8 (26.6), 42.6 (32.5) Physical functioning = 15.4 (27.7), 20.1 (29.2) Difficulty with activity = 20.8 (26.9), 25.0 (30.4) Sleep = 14.9 (18.0), 15.6 (18.6) Mental health = 11.5 (15.4), 13.9 (20.9) Energy/vitality = 23.7 (20.4), 26.3 (23.0) Self image = 27.7 (31.7), 36.2 (29.2) Sexual functioning = 15.4 (19.1), 15.6 (25.2) Significant improvement from baseline in both groups (<i>P</i> < 0.001). No difference between groups. MBL (menorrhagia score (SD)): Baseline = 46.2 (15.6) vs 45.6 (18.7) 3 months = 21.5 (11.9) vs 22.5 (11.5) 6 months = 18.4 (10.1) vs 21.4 (11.8) 12 months = 16.7 (10.2) vs figures no given Significant improvement from baseline in both groups (<i>P</i> < 0.001). No difference between groups.	Funding source: Boston Scientific Corp Study summary: The uterine fibroid quality of life score was significantly improved in both groups. No significant differences were observed in bleeding improvement, uterine volume reduction, uterine fibroid quality of life score improvement, and overall quality of life score improvement between groups. Patients receiving UAE required fewer days off work, fewer hospital days, and experienced fewer adverse events.

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			182.12 (SD 208.978) vs 226.92 (SD 196.394) Uterine volume (cm ³): Baseline = 658.4 vs 590.6 6 months = 404.3 vs 251 (<i>P</i> < 0.001 for change since baseline for both groups)				Duration of hospital stay (hours): 23.8 vs 61.6 (<i>P</i> < 0.0001) At least 1 adverse event: 33 vs 24 (<i>P</i> = 0.01) Total adverse events: 53 vs 43 Procedure-related adverse events: 24 vs 22 Major adverse events: 6 vs 1	
Gupta 2005 ⁴¹⁶	Systematic review; meta-analysis EL = 1+	3 RCTs included.	Population characteristics: Searched the Cochrane Menstrual Disorders and Subfertility Group Trials register (searched 10 August 2005), the Cochrane Central Register of Controlled Trials (CENTRAL) on the Cochrane Library, Issue 3, 2004), MEDLINE (January 1966 to November 2005) and EMBASE (January 1980 to November 2005). Contacted authors of potential ongoing studies. Country: UK	Uterine artery embolisation	N/A	Duration of operation (min); length of stay (days); length of recovery (days); Complications	Outcomes for UAE vs hysterectomy (outcome title; number of studies; number of participants statistical method; effect size): Duration of procedure (min): 1, 156, WMD (fixed) = -16.40 [95% CI -26.04 to -6.76] Intra-procedure blood loss (ml): 1, 156, WMD (fixed) = -405.20 [95% CI -512.71 to -297.69] Intra-procedural complications: 2, 216, OR (fixed) = 2.02 [95% CI 0.74 to 5.47] Need for blood transfusion: 2, 216, OR (fixed) = 0.04 [95% CI 0.00 to 0.33] Length of hospital stay (days): 2, 213, WMD (fixed) = -3.27 [95% CI -3.77 to -2.77] Unscheduled visits after discharge: 2, 217, OR (fixed) = 1.80 [95% CI 0.98 to 3.30] Readmission rates within 42 days: 2, 216, OR (fixed) = 6.00 [95% CI 1.14 to 31.53] Resumption to normal activities: 1, 59, WMD (fixed) = -26.68 [95% CI -36.15 to -17.21] Satisfaction with treatment: 1, 53, OR (fixed) = 0.47 [95% CI 0.09 to 2.48] UAE vs myomectomy (Outcome title; number of studies; number of participants; Statistical method; Effect size): Duration of procedure (minutes): 1, 63, WMD (fixed) = -34.50 [95% CI -48.74 to -20.26] Febrile morbidity: 1, 63, OR (fixed) = 0.90 [95% CI 0.24 to 3.32] Need for antibiotics: 1, 63, OR (fixed) = 1.12 [95% CI 0.25 to 4.92] Need for blood transfusion: 1, 63, OR (fixed) = 0.21 [95% CI 0.01 to 4.48] Length of hospital stay (days): 1, 63, WMD (fixed) = -1.60 [95% CI -2.47 to -0.73] Hospital stay 1 week: 1, 63, OR (fixed) = 0.11 [95% CI 0.01 to 2.08] Readmission to hospital: 1, 63, OR (fixed) = 2.29 [95% CI 0.20 to 26.58] Duration to full recovery (days): 1, 63, WMD (fixed) = -16.40 [95% CI -21.16 to -11.64] Relief of fibroid-related symptoms at 6 months follow-up: 1 54 OR (fixed) = 0.50 [95% CI 0.08 to 3.27] Total relief of all fibroid-related symptoms at 6 months follow-up: 1, 54, OR (fixed) = 0.36 [95% CI 0.12 to 1.11] Fibroid-related symptoms same or worse at 6 months follow-up: 1 54 OR (fixed) = 2.00 [95% CI 0.31 to 13.06] Serum FSH levels at 6 months follow-up: 1, 63, WMD (fixed) = 0.79 [95% CI -0.24 to 1.82] FSH levels 20 iu/l: 1, 63, OR (fixed) = 8.53 [95% CI 0.42 to 172.28] Fibroids detected by USS 4 cm by at least 6 months follow-up: 1, 63, OR (fixed) = 5.88 [95% CI 1.88 to 18.44] Re-intervention rate: 1, 63, OR (fixed) = 8.97 [95% CI 1.79 to 44.95]	Funding source: No financial support Study summary: UAE offers an advantage over hysterectomy with regards to a shorter hospital stay and a quicker return to routine activities. There is no evidence of benefit of UAE compared with surgery (hysterectomy / myomectomy) for satisfaction. The higher minor complications rate after discharge in the UAE group as well as the unscheduled visits and readmission rates require more longer term follow-up trials to comment on its effectiveness and safety profile. There is currently an ongoing trial (REST, U. K.) and EMMY trial yet to report on the long term follow up, the results of which are awaited with interest.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Hehenkamp 2005 ⁴¹⁸	randomised; multicentre; concealment and blinding not mentioned EL = 1+	349 eligible, 177 randomised (89 in hysterectomy group – 75 received hysterectomy, 14 had not. 88 in UAE group – 81 received UAE, 7 had not)	Population characteristics: Women; uterine fibroids; menorrhagia; pre-menopausal; scheduled for hysterectomy. Women excluded if – future fertility desired, active pelvic infection, allergic to contrast material, uterine malignancy, submucosal fibroids > 50% within uterine cavity. UAE vs hysterectomy: Age = 44.6 vs 45.4 Parity ≥ 1 58 vs 69 Previous treatment: none = 11 vs 15 hormonal = 59 vs 59 NSAIDs = 45 vs 41 Iron supplement = 50 vs 52 Surgery = 17 vs 11 Symptoms: Menorrhagia = 88 vs 89 Dysmenorrhoea = 47 vs 50 Duration of symptoms = 24 vs 24 Number of fibroids (median) = 2 vs 2 Uterine volume (median, cm ³) = 321 vs 313 Fibroid volume (median, cm ³) = 59 vs 89 Country: Netherlands	UAE; hysterectomy	2 years	Surgery completed; complications; duration of surgery; length of stay	Completed surgery: 72 of 81 completed. 5 with unilateral procedure due to technical failure on one-side, 4 with bilateral failure. 8 of 152 (5.3%) of arteries available were not embolised due to technical failure. Complications during hospital stay and at 6 weeks follow-up: At hospital (UAE vs hysterectomy): Nausea = 52 vs 42 Pain = 72 vs 71 Febrile morbidity = 4 vs 15 Minor complications = 23 vs 26 Major complications = 1 vs 1 At 6 weeks follow-up (UAE vs hysterectomy) Nausea = 25 vs 11 (RR = 2.10 (1.11 to 3.97)) Pain = 57 vs 52 Febrile morbidity = 17 vs 8 Minor complications = 68 vs 34 (RR = 1.45 (1.04 to 2.02), <i>P</i> = 0.024) Major complications = 3 vs 1 (RR = 2.78 (0.3 to 26.13), <i>P</i> = 0.62) Unscheduled visits to health professionals: UAE = 45 vs hysterectomy = 24 Readmission after UAE up to 6 weeks = 9 Duration of procedure (median): UAE = 75 min vs hysterectomy = 90 min (<i>P</i> = 0.007 for comparison of means) Blood loss (median, ml): UAE = 20 vs hysterectomy = 300 (<i>P</i> < 0.01 for comparison of means) Length of stay (days): UAE = 2 vs hysterectomy = 5.1	Funding source: ZonMw – Netherlands organisation for health research and development Study summary: UAE is a procedure similar to hysterectomy with a low major complication rate and with reduced length of hospital stay
Hehenkamp 2006 ⁴¹⁹	randomised; multicentre; concealment and blinding not mentioned EL = 1+	349 eligible, 177 randomised (89 in hysterectomy group – 75 received hysterectomy, 14 had not. 88 in UAE group – 81 received UAE, 7 had not)	Population characteristics: Women; uterine fibroids; menorrhagia; pre-menopausal; scheduled for hysterectomy. Women excluded if – future fertility desired, active pelvic infection, allergic to contrast material, uterine malignancy, submucosal fibroids > 50% within uterine cavity. UAE vs hysterectomy: Age = 44.6 vs 45.4 Parity ≥ 1 58 vs 69 Previous treatment: none = 11 vs 15 hormonal = 59 vs 59 NSAIDs = 45 vs 41	UAE; Hysterectomy		Pain; Return to daily activities	UAE (<i>n</i> = 72) vs Hysterectomy (<i>n</i> = 68) Analgesia use: Tablets only = 15 vs 5 Opiates = 46 vs 43 Epidural anaesthesia = 8 vs 20 Secondary epidural = 3 vs 0 Time to return to activity (days, SD): Paid work = 28.1 (25.7) vs 63.4 (33.2), <i>P</i> < 0.001 Voluntary work = 16.6 (8.9) vs 46.6 (30.1), <i>P</i> = 0.016 Usual household activities = 12.0 (12.4) vs 29.0 (30.1), <i>P</i> < 0.001 Heavy household activities = 20.7 (15.4) vs 53.7 (30.8), <i>P</i> < 0.001 Buying groceries = 14.0 (12.1) vs 35.0 (30.2), <i>P</i> < 0.001 Doing things around the house = 18.9 (14.4) vs 39.8 (24.7), <i>P</i> < 0.001 Leisure time activities = 14.8 (13.3) vs 40.4 (40.1), <i>P</i> < 0.001 Activities with children = 17.4 (14.2) vs 30.3 (20.6), <i>P</i> = 0.001	Funding source: ZonMw – government funded Study summary: In conclusion, pain appears to be less after UAE during hospital stay. Return to several daily activities was in favour of UAE in comparison with hysterectomy.

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			Iron supplement = 50 vs 52 Surgery = 17 vs 11 Symptoms: Menorrhagia = 88 vs 89 Dysmenorrhoea = 47 vs 50 Duration of symptoms = 24 vs 24 Number of fibroids (median) = 2 vs 2 Uterine volume (median, cm ³) = 471.9 vs 483.5 Fibroid volume (median, cm ³) = 121.5 vs 159.0 Country: Netherlands					
Katsumori 2003 ⁴³⁰	retrospective; comparative EL = 2–	152 (fibroids > 10 cm = 47, fibroids < 10 cm = 105)	Population characteristics: Women; Undergone UAE; Country: Japan	UAE in women with fibroids > 10 cm; UAE in women with fibroids < 10 cm;	Mean 17.5 months	Complication rates; duration of procedure (min); Reduction in fibroid volume (%); reduction in uterine volume (%); Time to recovery (days); patient satisfaction	Fibroid > 10 cm (<i>n</i> = 47), fibroid < 10 cm (<i>n</i> = 105): Complication rates: Major complications: 3 vs 2 Minor: 9 vs 16 Duration of procedure (min): 55.3 (SD 15.8) vs 46.6 (SD 14.3), <i>P</i> = 0.001 Symptom control: Reduction in fibroid volume (%): 4 months = 49.9 (SD 17.3) vs 56.2 (SD 20.7) 12 months = 63.6 (SD 20.5) vs 68.6 (SD 20.5) Reduction in uterine volume (%): 4 months = 35.9 (SD 13.9) vs 40.5 (SD 13.8) 12 months = 49.8 (SD 19.3) vs 54.3 (SD 12.8) Time to recovery (days): 13.6 (SD 13.0) vs 11.7 (SD 9.8) Patient satisfaction: 4 months: 1.80 (SD 0.46) vs 1.97 (SD 0.18), <i>P</i> = 0.004 1 year: 1.79 (SD 0.50) vs 1.90 (SD 0.30) 2 year: 1.83 (SD 0.40) vs 1.96 (SD 0.20)	Funding source: Not stated Study summary: We found no increased risk to patients undergoing uterine artery embolisation for fibroids on the basis of tumour size. Successful outcomes can be obtained for such lesions.
Pinto 2003 ⁴²⁰	randomised; concealed – sealed envelopes; blinding not mentioned EL = 1+	64 eligible. 57 randomised (38 in UAE group – 1 refused assignment and had hysterectomy, 19 in hysterectomy group – 3 refused assignment and had UAE, 1 of whom later had hysterectomy)	Population characteristics: Women; bleeding associated with uterine fibroids; patient with fibroid > 10 cm; contraindications to surgery; desire to maintain fertility and/or sensitivity to iodine were excluded from study. Baseline characteristics (UAE vs hysterectomy): Age (years) 46.4 vs 44.6 No pregnancies = 2.6 vs 3.2	UAE; hysterectomy	2 years	ER visits after surgery; complications; success on bleeding patterns; length of stay	Success of treatment on bleeding patterns: UAE = 31 of 36 (86%) had cessation of bleeding. Hysterectomy bleeding not measured. Visits to ER after surgery: UAE = 13, Hysterectomy = 4 Intra-operative complications: Minor – UAE = 11 vs 0 Major – UAE = 0 vs hysterectomy = 4 Post-operative complications: Minor – UAE = 20 vs hysterectomy = 3 Moderate – UAE = 19 vs hysterectomy = 2	Funding source: Not stated Study summary: Compared with hysterectomy, UAE is safe and effective treatment for bleeding fibroids, necessitates a shorter hospital stay, and results in fewer major complications.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			<p>Births = 2.2 vs 2.5</p> <p>Previous treatment:</p> <p>None = 23 vs 9</p> <p>Hormonal = 14 vs 10</p> <p>Myomectomy = 1 vs 0</p> <p>Number of fibroids = 1.6 vs 1.6</p> <p>Fibroid type:</p> <p>mural = 16 vs 13</p> <p>Submucosal = 15 vs 2</p> <p>Subserous = 7 vs 4</p> <p>Fibroid volume (cm³) = 72 vs 113</p> <p>Symptoms:</p> <p>menorrhagia = 37 vs 17</p> <p>Metrorrhagia = 19 vs 9</p> <p>Country: Spain</p>				<p>Major – UAE = 1 vs hysterectomy = 7</p> <p>Length of stay (based on intention to treat) – UAE = 1.71 days (SD 1.59), hysterectomy = 5.85 day (SD 2.52)</p>	
Prollius 2004 ⁴³¹	Prospective case-control EL = 2-	64 (51 with normal uterus, 12 with large uterus)	<p>Population characteristics:</p> <p>Women; symptomatic uterine fibroids – menorrhagia; women wanted to retain uterus; women excluded if – asymptomatic fibroids, pregnant, infertility as a result of fibroids, had not completed families</p> <p>Groups split based on uterus > 780 cm³ or not</p> <p>Country: South Africa</p>	Uterine Artery Embolisation	6 weeks, 3 months and 12 months	Menstrual blood loss; pressure effects of fibroid; complications of procedure	<p>Menstrual blood loss (volume) at 12 months (% improvement):</p> <p>Normal uterus = 85.1</p> <p>Large uterus = 91.7</p> <p>95% CI –33.7 to 15.6</p> <p>Clots:</p> <p>Normal uterus = 73.5</p> <p>Large uterus = 66.7</p> <p>95% CI –17.9 to 37.2</p> <p>Pressure effects of fibroid (% improvement):</p> <p>Discomfort:</p> <p>Normal uterus = 57.1</p> <p>Large uterus = 83.3</p> <p>95% CI –54.8 to 4.5</p> <p>Mass:</p> <p>Normal uterus = 40.8</p> <p>Large uterus = 50</p> <p>95% CI –48.7 to 14.9</p> <p>Deep dyspareunia:</p> <p>Normal uterus = 32.7</p> <p>Large uterus = 50</p> <p>95% CI –43.6 to 13.8</p> <p>Fibroid volume (cm³):</p> <p>Normal uterus – Pre-treatment = 411, 12 months = 282</p> <p>Large uterus – Pre-treatment 12 = > 780, 12 months 4 had uterus > 780</p> <p>Complications of procedure (including further treatment):</p> <p>Normal uterus = 30</p> <p>Large uterus = 3</p>	<p>Funding source: Not stated</p> <p>Study summary: The large uterus does not decrease UAE's efficacy. Although 33.3% of the study group still had a uterus of ≥ 780 cm³, symptom reduction was still similar for both groups. Women may thus still be left with a large uterine volume but without symptoms. This must be taken into consideration when counselling women with an extremely large uterus for UAE.</p>

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Razavi 2003 ⁴²⁴	Comparative cohort study EL = 2+	111 women undergoing abdominal myomectomy (AM) (<i>n</i> = 44) or uterine fibroid embolisation (UTE) (<i>n</i> = 67) for symptomatic uterine fibroids	Population characteristics: Mean age: AM – 37.7 years; UTE – 44.2 years Country: USA	abdominal myomectomy or uterine fibroid embolisation abdominal myomectomy or uterine fibroid embolisation	AM: 14.6 months UTE: 14.3 months	Success rate: significant reduction of menorrhagia and pain Complications hospital stay use of narcotics resumption of normal activities	Significant reduction in menorrhagia: AM: 64% UTE: 92% (<i>P</i> < 0.05) Significant reduction in pain: AM: 74% UTE: 52% (NS) Significant reduction in mass effect: AM: 91% UTE: 76% (<i>P</i> < 0.05) Complications: AM: 10 (25%) (3 blood transfusion, mean blood loss 376 ml, 2 wound infection, 2 adhesion, 1 readmission for ileus, 1 chronic pelvic pain, 1 incisional pain) UTE: 7 (11%) (<i>P</i> < 0.05) (Minimal blood loss, 1 endometritis, 1 pelvic pain, 1 groin numbness, 4 menopause Mean hospital stay: AM: 2.9 days UTE: 0 day (<i>P</i> < 0.05) Mean days taking pain medications: AM: 8.7 UTE: 5.1 (<i>P</i> < 0.05) Mean days till normal activity: AM: 36 UTE: 8 (<i>P</i> < 0.05) Secondary intervention: AM: 10% UTE: 8% (NS)	Funding source: not stated Study summary: UTE is less invasive and safer treatment than AM in women with symptomatic fibroids
Society of Obstetricians and Gynaecologists of Canada.; 2005 ⁴³²	Guideline EL = 2+	Not stated	Population characteristics: Not stated Country: Canada	Uterine Fibroid Embolisation	N/A	N/A	Recommendations: 1. Women considering treatment of fibroids should be counselled that while the early results of uterine artery embolisation are encouraging, no long-term data exist. (II-2-B) 2. UFE should only be considered for women with symptomatic or problematic fibroids who might otherwise be advised to have surgical treatment. (III-A) 3. UFE as a treatment for fibroids in patients wishing to preserve their fertility should be undertaken with full disclosure to the patient about the limitations of such a procedure and the lack of existing data regarding future fertility and pregnancy outcomes. (III-C) 4. UFE is contraindicated in women who have evidence of current genitourinary infection and/or malignancy. (II-2-B) 5. Women who choose UFE as an alternative to hysterectomy should be counselled regarding the risk of major complications of UFE where hysterectomy may be urgently required and potentially lifesaving. In view of this small but important risk, UFE is relatively contraindicated in women who are unwilling to have a hysterectomy under any circumstances. (III-C) 6. Genitourinary infection is the predominant cause of serious morbidity and mortality. Further research on the utility of prophylactic antibiotic therapy and	Funding source: SOGC funded

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							<p>the value of pre-treatment screening for infection is needed. (II-2-B)</p> <p>7. A gynaecologist who is familiar with UFE should evaluate all patients considered for UFE before the procedure is booked and a consensus on the suitability of the procedure achieved between the gynaecologist and radiologist. (III-C)</p> <p>8. Only radiologists with specialized embolisation experience and techniques should perform UFE. (III-C)</p> <p>9. The particular responsibilities of both gynaecologist and radiologist should be established prior to treatment and be set out in a relevant hospital protocol. A particular physician must be responsible for the patient at all times. (III-C)</p> <p>10. A Canadian national registry of numbers, indications, outcomes, complications, and successful pregnancies associated with UFE should be created and jointly administered and funded by the SOGC, CAR, and CIRA. (III-C)</p>	
Spies 2005 ⁴²¹	randomised; EL = 1-	36 randomised, 17 to PVA, 19 to TAGM	Population characteristics: Women; pre-menopausal; symptomatic fibroids; 30 to 55 years of age; < 24 week size uterus; no large pedunculated serosal fibroids Country: USA	Tris-acryl gelatin microspheres (TAGM); spherical polyvinyl alcohol particles (PVA)			<p>Outcomes for PVA vs TAGM:</p> <p>Duration of procedure (minutes) = 55 vs 57.5</p> <p>Complete infarction on MRI = 1 (7.1%) vs 6 (54.5%)</p> <p>Incomplete infarction = 13 (92.9%) vs 5 (45.5%)</p> <p>At least 90% infarction = 4 (28.6%) vs 8 (72.2%)</p> <p>Uninfarcted tumour = 44.3% vs 9.6%, $P = 0.004$</p> <p>QoL change score = 27.9 (SD 21.7) vs 49.0 (SD 25.5), $P = 0.02$</p> <p>No difference between groups for symptom score at 3 months, QoL at 3 months, Symptom change score, bleeding score, pain score, satisfaction score, percent change in uterine volume and percentage change in fibroid volume.</p>	<p>Funding source: Non-commercial, but not specified</p> <p>Study summary: The use of spherical PVA particles in the manner described herein results in an unacceptably high rate of failed tumour infarction in UAE.</p>
Spies 2004 ⁴²²	randomised; single blinded EL = 1-	100 (50 in PVA group, 50 in Tris-acryl gelatin microspheres)	Population characteristics: Women; Aged 30 to 55; Symptomatic uterine fibroids Baseline (TGM vs PVA): Age: 43.3 vs 42.5 BMI: 27 vs 26.7 Uterine volume (cm ³): 648.7 (SD 326.7) vs 603 (SD 343.3) Fibroid volume (cm ³): 138.4 (SD 139.5) vs 162.4 (SD 169.3) Fibroid specific symptom score: 57.4 (SD 19.8) vs 50.2 (SD 23.2) Fibroid specific QoL score: 47.6 (SD 21.1) vs 57.8 (SD 22.5), $P = 0.02$. Country: USA	UAE using polyvinyl alcohol particles; UAE using tris-acryl gelatin microspheres	3 months	Procedure outcomes; Length of stay; Analgesia use; Symptom score/change; Uterine volume (cm ³); Fibroid volume (cm ³); complications	<p>Tris-acryl vs PVA:</p> <p>Procedure outcomes:</p> <p>Mean total embolic volume per patient: 9.4 vs 3.0 ($P = 0.0001$)</p> <p>Frequency of catheter occlusion: 4 vs 28 ($P = 0.001$)</p> <p>No difference for fluoroscopy time, frequency of spasms, frequency of ovarian flow grade > 2 per artery.</p> <p>In-hospital pain scores:</p> <p>No difference between groups for VAS pain, PCA dose, patient temperature, analgesia use or symptoms scores.</p> <p>Symptom score/change:</p> <p>Mean change in bleeding scores: 3.2 vs 3.3 (NS)</p> <p>Mean change in pressure symptoms: 3.3 vs 3.4 (NS)</p> <p>Mean fibroid specific symptoms: 21.3 (SD 14.8) vs 23.4 (SD 18.5), $P = 0.02$</p> <p>Mean change in fibroid specific symptoms: -39.2 (SD 24.3) vs -26.8 (SD 24.9), $P = 0.02$</p> <p>Mean fibroid specific QoL: 81.9 (SD 15.7) vs 80.9 (SD 18.8), $P = 0.02$</p> <p>Percentage change in uterine volume (cm³): 35.1 vs 30.2 (NS)</p> <p>Percentage change in fibroid volume: 56.5 (SD 22.2) vs 42.5 (SD 25.8), $P = 0.01$.</p> <p>Frequency of uninfarcted dominant fibroid (%): 18 vs 5, $P = 0.02$</p> <p>No difference for other uninfarcted fibroids or presence of any uninfarcted fibroids or amenorrhoea rates</p> <p>Complications: 19 vs 11</p>	<p>Funding source: Non-commercial</p> <p>Study summary: No substantive difference were detected between outcomes of embolisation.</p>

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Spies 2004 ⁴³³	Prospective; cohort EL = 2+	102 in UAE, 50 in hysterectomy	Population characteristics: Women; symptomatic leiomyomas; aged between 30 and 50; For UAE > 50% of leiomyomas within uterine cavity or dominant pedunculated serosal leiomyoma excluded. Average age: UAE = 42.6, Hysterectomy = 41.6 Number of leiomyoma: 1 = 26%, 40% 2 = 32%, 38% > 3 = 41%, 20% Largest leiomyoma volume (ml): 146.8, 90.6 Previous treatment: None = 52%, 70% Hormonal = 39%, 24% Surgery = 53%, 20% Country: USA	UAE; hysterectomy UAE vs Baseline UAE vs hysterectomy	12 months	PBAC score; Menorrhagia questionnaire; SF-12; complications	Baseline symptoms: Menstrual flow: Heavy: UAE = 96%, Hysterectomy = 84% Normal = 2%, 8% Menstrual bleeding score: UAE = 467.4, Hysterectomy = N/A SF-12 physical score: UAE = 44.4 (SD 8.3), Hysterectomy = 42.0 (SD 10.1) SF-12 mental score: UAE = 44.7 (SD 11.8), Hysterectomy = 40.3 (SD 10.8) UAE baseline vs 6 month follow-up results: PBAC score at baseline = 435.6 (SD 286.5), 6 months = 140.6 (SD 110.1), -58.1% (SD 36.6) Menorrhagia questionnaire score at baseline = 47.2 (SD 13.8), 6 months = 19.2 (SD 8.3), -56.6% (SD 20.3) Comparison of UAE and hysterectomy for SF-12 scores: SF-12 physical for UAE at baseline = 45.1 (SD 8.2), 12 months = 53.6 (SD 6.1), +22.6% (SD 27.1), $P < 0.001$ SF-12 physical for hysterectomy at baseline = 43.0 (SD 9.9), 12 months = 51.4 (SD 6.9), +25.4 (SD 32.7), $P < 0.001$ SF-12 mental for UAE at baseline = 45.4 (SD 11.5), 12 months = 52.6 (SD 7.9), +23.4% (SD 37.7), $P < 0.001$ SF-12 mental for hysterectomy at baseline = 40.6 (SD 11.1), 12 months = 51.1 (SD 11.2), $P < 0.001$ Complications: On SCVIR: UAE = 4 (3.9%), hysterectomy = 6 (12.0%) On ACOG: UAE = 15 (14.7%), Hysterectomy = 17 (34%)	Funding source: Biosphere Medical Study summary: Both procedures substantially improved symptoms for most patients, with an advantage for hysterectomy at 12 months for pelvic pain. Serious complications were infrequent in both groups.
Vilos 2006 ⁴²³	Randomised EL = 1-	26 included, 14 UAE only, 12 UAE and GnRH-a. 10 UAE and 12 UAE and GnRH-a analysed. 7 UAE and 9 UAE and GnRH-a analysed at 12 months.	Population characteristics: Women; symptomatic uterine fibroids; no other gynaecological pathology Country: Canada	UAE only; UAE and GnRH-a	12 months	Uterine volume (cm ³); Dominant fibroid volume (cm ³)	Outcomes for UAE only vs UAE and GnRH-a: Uterine volume (cm ³): Baseline = 476.6 (SD 279.3) vs 556 (SD 271.8), NS 12 months = 200.6 (SD 74.1) vs 305.1 (SD 141.3) Dominant fibroid volume (cm ³) Baseline = 257.3 (SD 302.9) vs 226 (SD 182.9) 12 months = 34.9 (SD 42.4) vs 94.7 (SD 88.9)	Funding source: Not stated Study summary: The addition of goserelin therapy to UAE did not alter the reduction rate or volume of uterine myomas.
Siskin et al 2006 ⁴²⁶	Prospective; cohort EL = 2+	146 in total. 77 in UAE and 69 in myomectomy	Population characteristics: Inclusion criteria: Women; Age ≥ 30 ; symptomatic fibroids; Pelvic MRI scan; menstrual cycle every 22 to 35 days; recent Pap smear; not drug treatment for fibroids within 3 months. Exclusion criteria: presence of hysteroscopically resectable fibroid; active pelvic infection; gynaecological malignancy; pregnant; unexplained AUB; wish for future fertility (UAE only).	UAE – using polyvinyl alcohol microspheres; myomectomy	12 and 24 months		UAE vs myomectomy: Adverse events: 26 in 77 vs 53 in 69	Funding source: Boston Scientific

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			Baseline figures (UAE vs myomectomy): Dominant symptom: AUB 53 vs 21 Pressure = 11 vs 20 Pelvic pain = 12 vs 21 Infertility = 0 vs 3 Other = 1 vs 3 UAE group were older and had more previous pregnancies. Country: USA					

Table 11.2 Radiological interventions for treatment of uterine fibroids – additional non-comparative studies

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Bruno 2004 ⁴³⁴	Prospective; cohort; non-comparative EL = 3	UAE	99	Women; UAE for symptomatic fibroids Baseline: Age: 43.0 (SE 0.52) BMI: 26.9 (SE 0.44) Race: African-American = 61, Caucasian = 34, other = 1. Uterine volume (cm ³): 628 (SE 34.1) Fibroid volume: 150 (SE 15.7) Fibroid specific symptom score: 54.1 (SE 2.19) Fibroid specific QoL score: 52.3 (SE 2.24) Country: USA	Pain scores; Temperature scores; Symptom summary scores; PCA use; Analgesia use	At 7 day follow-up: Pain scores: VAS score in hospital: 3.03 (SE 0.26) VAS score in first week: 4.89 (SE 0.26) Temperature scores: Maximum temperature in hospital :37.1 (SE 0.05) Maximum temperature in first week: 37.4 (SE 0.05) Symptom summary scores: Week 1 = 26.6 (SE 1.73) Week 2 = 5.93 (SE 0.34) Week 3 = 4.68 (SE 0.38) Week 4 = 4.86 (SE 0.41) PCA use: Doses given: 28.1 (SE 1.62) Total PCA dose (morphine mg): 46.7 (SE 3.48) Analgesia use: Paracetamol: 10.7 (SE 1.19) Ibuprofen: 17.9 (SE 0.58) Multiple regression on baseline factors influencing pain scores, temperature or symptoms scores found only one significant result for: African-American on symptom summary at weeks 2 to 4.	Funding source: Non-commercial funding Study summary: Despite the reputation of UAE to the contrary, when current techniques are used, recovery after UAE for fibroids is relatively mild, with few instances of severe pain, high fever, or severe constitutional symptoms.
Huang 2006 ⁴³⁵	Retrospective; cohort EL = 3	UAE	233	Women; undergone UAE for uterine fibroids Country: Canada	Hysterectomy rate; myomectomy rate; additional UAE rate	Hysterectomy rate = 16 Myomectomy rate = 6 Additional UAE rate = 3 (all had subsequent surgery) Total = 22 (9.4%) Failure (<i>n</i> = 22) vs asymptomatic group (<i>n</i> = 211) Uterine volume (cm ³): Baseline = 590.2 (SD 153.1) vs 525.3 (SD 30.2) 6 months = 253.4 (SD 29.7) vs 393.1 (SD 27.8) Dominant fibroid (cm ³): Baseline = 355.2 (SD 109.3) vs 183.8 (SD 15.7) 6 months = 161.9 (SD 60.5) vs 117 (SD 18.5)	Funding source: Not stated Study summary: The overall failure rate of UFE is 9.4%. Failure is mainly due to persistent menorrhagia and abdominal pain. Shrinkage of the uterus after UFE does not necessarily correlate with long-term success of UFE.
Hutchins 1999 ⁴³⁶	Prospective case series EL = 3	uterine artery embolisation	305	Women; pre-menopausal; leiomyomas; menorrhagia - subjective; excluded if – pregnant, active pelvic infection, allergy to contrast substance, arteriovenous fistula, undiagnosed pelvic mass. Age range 26 to 52 Country: USA	Technical completion of surgery; complications; menstrual bleeding patterns; fibroid symptoms; patient satisfaction; additional treatment	Technical completion of surgery: 13 of 205 procedures were not completed. Complications: No major and 2 minor complications Menstrual bleeding patterns: 3 months: 155 had improved, 11 had not 6 months: 101 had improved, 8 had not 12 months: 50 had improved, 2 had not. Fibroid symptoms – bulk: 3 months: 103 had improved, 13 had not 6 months: 71 had improved, 13 had not 12 months: 36 had improved, 4 had not.	Funding source: Not stated Study summary: Uterine artery embolisation appears to be a highly effective treatment for symptomatic uterine leiomyomata. Its impact on fertility and pregnancy remain to be investigated fully.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
						<p>Patient satisfaction with treatment:</p> <p>3 months: 155 of 185</p> <p>6 months: 103 of 121</p> <p>12 months: 51 of 59</p> <p>Additional treatment: 2 arteriograms, 6 hysterectomies, 5 myomectomies</p>	
Katsumori 2006 ⁴³⁷	Case series EL = 3	UAE	96 underwent treatment, 16 lost to follow-up	Women; symptomatic uterine fibroids Country: Japan	Complications rates; Treatment failure rates	<p>UAE outcomes by 5 years:</p> <p>Primary failure of symptom control = 0%</p> <p>Symptom recurrence = 10.5%</p> <p>Gynaecologic interventions = 10.5%</p> <p>Complication-related gynaecologic interventions = 2.1%</p> <p>Symptom control = 89.5%</p> <p>Overall failure of UAE = 12.7%</p> <p>Total number of complications = 25</p> <p>Major complications:</p> <p>Sloughing fibroids = 2</p> <p>Sexual dysfunction = 1</p>	<p>Funding source: Not stated</p> <p>Study summary: Uterine artery embolisation using gelatin sponge particles alone can achieve long-term symptom control for fibroids in most cases.</p>
Marret 2005 ⁴³⁸	Case series EL = 3	UAE	85	Women; undergone UAE Country: France	Risk factors for recurrence	<p>Increase in fibroid size ($P < 0.008$), size of largest fibroid ($P = 0.009$) and number of fibroids ($P = 0.02$) were only significant factors in recurrence of fibroids after UAE.</p> <p>Location of fibroid, patient age, nulliparity, BMI, Bulk symptoms, pain were all non-significant.</p>	Funding source: Not stated
McLucas 2000 ⁴³⁹	Case series EL = 3	UAE	152	Women; undergone UAE Baseline: Age = 43 Country: USA	Change in fibroid size; change in fibroid related symptoms	<p>Change in fibroid size by 6 weeks ($n = 115$): changed from 7.7 cm to 6.0 cm (-22%)</p> <p>Change in fibroid size by 6 months ($n = 115$): changed from 7.7 cm to 4.9 cm (-36%)</p> <p>67% reported cessation of menorrhagia.</p> <p>74% reported relief from pain and pressure symptoms.</p> <p>6 complications reported</p>	Funding source: Not stated
McLucas 1999 ⁴⁴⁰	Case series EL = 3	UAE	300	Women; menorrhagia secondary to uterine fibroids. Average age = 43 Country: USA	Success – symptom relief or fibroid shrinkage or no additional surgery	<p>Success:</p> <p>44 of 300 classified as failures.</p> <p>Demographics and gynaecological conditions did not correlate with success of treatment.</p> <p>Fibroid size > 8.5 cm did correlate with success of treatment.</p>	Funding source: Not stated
McLucas 2001 ⁴⁴¹	Case series EL = 3	UAE	167	women; menorrhagia or post-menopausal bleeding associated with uterine fibroids Country: USA	Change in uterine volume (ml); change in fibroid related symptoms	<p>Change in uterine size (ml) and myoma size (cm):</p> <p>Baseline ($n = 155$): 1389 (range 117 to 8804); 7.8 (1.5 to 16.3)</p> <p>6 weeks ($n = 125$): 864 (102 to 4640); 6.1 (1.1 to 14.2)</p> <p>6 months ($n = 98$): 619 (75 to 3474); 5.4 (1.8 to 13.7)</p> <p>12 months ($n = 46$): 608 (103 to 3716); 5.0 (1.4 to 11.0)</p> <p>Change in symptoms:</p> <p>123 of 150 reported improvement in menorrhagia</p> <p>133 of 150 reported improvement in pressure and pain symptoms.</p> <p>Complications:</p> <p>7 were readmitted due to pain.</p> <p>12 reported fever</p> <p>8 reported passing of myoma</p> <p>6 patients had had hysterectomy</p> <p>21 of 167 were considered failures – had hysterectomy, no improvement or worsening of symptoms.</p>	Funding source: Not stated

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Pelage 2000 ⁴⁴²	Prospective case series EL = 3	Uterine Artery Embolisation	80	Women; menorrhagia; failed medical treatment to treat menorrhagia; uterine fibroids found via ultrasound. Mean average age: 44.7 years 15 women had undergone myomectomy to treat fibroids Location of fibroids: Intramural = 79% Submucosal = 8% Mixed = 14% Number of fibroids: 1 = 31% 2 = 16% 3 = 21% > 3 = 31% Country: France	Menstrual bleeding pattern; completed procedure; Complications; Fibroid size	In 76 of 80 women the procedure was completed. 5 of 76 women reported no improvement in menstrual bleeding symptoms after treatment. Complications: 6 women complained of amenorrhoea. 68 of 76 women complained of post-operative pain. Fibroid size: Pre-treatment fibroid = 58 mm (range 21 to 100) At 6 months = 38 mm (range 18 to 68)	Funding source: Not stated Study summary: Super selective arterial embolisation of the uterine arteries is an effective means of controlling symptomatic uterine leiomyoma. However, the ideal embolic regimen remains to be determined.
Pron 2003 ⁴⁴³	Prospective; cohort EL = 3	Uterine Artery Embolisation – polyvinyl alcohol particles	538	Women; symptomatic uterine fibroids; excluded if – active pelvic inflammatory disease, undiagnosed pelvic mass, endometrial carcinoma, pregnancy, or renal insufficiency Baseline characteristics: Number of fibroids: 1 = 150 2 to 4 = 220 > 5 = 133 Country: USA	Change in uterus size; change in fibroid size; Symptom change; Patient satisfaction; Patient QoL	Baseline uterus size (cm ³): 704 (SD 586) Uterus size at 3 months (cm ³): 428 (SD 322) Mean % change in uterus size: 27 (95% CI 23 to 32) Baseline fibroid size (cm ³): 308 (SD 380) Fibroid size at 3 months (cm ³): 170 (SD 215) Mean % change in fibroid size: 33 (95% CI 28 to 38) Symptom change: Menorrhagia: improved = 358, unchanged = 43, worse = 28 Dysmenorrhoea: improved = 249, unchanged = 43, worse = 30 Bulk: improved = 388, unchanged = 72, worse = 4 Urinary urgency/frequency: improved = 263, unchanged = 41, worse = 2 Patient satisfaction at 3 months: 91% satisfied Patient QoL: Life impact score changed from 8 to 3 by 3 months ($P < 0.001$)	Funding source: Not stated Study summary: UAE reduced fibroid uterine volume and provided significant relief of menorrhagia that was unrelated to initial fibroid uterine size or volume reduction. Patient satisfaction with short-term UAE treatment outcomes was high.
Pron 2003 ⁴⁴⁴	Prospective; cohort EL = 3	Uterine Artery Embolisation	555 entered study, 539 completed baseline questionnaire	Women; symptomatic uterine fibroids; excluded if – active pelvic inflammatory disease, undiagnosed pelvic mass, endometrial carcinoma, pregnancy, or renal insufficiency Country: Canada	N/A	Baseline characteristics: Mean age = 43 (SD = 6.04; range 18 to 59). 167 of 539 were < 40 years. General health: Excellent = 89 (17%) Very good = 215 (40%) Good 196 (37%) Not very good = 35 (7%) Menopausal status: pre-menopausal = 431 (80%) Peri-menopausal = 92 (17%) Postmenopausal = 14 (3%) Family intentions: No children = 168 (50%) decided not to have = 95 (18%) would like to have = 127 (24%) Unable to have = 35 (7%)	Funding source: Not stated Study summary: Our study illustrates that large numbers of women with highly symptomatic fibroid disease are averse to surgery despite their burden of suffering and are actively seeking alternatives to hysterectomy.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
						<p>Children = 269 (50%) Decided no more = 196 (36%) Would like more = 37 (7%) Unable to have more = 30 (6%)</p> <p>Number of fibroids: 1 = 150 (30%) 2 to 4 = 220 (44%) ≥ 5 = 125 (26%)</p> <p>Fibroid volume (cm³): 0 to 100 = 174 (35%) 101 to 200 = 114 (23%) 201 to 400 = 91 (18%) ≥ 401 = 121 (24%) Mean average = 293 (95% CI 259 to 327)</p> <p>Uterine volume (cm³): 0 to 250 = 106 (22%) 251 to 500 = 131 (27%) 501 to 1000 = 149 (31%) ≥ 1000 = 102 (21%) Mean average = 680 (95% CI 626 to 734)</p> <p>Symptoms: Pelvic pain only = 68 (13%) Pain with bleeding = 337 (63%) Bleeding only = 89 (17%) Bulk/mass effects = 45 (8%)</p> <p>Symptom durations (years): < 1 = 20 (4%) 1 to 4 = 278 (54%) 5 to 9 = 122 (24%) ≥ 10 = 94 (18%) Mean average = 5 (95% CI 4.8 to 5.7)</p> <p>Prior myomectomy = 73 (14%)</p> <p>Fibroid impact score: 1 to 3 = 90 (17%) 4 to 6 = 135 (26%) 7 to 10 = 304 (58%)</p>	
Pron 2003 ⁴⁴⁵	Prospective; cohort/single arm trial; multicentre EL = 3	Uterine Artery embolisation	555 (11 centre)	Women; UAE for symptomatic fibroids Country: Canada	Intra-procedural pain; post-procedural pain; Length of stay; complications; readmission rates	<p>Intra-procedural pain: Categorical scale: None = 386 Minor = 33 Uncomfortable = 54 Very uncomfortable = 50 Unbearable = 23 Numeric scale (0 to 10): 0 = 386 1.0 to 2.0 = 13</p>	Funding source: Boston scientific partially funded study

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
						3.0 to 4.0 = 26 5.0 to 6.0 = 43 7.0 to 10.0 = 80 Post-procedural pain; Categorical scale: None = 44 Minor = 86 Uncomfortable = 103 Very uncomfortable = 188 Unbearable = 116 Ineffective pain management = 24 Numeric scale (0 to 10): 0 = 44 1.0 to 2.0 = 25 3.0 to 4.0 = 63 5.0 to 6.0 = 95 7.0 to 10.0 = 313 Ineffective pain management = 57 Length of stay: 1.3 days Complications: Pain/nausea/vomiting = 75 Pain/fever = 16 Hypertension = 3 Respiratory depression = 1 Aspiration pneumonia = 1 Pulmonary oedema = 1 Seizure = 1 Dissatisfaction with interventional care = 17 Post-embolisation symptoms: Discharge = 115 Spotting = 120 Bleeding = 173 Swelling = 252 Fever = 157 Dysuria = 12 Hot flushes = 163 Mood swings = 41 Leg pain = 46 Fibroid passage = 19 Hypertension = 7 Emergency room returns: 57 Readmission rates: 16 Recovery time (days): 13.1 Pain levels linked with length of stay ($P = 0.004$)	

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Rajan 2004 ⁴⁴⁶	Retrospective; case series EL = 3	Uterine Artery Embolisation	414	Women; undergone UAE Country: Canada	Factors linked to risk of uterine infection	410 of 414 procedures were technically successful. 103 of 414 received antibiotics 5 of 414 had uterine infections (none had history of pelvic disease). Risk factors for uterine infection: Submucosal vs non-submucosal, $P = 0.079$ Use of pre-procedure antibiotics, $P = 0.81$ Type of embolic agent, $P = 0.71$ Vials of embolic particles used, $P = 0.33$ Size of dominant fibroid, $P = 0.74$ Location of dominant fibroid, $P = 1.0$	Funding source: Not stated Study summary: No risk factors for uterine infection after UAE were identified.
Ravina 1999 ⁴⁴⁷	Prospective; cohort EL = 3	Uterine Artery Embolisation (polyvinyl alcohol)	184 treated, 8 procedure failures, 19 lost to follow-up, 157 assesses	Women; Uterine fibroids Country: France	Reduction in fibroid size; Complications	Reduction in fibroid size: 0 to 24% (failure) = 7% Vanished = 6% Expelled = 4% Complications: Fever = 20 Menorrhagia = 19 UTI = 3 Aseptic necrobiosis = 1 Expelled fibroid = 6 Uterine necrosis = 1 Amenorrhoea = 20 (10 UAE related)	Funding source: Not stated
Roth 2000 ⁴⁴⁸	Prospective; cohort/single arm trial EL = 3	Uterine Artery Embolisation	81	Women; UAE for symptomatic fibroids Country: USA	Factors linked to post-operative pain	Regression analysis results for relationship between analgesia use and uterine volume: Attempted doses (self-administered) $R^2 = 0.035$ (NS) Doses given, $R^2 = 0.032$ (NS) Total morphine dose, $R^2 = 0.10$ (NS) Numeric pain rating scale, $R^2 = 0.012$ (NS) Regression analysis results for relationship between analgesia use and fibroid volume: Attempted doses (self-administered) $R^2 = 0.029$ (NS) Doses given, $R^2 = 0.013$ (NS) Total morphine dose, $R^2 = 0.10$ (NS) Numeric pain rating scale, $R^2 = 0.00016$ (NS)	Funding source: Not stated Study summary: Use of analgesia was not related to uterine volume or fibroid size.
Shan 2004 ⁴⁴⁹	Prospective; one-arm trial EL = 3	UAE using PLE (pingyangmycin-lipiodol emulsion)	100	Women; menorrhagia associated with uterine fibroids; ultrasound confirmed fibroids Country: China	Menorrhagia; bulk-symptoms; postoperative pain; complications; change in uterine size	Menorrhagia: 99 of 100 reported reduced blood loss Bulk-symptoms: 44 of 64 reported improvement in bulk symptoms. Postoperative pain: 83 of 100 reported resolution of pain within 7 days Complications: 2 reported Change in uterine size: mean reduction in volume was 42% by 3 months, and 48% by 6 months	Funding source: Not stated Study summary: PLE is effective in the management of uterine leiomyoma, having superiority in alleviating post-procedure-related pain.
Spies 2001 ⁴⁵⁰	Case series EL = 3	Uterine Artery Embolisation	200	Women; uterine fibroids; symptoms associated with fibroids – menorrhagia, pelvic pain or pressure, urinary symptoms. Women excluded if – pregnant, primary aim was pregnancy. Average age = 43	Menstrual bleeding symptoms; bulk symptoms; satisfaction with symptoms; complications; completion of treatment; subsequent surgery; uterine and fibroid volume	198 of 200 procedures were technically completed. 97% discharged within 1 day of procedure. Mean average days until return to work = 8 Menstrual symptoms (% improved): 3 months = 87, 6 months = 89, 12 months = 90 Bulk symptoms (% improved): 3 months = 93, 6 months = 92, 12 months = 91 Satisfaction with symptoms (%): 3 months = 93, 6 months = 93, 12 months = 92	Funding source: Public and private funded (Boston Scientific) Study summary: Uterine artery embolisation is safe and controls the symptoms caused by leiomyomas in

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
				Menorrhagia = 85% Pelvic pain or pressure = 83% Urinary symptoms = 54% Mean uterine volume (cm ³) = 714 (SD 482) Mean fibroid volume (cm ³) = 240 (SD 279) Location of primary fibroid: Submucosal = 19% Intramural = 59% Subserosal = 21% Country: USA		Uterine volume at 3 months (<i>n</i> = 174) was reduced by 27%, and by further 38% by 12 months (<i>n</i> = 116) Fibroid volume at 3 months was reduced by 44% and by 58% by 12 months Complications: minor = 13 Major = 1 Subsequent surgery: 21 including 9 hysterectomies	most patients.
Spies 2005 ⁴⁵¹	Prospective; single arm-trial/cohort; non-comparative EL = 3	Uterine Artery embolisation	200	Women; Undergone UAE for symptomatic uterine fibroids; Excluded if – pregnant, suspicion of cancer. Baseline: age = 43.1 Race: African-American = 101 White = 90 Other 9 Number of fibroids: 1 = 28 2 to 5 = 138 > 5 = 23 Missing = 11 Location of fibroids: Intramural = 108 Submucosal = 35 Subserosal = 39 Missing = 18 Uterine volume (ml) = 717 (95% CI 648.8 to 785.2) Largest fibroid (ml) = 240.0 (95% CI 200.8 to 279.3) Country: USA	Change in symptoms; Major interventions; menstrual cycles; Bleeding score; pain score	Change in symptoms (improved vs not improved, <i>n</i> = 200)) 3 months: 180 vs 9 1 year: 166 vs 10 2 years: 136 vs 8 3 years: 152 vs 7 4 years: 143 vs 6 5 years: 133 vs 10 Major intervention (hysterectomy, myomectomy, redo UAE): 3 months: 7 1 year: 15 2 years: 6 3 years: 11 4 years: 6 5 years: 8 Change in bleeding score (from –5 to +5, positive means improvement): 3 months: 3.33 1 year: 3.73 2 years: 3.83 3 years: 3.84 4 years: 4.07 5 years: 3.98 Change in pain score (from –5 to +5, positive means improvement): 3 months: 3.47 1 year: 3.68 2 years: 3.56 3 years: 3.81 4 years: 3.84 5 years: 3.72 Change in uterus at 12 months: –39.4% Change in fibroid size at 12 months: – 57.8%	Funding source: Not stated Study summary: Uterine embolisation provides durable symptom relief for most patients, with a 25% chance of failure of symptom control or recurrence over the course of a 5 year follow-up.
Spies 2005 ⁴²⁸	Cohort EL = 3	Uterine Artery Embolisation	2112	Women; Undergone UAE Country: USA	Symptoms score; QoL score; subsequent treatment	Outcomes (baseline <i>n</i> = 2122, 6 months, <i>n</i> = 1798, 12 months, <i>n</i> = 1701) Symptom score (0 to 100; baseline, 6 months, 12 months; Mean (SD)): 58.61 (20.82), 19.87 (18.61), 19.23 (17.94) HRQOL score (0 to 100; baseline, 6 months, 12 months; Mean (SD)): 46.95 (23.03), 85.04 (20.06), 86.68 (18.15)	Funding source: Commercial and government sources Study summary: Uterine embolisation results in substantial symptom improvement for most

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
						<p>Subsequent care:</p> <p>Medical treatment: 0 to 6 months = 6.96%, 6 to 12 months = 7.11%</p> <p>Gynaecological interventions: 0 to 6 months = 3.56, 6 to 12 months = 5.88%</p> <p>Unplanned ER or hospital visit: 0 to 6 months = 5.51, 6 to 12 months = 3.06%</p> <p>Multivariate analysis on change in symptoms scores (adjusted, negative figure means less improvement in score):</p> <p>Predominant symptoms:</p> <p>HMB = -16.6 (-26.1 to -7.12)</p> <p>Bulk symptoms = -8.22 (-17.3 to 1.92)</p> <p>Pain = -7.71 (-18.3 to 1.96)</p> <p>Fibroid size = 1.020 (0.60 to 1.44)</p> <p>Prior medication = -4.11 (-6.44 to -1.77)</p> <p>Fibroid morphology = -4.73 (-8.0 to -1.46)</p> <p>Age = 0.21 (0.01 to 8.56)</p> <p>Multivariate analysis on change in QOL scores (adjusted):</p> <p>Predominant symptoms:</p> <p>HMB = 17.94 (8.02 to 27.87)</p> <p>Bulk symptoms = 6.50 (-4.00 to 16.98)</p> <p>Pain = 7.07 (-2.98 to 17.12)</p> <p>Fibroid size = -0.937 (-1.37 to -0.51)</p> <p>Prior medication = 6.166 (3.77 to 8.56)</p> <p>Fibroid morphology = 4.87 (1.60 to 8.15)</p> <p>Age = -3.81 (-6.54 to -1.08)</p>	patients, with hysterectomy required in only 2.9% of patients in the first 12 months after therapy.
Spies 2002 ⁴⁵²	Prospective; one arm trial EL = 3	UAE	200, 182 at 3 months, 184 at 12 months	Women; UAE Country: USA	Factors associated with fibroid volume change	<p>Factors associated with reduction in fibroid volume by 3 months:</p> <p>Submucosal, baseline uterine volume significant factors ($P < 0.05$). Number of fibroids, race, birth control use, GnRH, prior pregnancies, prior births, baseline uterine volume and age.</p> <p>Factors associated with reduction in fibroid volume by 12 months:</p> <p>baseline uterine volume significant factors ($P < 0.05$). Type of fibroid, number of fibroids, race, birth control use, GnRH, prior pregnancies, prior births, baseline uterine volume and age</p>	Funding source: Not stated Study summary: Smaller baseline leiomyoma size and submucosal location are more likely to result in a positive imaging outcome. There are limited associations between other baseline parameters and either symptom change or imaging outcome.
Spies 2002 ⁴⁵³	Prospective; cohort EL = 3	Uterine Artery embolisation	400	Women; uterine fibroids; undergoing UAE. No demographic figures provided. Country: USA	Complications	<p>Complications after UAE:</p> <p>None = 358</p> <p>Allergic reaction = 10</p> <p>Leiomyoma passage = 10</p> <p>Prolonged pain = 5</p> <p>UTI = 4</p> <p>Endometritis = 2</p> <p>Femoral nerve injury = 3</p> <p>Vessel injury = 2</p> <p>Urinary retention = 2</p> <p>Vaginal discharge = 1</p> <p>DVT = 1</p> <p>Drug reaction = 1</p>	Funding source: Not stated Study summary: The short-term complication rate was low in women undergoing uterine embolisation.

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
						Thrush = 1 <i>Clostridium difficile</i> infection = 1 Intravenous phlebitis = 1 Arterial thrombosis = 1 Pulmonary embolism = 1 In-hospital = 10 Within 30 days of discharge = 37 After 30 days of discharge = 10	
Walker 1999 ⁴⁵⁴	Case series EL = 3	Uterine Artery Embolisation	200	Women; undergone UAE for symptomatic uterine fibroids Country: UK	Menstrual symptoms; pressure symptoms; complications; failures; fibroid volume	In 7 of 200 patients it was not possible to complete procedure. 111 of 200 responded to follow-up questionnaire. Menstrual symptoms were improved in 79% of patients. Pressure symptoms were improved in 92% of women. 2 serious complications were reported. Volume reduction of fibroid by ultrasound at 12 months = 69%.	Funding source: Not stated
Walker 2002 ⁴⁵⁵	Prospective case series EL = 3	Uterine artery embolisation	400	Women; symptomatic uterine fibroids; menorrhagia or bloating Mean age = 43.2 HMB = 78% Painful periods = 59% Country: UK	Menstrual symptoms; fibroid symptoms; fibroid volume; patient satisfaction with treatment; complications; recovery time	84% of women reported improvement in menorrhagia symptoms. 97% of women satisfied with treatment and outcome Days of pain after surgery: mean = 17.2 Days until returned to normal activities: mean = 13.6 Days till back to work: mean = 16.6 Uterus and fibroid volume by ultrasound (cm ³): pre-treatment: Uterus = 787 (SD 648) Fibroid = 248 (SD 354) Post-treatment: Uterus = 326 (SD 246) Fibroid = 88 (SD 158) $P = 0.0001$ from change in volume of uterus and fibroid. 12 of 400 treatments failed to improve symptoms. 11 of 400 had temporary improvement in symptoms. Of 23 failures: 3 had second UAE, 4 had myomectomy, 9 had hysterectomy, 1 had ablation, 2 had hysteroscopies. 3 cases on infective complications. 13 pregnancies in 12 women – 9 successful.	Study summary: Uterine artery embolisation is associated with a high clinical success rate and good fibroid volume reduction. Infective complications requiring hysterectomy, amenorrhoea under the age of 45 and chronic vaginal discharge may complicate the procedure.
Watson 2002 ⁴⁵⁶	Case series EL = 3	UAE	114 women and 165 fibroids.	Women; undergoing UAE Baseline: Age: 42 Country: UK	Fibroid volume	Change in fibroid volume pre- to post- treatment: All = -58% In 10 women fibroid had disappeared. In 5 women a > 98% reduction was found.	Funding source: Not stated Study summary: The majority of women were satisfied with their outcome. We have shown that uterine artery embolisation is a successful treatment for symptomatic fibroids of all types, sizes and signal characteristics.
Worthington 2005 ⁴²⁷	Prospective; cohort; non-comparative EL = 3	UAE	3160	Women; Undergone UAE baseline characteristics ($n = 3005$): Age = 43.5 (SD 5.6)		Adverse events ($n = 3041$): In hospital events: None = 2952 1 event = 89	Funding source: Mixed commercial and non-commercial funding Study summary: Uterine embolisation for

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
				<p>Race:</p> <p>African-American = 48%</p> <p>White, non-Hispanic = 44.4%</p> <p>White, Hispanic = 3.6%</p> <p>Asian = 2.8%</p> <p>Other = 1.3%</p> <p>Co-morbidities:</p> <p>Obesity = 12.1%</p> <p>Diabetes = 2.9%</p> <p>Hypertension = 12.8%</p> <p>Current smoker = 12.2%</p> <p>Reproductive history:</p> <p>irregular menses = 28%</p> <p>Postmenopausal = 2.6%</p> <p>History of infertility = 10.7%</p> <p>Nulliparous = 44.1%</p> <p>Preterm delivery = 10.6%</p> <p>Symptoms:</p> <p>HMB = 84.5%</p> <p>Pelvic pain = 62.1%</p> <p>Bulk-related = 83.9%</p> <p>Other symptoms = 12.3%</p> <p>Pre-dominant symptoms:</p> <p>HMB = 64.7%</p> <p>Pelvic pain = 10.5%</p> <p>Bulk-related = 23.3%</p> <p>Other symptoms = 1.5%</p> <p>Symptom severity:</p> <p>Symptom severity index = 59 (44 to 72)</p> <p>UFS-QOL = 46 (29 to 65)</p> <p>Prior procedures for uterine fibroids:</p> <p>Any invasive procedure = 34.7%</p> <p>Multiple procedures = 7.6%</p> <p>D&C = 18.7%</p> <p>Myomectomy = 13.7%</p> <p>Hysteroscopy = 5.6%</p> <p>Endometrial ablation = 1.4%</p> <p>Other = 4.0%</p> <p>UAE = 0.4%</p> <p>Mean uterine volume = 677.7 (SD 520.4)</p> <p>Number of uterine fibroids:</p> <p>Any demonstrable = 95.7%</p> <p>1 to 2 = 43.4%</p> <p>3 to 4 = 24.1%</p>		<p>2 events = 5</p> <p>Major event = 20</p> <p>Nausea = 4</p> <p>Prolonged pain = 6</p> <p>Drug reaction = 1</p> <p>Vessel injury = 3</p> <p>Other complications = 4</p> <p>Urinary retention = 1</p> <p>Contrast reaction = 1</p> <p>Minor events = 74</p> <p>Contrast reaction = 3</p> <p>Drug reaction = 5</p> <p>Device related = 1</p> <p>Groin haematoma = 22</p> <p>Nausea = 0</p> <p>Nontarget embolisation = 1</p> <p>Prolonged pain = 0</p> <p>Urinary retention = 11</p> <p>Vessel injury = 13</p> <p>Other = 18</p> <p>Post discharge adverse events (<i>n</i> = 2729)</p> <p>None = 2019</p> <p>1 event = 519</p> <p>2 events = 128</p> <p>3 events = 49</p> <p>4+ events = 14</p> <p>Any event = 710</p> <p>Major events = 135</p> <p>Persistent bleeding = 7</p> <p>Infection = 17</p> <p>New hot flushes = 2</p> <p>Thromboembolism = 4</p> <p>Recurrent pain = 65</p> <p>Sloughing or passing fibroid = 19</p> <p>Spinal headache = 1</p> <p>Others = 20</p> <p>Minor events = 848</p> <p>Bleeding = 55</p> <p>Headache = 18</p> <p>New hot flushes = 156</p> <p>Infection = 82</p> <p>Pain = 264</p> <p>Sloughing = 123</p> <p>Other = 150</p> <p>Multivariate analysis showed that:</p> <p>Any prior procedures, OR = 1.235 (<i>P</i> < 0.001)</p> <p>DVT prophylactic use: OR = 0.757 (<i>P</i> = 0.005)</p> <p>Duration of procedure: OR = 1.004 (<i>P</i> = 0.009)</p> <p>African-American: OR = 1.129 (<i>P</i> = 0.021)</p> <p>Current or recent smoker: OR = 1.141 (<i>P</i> = 0.039)</p>	leiomyomata is a low-risk procedure with little variability in short-term outcome based on either patient demographics or practice setting.

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
				5 or more = 32.6% Morphology of uterine fibroids: Intramural = 42.8% Transmural = 20.3% Subserosal = 14.3% Submucosal = 13.1%		were significant factors associated with adverse events.	

Table 11.3 Myomectomy for treatment of uterine fibroids – comparative studies

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Agostini 2005 ⁴⁷⁰	randomised EL = 1–	94 randomised; 47 to oxytocin; 47 to placebo	Population characteristics: Women; symptomatic uterine fibroids; scheduled for myomectomy Baseline characteristics (oxytocin vs placebo): Age = 40 vs 39 Weight of fibroid (g) = 286 (SD 206) vs 268 (SD 253) Indication for surgery: bleeding = 24 vs 21 Pelvic pain = 17 vs 20 Fertility = 6 vs 6 Country: France	oxytocin pre-treatment before myomectomy; placebo pre-treatment before myomectomy	2 days	Intra-operative blood loss (ml); Change in haemoglobin (g/dl); blood transfusion rates	Oxytocin ($n = 47$) vs placebo ($n = 47$) Intra-operative blood loss (ml): 508 (SD 558) vs 451 (SD 336), $P = 0.55$ Change in haemoglobin (g/dl): 1.89 (SD 1.26) vs 1.93 (SD 1.2), $P = 0.87$ Blood transfusion rates: 7 of 47 vs 2 of 47, $P = 0.09$	Funding source: Not stated
Broder 2002 ⁴²⁵	Comparative cohort study EL = 2+	81 women undergoing abdominal myomectomy (AH) ($n = 30$) and uterine artery embolisation (UAE) ($n = 51$) for symptomatic fibroids	Population characteristics: Mean age: UAE: 43.5 years AH: 37.6 years ($P < 0.001$) More likely to have previous myomectomy ($P < 0.001$) Country: Germany	abdominal myomectomy vs uterine artery embolisation abdominal myomectomy vs uterine artery embolisation	AH: mean 49 months UAE: mean 46 months	Further invasive treatment overall symptoms improvement patient satisfaction	Further invasive treatment UAE: 15 (29%) (12% hysterectomy, 16% myomectomy, 2% UAE) AM: 1 (3%) (0=0.04) (3% hysterectomy, 0 myomectomy, 0 UAE) overall symptoms improvement UAE: 92% AM: 90% (NS) Patient satisfaction: Dissatisfied: UAE: 6% AM: 21% ($P = 0.06$) Clinical failure: UAE: 39% AM: 30% (NS) Using logistic regression: UAE more likely to have further invasive therapy (OR 12.5, 95%CI 1.4 to 110.1)	Funding source: not stated Study summary: UAE more likely than AM to need further invasive therapy 3–5 years after index procedures
Celik 2003 ⁴⁷¹	Randomised; double-blind EL = 1–	25 randomised; 12 placebo pre-treatment; 13 vaginal misoprostol (400 µg)	Population characteristics: Women; symptomatic uterine fibroids; scheduled for myomectomy Baseline (misoprostol vs placebo): Age = 31.7 vs 32.2 Parity = 2.2 vs 2.3 BMI = 28.3 vs 28.5 Number of myoma = 5.5 vs 5.3 Largest myoma (mm) = 150.7 vs 154.2 Uterus size (weeks) = 15.7 vs 15.5 Intramural fibroids = 79% vs 81% Subserous = 20% vs 18% No statistical difference between groups Country: Turkey	Misoprostol prior to myomectomy; placebo prior to myomectomy	1 day	Haemoglobin levels (g/dl); Estimate intra-operative blood loss (ml); need for transfusions; operating time (min); length of stay (days)	Misoprostol ($n = 13$) vs placebo ($n = 12$): Haemoglobin levels (g/dl): Pre-operative = 12.6 vs 12.3 (NS) Post-operative 1 hour = 10.6 vs 9.7 ($P < 0.05$) Postoperative 24 hours = 9.7 vs 8.9 ($P < 0.05$) Estimate intra-operative blood loss (ml): 472 (SD 77) vs 621 (SD 121); $P < 0.05$ Need for transfusions: 2 vs 4 ($P < 0.05$) Operating time (min): 48.5 vs 58 Length of stay (days): 4.2 vs 4.2	Funding source: Not stated

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Corson 1994 ⁴⁷²	Placebo; double-blind; randomised – double-blind EL = 1–	64 women in total – not stated how many in each group.	Population characteristics: Women; benign pathology – uterine fibroids, polyps; scheduled for hysteroscopic surgery – ablation, myomectomy, polypectomy. Variation in pre-treatment for women Country: USA	Dilute vasopressin (20 units); placebo	Not stated	Blood loss (ml)	Minimal operative bleeding: 81% in vasopressin vs 42% in placebo ($P = 0.0002$)	Funding source: Not stated
Derman 1991 ⁴⁵⁹	Comparative case series – chart review EL = 2–	156 women (94 undergoing hysteroscopic submucous resection of uterine leiomyomas, 62 endometrial ablation)	Population characteristics: 94 women undergoing submucous resection Mean age: 36.6 years (26–50) Indications: 83% menorrhagia/metrorrhagia, 16% infertility, 1% post-menopausal bleeding Country: USA	hysteroscopic submucous resection an/or endometrial ablation None	up to 9 years	peri-operative complications fertility length of hospital stay recurrence of symptom requiring repeat hysteroscopic or major abdominal surgery	Hysteroscopic submucous resection: peri-operative complications: 0 heart failure 0 adverse reaction to Hyskon 4 blood transfusion 23 (24.5%) reported problems (recurrent abnormal bleeding, uterine rupture and pain) 16% further surgery, 84% did not require further surgery at 9 year follow-up Fertility – 21 became pregnant (2 aborted and 5 TOP; 18 infants delivered) Endometrial ablation: 0 blood transfusion 22.5% recurrence in increased bleeding 8% had another surgical procedure 91.3% had not required further surgery at 6 year follow-up Fertility – 0 became pregnant Mean length of stay – 2.06 nights	Funding source: Not stated Study summary: hysteroscopic submucous resection of uterine leiomyomas and endometrial ablation appeared to be effective treatment of menorrhagia and leiomyoma over the long term, although effectiveness appears to diminish with time
Fedele 1990 ⁴⁷³	RCT EL = 1+	$n = 24$: GnRH-a (buserelin) prior to myomectomy ($n = 8$) Immediate myomectomy ($n = 16$)	Population characteristics: Women with symptomatic multiple uterine leiomyomas, prevalent symptoms of infertility ($n = 18$) and menorrhagia ($n = 6$) Mean age: 33.6 years (24–38) Country: Italy	GnRH-a (buserelin) prior to myomectomy or immediate myomectomy Intranasal GnRH-a (buserelin) prior to myomectomy vs immediate myomectomy	6 months	Intra-operative blood loss post-operative morbidity short-term myoma recurrence	Intra-operative blood loss (mean): GnRH-a + myomectomy – 235 ml (SEM 22) immediate myomectomy – 275 ml (SEM 35): NS Post-operative morbidity (pyrexia $\geq 39^\circ\text{C}$): GnRH-a + myomectomy – 2 women immediate myomectomy – 3 women (NS) Short-term myoma recurrence: At 3 months – negative in both groups At 6 months – Myoma < 1.5 cm recurrence detected by ultrasound: GnRH-a + myomectomy – 5 (63%) immediate myomectomy – 2 (13%) ($P < 0.05$)	Funding source: not stated Study summary: A period of induction with hypo-estrogen prior to myomectomy may favour short-term recurrence of myomas, limiting the efficacy of surgery
Fletcher 1996 ⁴⁷⁴	randomised EL = 1–	52 randomised; 26 to vasopressin; 26 to tourniquet	Population characteristics: Women; aged 24 to 45; symptomatic uterine fibroids; uterus size = 10 weeks gestation; excluded if – contraindications to vasopressin. Baseline characteristics: Age = 33.2 vs 35.2 Uterus size (weeks) = 16.5 vs 16.6 Number of fibroids = 10.1 vs 9.2	Vasopressin; tourniquet	Not stated	Intra-operative blood loss (ml); Haemoglobin level; post-operative fever;	Vasopressin ($n = 26$) vs tourniquet ($n = 26$): Intra-operative blood loss (ml): 287.3 (SD 195) vs 512.7 (SD 200), $P = 0.036$ Blood loss > 1 litre = 0 vs 6, $P = 0.023$ Transfusions = 1 vs 5, $P = 0.191$ Haemoglobin level: Baseline = 11.9 vs 12.2 Post-operative = 10.2 vs 9.8	Funding source: Not stated

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			Largest fibroid diameter = 6.6 vs 9.4 Country: Jamaica				(no effect caused by transfusions) Post-operative fever: 3 vs 5, $P = 0.703$	
Frederick 1994 ⁴⁷⁵	Randomised; single blind EL = 1-	20 randomised (10 to vasopressin; 10 to placebo)	Population characteristics: Women; scheduled for myomectomy; symptomatic uterine fibroids; uterine size > 14 weeks. Baseline characteristics (vasopressin vs placebo): Age = 32 vs 32 Parity = 0 vs 0 Size of uterus (weeks) = 17 vs 18 Number of fibroids = 14 vs 8 Size of largest fibroid (sm) = 8.6 vs 10 Country: Jamaica	Dilute vasopressin (20 u/ml); saline (20 ml)	Not stated	Blood loss (ml); Haemoglobin fall (g/dl); haematocrit fall (g/dl)	Vasopressin vs placebo: Blood loss (ml): 225 (150 to 400) vs 675 (500 to 800) ($P = 0.0001$) Haemoglobin fall (g/dl): 1.7 vs 5.3 ($P = 0.0002$) haematocrit fall (g/dl): 5 vs 13 ($P = 0.0003$)	Funding source: Not stated
Ginsburg 1993 ⁴⁷⁶	randomised EL = 1-	21 women randomised; 10 to vasopressin; 11 to tourniquet	Population characteristics: Women; symptomatic uterine fibroids; scheduled for myomectomy. Excluded if – prior myomectomy, abdominal adhesions, adnexal masses, or coagulopathy Baseline characteristics (vasopressin vs tourniquet): Age = 36 vs 36 Uterine volume (cm ³) = 833 vs 650 Country: USA	Vasopressin prior to myomectomy; tourniquet prior to surgery	Not stated	Total blood loss (ml); Operating time (minutes); ; Number of subjects transfused; length of stay (days); hematocrit (%)	Vasopressin ($n = 10$) vs tourniquet ($n = 11$): Total blood loss (ml): 461 (SD 177) vs 379 (SD 95) Operating time (minutes): 72 (SD 6) vs 66 (SD 7) Number of subjects transfused: 1 vs 3 Length of stay (days): 3.6 vs 4.0 Hematocrit (%): Pre-operative = 34.0 vs 35.5 Post-operatively = 29.5 vs 29.9 No statistical difference for any comparison.	Funding source: Not stated
Jasonni 2001 ⁴⁷⁷	randomised EL = 1-	36 randomised; 20 to long-term GnRH; 16 to short-term GnRH	Population characteristics: Women; symptomatic uterine fibroids; scheduled for myomectomy. Country: Italy	GnRH-a for 6 months prior to myomectomy; GnRH-a for 2 months prior to myomectomy	Not stated	Uterine volume (cm ³); intra-operative blood loss (ml); LH, FSH and estradiol plasma levels	Long-term vs short-term: Uterine volume (cm ³): 680 (SD 276) vs 745 (SD 320) Intra-operative blood loss (ml): 315 (SD 93) vs 336 (SD 88) LH, FSH and stradiol plasma levels: rReduction in both groups, and no differences between groups	Funding source: Not stated
Lethaby 2001 ⁴⁶⁹	Systematic review; meta-analysis EL = 1+	26 trials included – 3 waiting to be reviewed	Population characteristics: Search strategy using keywords and MeSH headings. Hand searching of bibliographies and specific journals. Search undertaken on MEDLINE, EMBASE, Cochrane library, Current contents, NRR and NLMCTR Country:	GnRH pre-treatment for hysterectomy or myomectomy in presence of fibroids		Uterus size; operative complications	62 outcomes are reported. Only most relevant are reported here. GnRH vs placebo pre-treatment for hysterectomy: Uterine volume (ml) ($n = 15$, $n = 978$), WMD = -159.04 [-169.05 to -149.03] in favour of GnRH. Duration of operation (min): WMD = -5.18 [-8.62 to -1.75] in favour of GnRH. Proportion undergoing vaginal rather than abdominal hysterectomy: OR = 4.70 [2.97 to 7.45]. Post-operative complications: OR = 0.62 [0.39 to 0.97]. Difficulty with surgery: OR = 0.72 [0.52 to 1.00]. Intra-operative blood loss (ml): WMD = -57.98 [-75.66 to -40.30] in favour of hysterectomy. No difference between groups for 12 of 16 operative adverse events. Wide confidence intervals for all adverse events.	Funding source: Health Research Council, New Zealand Study summary: Use of GnRH for 3 to 4 months prior to surgery reduces fibroid size.

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							<p>GnRH vs placebo pre-treatment in myomectomy:</p> <p>Intra-operative blood loss (ml) (8 studies, $n = 263$): WMD = -67.46 [-90.55 to -44.37].</p> <p>Duration of surgery (min) (5 studies, $n = 190$): WMD = 4.20 [-2.69 to 11.08].</p> <p>Decrease in myomas diameter (1 study, $n = 46$): WMD = 19.20 [6.43 to 31.97].</p> <p>7 of 9 operative adverse events showed no difference between groups. Wide confidence intervals for all adverse event measures.</p> <p>For most outcomes there was no difference between groups, and all associated with wide confidence intervals.</p>	
Liu 2004 ⁴⁶⁰	controlled study with no randomisation EL = 2+	342 women with symptomatic fibroids	Population characteristics: Mean age: 39 years (24 to 49) Country: Taiwan	Myomectomy only ($n = 108$) (Group 1) Combined uterine depletion and myomectomy ($n = 234$) – (Group 2) Combined uterine depletion and myomectomy vs myomectomy only	25.4 months (14–52)	Operation time Intra-operative blood loss Post-op symptoms improvement Fibroid recurrence	<p>Symptoms resolution</p> <p>Menorrhagia: Group 1: 79/94 (84%) Group 2: 194/194 (100%)</p> <p>Dysmenorrhoea: Group 1: 31/36 (86%) Group 2: 104/106 (98%)</p> <p>Compression: Group 1: 16/16 (100%) Group 2: 37/37 (100%)</p> <p>Total: Group 1: 88/108 (82%) Group 2: 232/234 (99%)</p> <p>Operation time: Group 1: 55 min (40–85) Group 2: 68 min (48–115)</p> <p>Intra-operative mean blood loss: Group 1: 250 ± 133 ml (30–850) Group 2: 50 ± 27 ml (20–350) ($P < 0.001$)</p> <p>Post-op hospital stay: Group 1: 3.4 ± 0.9 days Group 2: 3.2 ± 1.0 days</p> <p>Fibroid recurrence: Group 1: 21 (19%) recurrence at 16 month follow-up, 5 (24%) underwent second myomectomy Group 2: 0% ($P < 0.001$)</p>	<p>Funding source: Not stated</p> <p>Study summary: The procedure of uterine depletion before myomectomy (for the management of uterine), reduces intra-operative blood loss, resulted in complete resolution of fibroid-related menorrhagia and has the potential to prevent fibroid recurrence.</p>
Loffer 2005 ⁴⁵⁸	Comparative study EL = 2+	177 women Hysteroscopic myomectomy without endometrial ablation (EA) ($n = 104$) Hysteroscopic	Population characteristics: Indications: menorrhagia and menometrorrhagia Women with EA: Mean age 44 years, 80% had endometrial pre-treatment Women without EA: Mean age 37.6 years, 26% had endometrial pre-treatment Country: USA	Hysteroscopic myomectomy without endometrial ablation (EA) Hysteroscopic myomectomy without endometrial ablation (EA) vs	up to 15 years	Control of bleeding No of subsequent hysterectomy	<p>Control of bleeding: Women with EA: 96% bleeding was controlled at up to 15 years</p> <p>Women without EA: 81% bleeding was controlled at up to 15 years (OR 0.18, 95% CI 0.05 to 0.63)</p> <p>In women who had complete removal of myoma:</p>	<p>Funding source: Not stated</p> <p>Study summary: Endometrial ablation at the time of hysteroscopic myomectomy improves results in the control of bleeding</p>

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
		myomectomy with concomitant endometrial ablation (<i>n</i> = 73)		Hysteroscopic myomectomy with concomitant endometrial ablation			<p>bleeding was controlled in 90%</p> <p>In women who had incomplete removal of myoma: bleeding was controlled in 76% (OR 0.39, 95% CI 0.16 to 0.99)</p> <p>In women who had complete removal of myoma and EA: bleeding was controlled in 97%</p> <p>In women who had complete removal of myoma and no EA: bleeding was controlled in 84% (OR 0.19, 95% CI 0.04 to 0.87)</p> <p>In women who had incomplete removal of myoma and EA: bleeding was controlled in 92%</p> <p>In women who had incomplete removal of myoma and no EA: bleeding was controlled in 70% (OR 0.20, 95% CI 0.02 to 1.79) (NS)</p> <p>Myoma completely removed + EA vs myoma not completely removed + EA: significant success in control of bleeding (common OR 5.25, 95% CI 1.49 to 18.5)</p> <p>Subsequent hysterectomy:</p> <p>In women with EA: 18%</p> <p>In women with no EA: 22% (NS)</p> <p>In women with complete resection: 18%</p> <p>In women with incomplete resection: 30% (NS)</p> <p>Complete myoma removal + EA: 18%</p> <p>Complete myoma removal with no EA: 17% (NS)</p> <p>Incomplete myoma removal + EA: 15%</p> <p>Incomplete myoma removal with no EA: 37% (NS)</p>	
Palomba 2002 ⁴⁷⁸	randomised; open EL = 1–	66 randomised; 22 to GnRH, iron and tibolone group; 22 to GnRH and iron and placebo; 22 to iron only. 5 women dropped out of study, but no information on from which groups.	Population characteristics: Women; pre-menopausal; symptomatic uterine fibroids; largest fibroid between 400 and 500 cm ³ ; maximum of 3 fibroids. Excluded if – systemic disease or malignancy, pregnant, submucosal fibroids. Baseline (tibolone vs GnRH vs iron only): Age = 24.9 vs 27 vs 26.6 Parity = 1.1 vs 1.0 vs 1.0 BMI = 23.6 vs 24.4 vs 24.2 Country: Italy	GnRH, iron tablets, and tibolone; GnRH, iron tablets and placebo; iron tablets only. All prior to surgery.	3 months	Hot flushes (pre-surgery); Uterine volume (cm ³); fibroid volume (cm ³); fibroid symptoms; duration of surgery (minutes)	<p>Tibolone vs GnRH vs Iron only:</p> <p>Hot flushes (pre-surgery):</p> <p>Tibolone group significantly less than placebo group (<i>P</i> < 0.05). (Data presented on weekly basis so not summarised.)</p> <p>Uterine volume (cm³):</p> <p>Baseline = 528 (SD 83) vs 504 (SD 92) vs 496 (SD 99). 1 week prior to surgery = 373 (SD 51) vs 337 (SD 50) vs 498 (SD 97). 1 week post-surgery = 198 (SD 27) vs 193 (SD 18) vs 201 (SD 19).</p> <p>Reduction in volume significant for tibolone and GnRH groups, and no difference between groups.</p> <p>Fibroid volume (cm³):</p> <p>Baseline = 179 (SD 48) vs 167 (SD 41) vs 163 (SD 38). 1 week prior to surgery = 130 (SD 31) vs 113 (SD 23) vs 164 (SD 39).</p> <p>Reduction in volume significant for tibolone and GnRH groups, and no difference between groups.</p> <p>Fibroid symptoms (10 cm VAS):</p>	Funding source: Not stated

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							Menorrhagia: Baseline = 6.8 vs 7.1 vs 6.8 1 week prior to surgery = 3.5 vs 1.8 vs 7.4 (Not measured post-operatively) Duration of surgery (minutes): 99.8 (SD 22.7) vs 91.5 (SD 17.6) vs 117.3 (SD 16.1) Intra-operative blood loss (ml): 186.8 (SD 62.2) vs 171.2 (SD 64.3) vs 245.8 (SD 53.0), $P < 0.05$ for iron vs other groups.	
Phillips 1995 ⁵⁷⁵	Case series; prospective EL = 2+	208 (120 with transcervical electrosurgical resection, and 88 with additional transcervical endometrial resection)	Population characteristics: TSR – Women; uterine fibroids; menorrhagia – subjective; desire to preserve fertility TEMR (as above) but no desire for fertility; poor surgical risk; refused hysterectomy; post-menopausal bleeding. Demographic information (TSR vs TSR-TEMR) Mean age (years) = 37.9, 43.2 Mean leiomyoma diameter (cm ³) = 2.6, 3.2 Mean uterine size (gestational weeks) = 7.2, 6.8 Country: USA	transcervical electrosurgical resection; transcervical endometrial resection; GnRH pre-treatment for women with > 50% of cavity occupied by fibroid.	Up to 6 years	Operative time; length of stay; Complications; menstrual bleeding patterns; Additional surgery	Operative time (TSR vs TSR-TEMR, minutes) = 30.2 vs 39.5 Mean length of stay (TSR vs TSR-TEMR, hours) = 4.3 vs 4.7 Complications (TSR vs TSR-TEMR) = 5 vs 3 Mean fluid absorbed (TSR vs TSR-TEMR, ml) = 578 vs 677 ($P < 0.05$) Bleeding patterns at 6 months (TSR vs TSR-TEMR): Amenorrhoea = 0 vs 62 Hypomenorrhoea = 0 vs 16 Eumenorrhoea = 113 vs 7 Unsatisfactory = 7 vs 3 Satisfactory = 113 (94.2%) vs 85 (96.6%) Additional surgery by 6 months (TSR vs TSR-TEMR) = 8 vs 6 Bleeding patterns by 6 years follow-up (TSR vs TSR-TEMR): Amenorrhoea = 8 vs 49 Hypomenorrhoea = 0 vs 11 Eumenorrhoea = 82 vs 9 Unsatisfactory = 16 vs 9 Satisfactory = 90 (84.1%) vs 69 (88.5%)	Funding source: Not stated Study summary: TSR with or without TEMR is an effective and safe treatment for women with submucous leiomyomas suffering from chronic menorrhagia.
Razavi 2003 ⁴²⁴	Comparative cohort study EL = 2+	111 women undergoing abdominal myomectomy (AM) ($n = 44$) or uterine fibroid embolisation (UTE) ($n = 67$) for symptomatic uterine fibroids	Population characteristics: Mean age: AM – 37.7 years; UTE – 44.2 years Country: USA	abdominal myomectomy or uterine fibroid embolisation abdominal myomectomy or uterine fibroid embolisation	AM: 14.6 months UTE: 14.3 months	Success rate: significant reduction of menorrhagia and pain Complications hospital stay use of narcotics resumption of normal activities	Significant reduction in menorrhagia: AM: 64% UTE: 92% ($P < 0.05$) Significant reduction in pain: AM: 74% UTE: 52% (NS) Significant reduction in mass effect: AM: 91% UTE: 76% ($P < 0.05$) Complications: AM: 10 (25%) (3 blood transfusion, mean blood loss 376 ml, 2 wound infection, 2 adhesion, 1 readmission for ileus, 1 chronic pelvic pain, 1 incisional pain). UTE: 7 (11%) ($P < 0.05$) (Minimal blood loss, 1 endometritis, 1 pelvic pain, 1 groin numbness, 4	Funding source: not stated Study summary: UTE is less invasive and safer treatment than AM in women with symptomatic fibroids

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							menopause. Mean hospital stay: AM: 2.9 days UTE: 0 day ($P < 0.05$) Mean days taking pain medications: AM: 8.7 UTE: 5.1 ($P < 0.05$) Mean days till normal activity: AM: 36 UTE: 8 ($P < 0.05$) Secondary intervention: AM: 10% UTE: 8% (NS)	
Sapmaz 2003 ⁵⁷⁶	Randomised EL = 1–	51 randomised; 26 in bilateral ligation; 25 in tourniquet	Population characteristics: Women; symptomatic uterine fibroids; scheduled for myomectomy Baseline (ligation vs tourniquet): Age = 32 vs 33 Parity = 1.1 vs 1.3 Menorrhagia = 12 vs 12 Pelvic pain = 9 vs 10 Pollaciuria = 4 vs 3 Infertility = 0 vs 0 Number of myoma = 5.5 vs 5.5 Maximum myoma volume = 205 vs 207 Country: Turkey	bilateral ligation prior to myomectomy; tourniquet prior to myomectomy	6 months	Intra-operative blood loss (ml); duration of operation (min); Haemoglobin levels (g/dl)	Ligation ($n = 26$) vs tourniquet ($n = 25$): Intra-operative blood loss (ml): 220 (SD 50) vs 294 (SD 60) Duration of operation (min): 67 vs 68 Haemoglobin levels (g/dl): Baseline = 12 vs 12 After myomectomy = 11.4 vs 10.9 ($P < 0.05$) At 24 hours = 11.3 vs 10.8 ($P < 0.05$) No blood transfusion in either group.	Funding source: Not stated
Taylor 2005 ⁵⁷⁷	Randomised – computer generated; opaque envelopes; single blind; EL = 1+	171 eligible; 28 randomised; 14 to control group; 14 to tourniquet group.	Population characteristics: Women; symptomatic fibroids; ≥ 14 week gestation; requesting myomectomy; excluded if – history of bleeding disorder, concurrent anticoagulant therapy, or haemoglobin < 10.5 g/dl Baseline characteristics (control vs tourniquet): Age = 39.5 vs 42.6 Parity = 0 vs 0 Hb (g/dl) = 11.8 vs 12.2 GnRH-a = 1 vs 2 Previous surgery = 2 vs 3 Uterine size (weeks) = 18 vs 17 Country: UK	Tourniquet; no treatment	6 months	Blood loss; transfusion rates; complication rates	Control ($n = 14$) vs tourniquet ($n = 14$): Operative details: Operating time (min) = 118 vs 114 Tourniquet time = – vs 52 Number of fibroids removed = 4.5 vs 10.5 Weight of fibroids = 481 vs 395 Blood loss (ml) = 2359 vs 489 ($P = 0.0001$) Post-operative blood loss: Drained in 48 hours = 220 vs 150 ($P = 0.165$) Transfusion = 59 vs 2 ($P = 0.0005$) Patients transfused = 11 vs 1 ($P = 0.0003$) Episodes of post-operative morbidity: 8 vs 1 ($P = 0.0128$)	Funding source: Not stated
Vercellini 2003 ⁴⁷⁹	randomised – computer generated; concealed – opaque envelopes EL = 1+	162 eligible; 100 randomised; 50 to GnRH (49 completed); 50 to immediate surgery (48 completed).	Population characteristics: Women; pre-menopausal; 18 to 40 years old; symptomatic uterine fibroids – intramural or subserous; excluded if – previous surgery for fibroids, uterine malformations, past pelvic inflammatory disease, coagulation disorders, or unstable general condition, haemoglobin < 10 g/dl. Baseline characteristics (GnRH vs immediate	GnRH-a for 2 months prior to myomectomy; myomectomy	6 months	Intra-operative blood loss (ml); Operating time (minutes); difficulty of surgery	Uterine volume decreased to 269 (SD 119) in the GnRH-a group, immediate group not assessed. GnRH vs Immediate surgery: Intra-operative blood loss (ml): 265 (SD 181) vs 296 (SD 204) Operating time (minutes): 93 (SD 32) vs 90 (SD 32) Difficulty of surgery: Easier = 3 vs 2	Funding source: Not stated

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			surgery): Age = 34 vs 33 BMI = 22 vs 23 Uterine volume (weeks) = 12 vs 12 Uterine volume (ml) = 343 vs 338 Diameter of largest fibroid = 69 vs 66 Country: Italy				Same = 38 vs 39 Difficult = 8 vs 7 No statistical difference between groups. No difference between groups based on size of uterus, number of fibroids removed or length of incisions.	
Zullo 2004 ⁴⁸⁰	randomised EL = 1-	60 randomised; 30 therapy (28 assessed); 30 to placebo (28 assessed)	Population characteristics: Women; pre-menopausal; symptomatic uterine fibroids; excluded if – systemic disease, malignancy, fibroids not between 3 to 5 cm, calcification or hypoechoic fibroids, pregnant Country: Italy	Bupivacaine plus epinephrine; placebo	2 days	Intra-operative blood loss (ml); duration of surgery; vials of analgesia used (<i>n</i>)	Therapy vs placebo: Intra-operative blood loss (ml): 143.9 (SD 48.1) vs 212.5 (SD 51.), $P < 0.001$ Duration of surgery: 78.7 (SD 13.1) vs 109.2 (SD 15.2), $P < 0.001$ Vials of analgesia used (<i>n</i>): 4 vs 7.6, $P < 0.01$	Funding source: Not stated
Sawin 2000 ⁴⁵⁷	Comparative cohort study EL = 2+	394 women Abdominal myomectomy (AM): <i>n</i> = 197 Abdominal hysterectomy (AH): <i>n</i> = 197	Population characteristics: Mean age AM: 36 years AH: 44 years ($P < 0.0001$) Mean weight AM: 156 lbs AH: 174 lbs ($P < 0.0001$) Mean parity: AM: 0.5 AH: 1.6 ($P < 0.0001$) Pre-op uterus size (weeks equivalent) AM: 14 AH: 16 ($P < 0.0001$) Indications: AM: vaginal bleeding (37%) or pain (39%), recurrent miscarriage, infertility AH: vaginal bleeding (62%) or pain (31%) Country: USA	AM vs AH AM vs AH	Chart review over a period of 2 years	Morbidity Post op care	Morbidity: Overall morbidity: AM: 39%; AH: 40% (OR 0.93, 95% CI 0.63 to 1.40) Febrile morbidity: AM: 33%; AH: 26% (OR 1.41, 95% CI 0.91 to 2.17) Haemorrhage: AM: 10%; AH: 14% (OR 0.46, 95% CI 0.26 to 0.83) Unintended procedure: AM: 4.5%; AH: 0.6% (OR 0.45, 95% CI 0.20 to 0.99) Life threatening event: AM: 1.5%; AH: 1% (OR 1.51, 95% CI 0.17 to 18.00) Readmission: AM: 1.5%; AH: 2.5% (OR 0.59, 95% CI 0.09 to 3.10) Post-op care: Mean operative time (min): AM: 201; AH: 176 ($P < 0.00002$) Estimated blood loss (ml): AM: 227; AH: 484 ($P < 0.00001$) Length of hospital stay (days): AM: 4; AH: 4.4 ($P < 0.048$) Max drop in Hgb: AM: 2.5; AH: 4 (NS) Transfusion (no.): AM: 9%; AH: 13% (NS)	Funding source: Not stated Study summary: No clinical difference in peri-operative morbidity between myomectomy and hysterectomy. Myomectomy should be considered a safe alternative to hysterectomy
Gupta 2005 ⁴¹⁶	Systematic review; meta-analysis EL = 1+	3 RCTs included.	Population characteristics: Searched the Cochrane Menstrual Disorders and Subfertility Group Trials register (searched 10 August 2005), the Cochrane Central Register of Controlled Trials (CENTRAL) on the Cochrane Library, Issue 3, 2004), MEDLINE (January 1966 to November 2005) and EMBASE (January 1980 to November 2005). Contacted authors of potential ongoing studies. Country: UK	Uterine artery embolisation	N/A	Duration of operation (min); length of stay (days); length of recovery (days); Complications	Outcomes for UAE vs hysterectomy (outcome title; number of studies; number of participants statistical method; effect size): Duration of procedure (min): 1, 156, WMD (fixed) -16.40 [95% CI -26.04 to -6.76]. Intra-procedure blood loss (ml): 1, 156, WMD (fixed) -405.20 [95% CI -512.71 to -297.69]. Intra-procedural complications: 2, 216, OR (fixed) 2.02 [95% CI 0.74 to 5.47]. Need for blood transfusion: 2, 216, OR (fixed) 0.04 [95% CI 0.00 to 0.33]. Length of hospital stay (days): 2, 213, WMD (fixed) -3.27	Funding source: No financial support Study summary: UAE offers an advantage over hysterectomy with regards to a shorter hospital stay and a quicker return to routine activities. There is no evidence of benefit of UAE compared with surgery (hysterectomy / myomectomy) for

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							<p>[95% CI -3.77 to -2.77].</p> <p>Unscheduled visits after discharge: 2, 217, OR (fixed) 1.80 [95% CI 0.98 to 3.30].</p> <p>Readmission rates within 42 days: 2, 216, OR (fixed) 6.00 [95% CI 1.14 to 31.53]</p> <p>Resumption to normal activities: 1, 59, WMD (fixed) -26.68 [95% CI -36.15 to -17.21].</p> <p>Satisfaction with treatment: 1, 53, OR (fixed) 0.47 [95% CI 0.09 to 2.48]</p> <p>UAE vs myomectomy (Outcome title; number of studies; number of participants; Statistical method; Effect size)@</p> <p>Duration of procedure (minutes): 1, 63, WMD (fixed) -34.50 [95% CI -48.74 to -20.26].</p> <p>Febrile morbidity: 1, 63, OR (fixed) 0.90 [95% CI 0.24 to 3.32].</p> <p>Need for antibiotics: 1, 63, OR (fixed) 1.12 [95% CI 0.25 to 4.92].</p> <p>Need for blood transfusion: 1, 63, OR (fixed) 0.21 [95% CI 0.01 to 4.48].</p> <p>Length of hospital stay (days): 1, 63, WMD (fixed) -1.60 [95% CI -2.47 to -0.73].</p> <p>Hospital stay 1 week: 1, 63, OR (fixed) 0.11 [95% CI 0.01 to 2.08].</p> <p>Readmission to hospital: 1, 63, OR (fixed) 2.29 [95% CI 0.20 to 26.58].</p> <p>Duration to full recovery (days): 1, 63, WMD (fixed) -16.40 [95% CI -21.16 to -11.64].</p> <p>Relief of fibroid-related symptoms at 6 months follow-up: 1 54 OR (fixed) 0.50 [95% CI 0.08 to 3.27].</p> <p>Total relief of all fibroid-related symptoms at 6 months follow-up: 1, 54, OR (fixed) 0.36 [95% CI 0.12 to 1.11].</p> <p>Fibroid-related symptoms same or worse at 6 months follow-up: 1 54 OR (fixed) 2.00 [95% CI 0.31 to 13.06].</p> <p>Serum FSH levels at 6 months follow-up: 1, 63, WMD (fixed) 0.79 [95% CI -0.24 to 1.82].</p> <p>FSH levels 20 iu/l: 1, 63, OR (fixed) 8.53 [95% CI 0.42 to 172.28].</p> <p>Fibroids detected by USS 4 cm by at least 6 months follow-up: 1, 63, OR (fixed) 5.88 [95% CI 1.88 to 18.44].</p> <p>Re-intervention rate: 1, 63, OR (fixed) 8.97 [95% CI 1.79 to 44.95].</p>	<p>satisfaction. The higher minor complications rate after discharge in the UAE group as well as the unscheduled visits and readmission rates require more longer term follow-up trials to comment on its effectiveness and safety profile. There is currently an ongoing trial (REST, U. K.) and EMMY trial yet to report on the long term follow up, the results of which are awaited with interest.</p>
Seracchioli, R 2000 ⁴⁶¹	RCT EL = 1-	131					<p>It reported a significantly higher incidence of febrile morbidity (> 38 °C) in the abdominal group than in the laparoscopic group (26.2% vs 12.1%; $P < 0.05$). The mean drop in haemoglobin was more pronounced in the abdominal group (2.17 ± 1.57 vs 1.33 ± 1.23; $P < 0.001$).</p>	

Table 11.4 Myomectomy for treatment of uterine fibroids – non-comparative studies

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
De Blok 1995 ⁴⁶⁵	case series; retrospective EL = 3	Transcervical resection of fibroids	163 (109 TCRM, 54 other treatment)	Women; menorrhagia related to submucous fibroids Country: Netherlands	Treatment pattern; number of resections needed; uterine assessment	Grade of fibroids: 0 – pedunculated, no intramural extension. I – < 50% intramural and > 50% intra-cavitary. II – > 50% intramural and < 50% intra-cavitary. Number of patients by fibroid grade: TCRM – grade 0 = 53, grade I = 63, grade II = 47. No TCRM – grade 0 = 2, grade I = 17, grade II = 35 Number of procedures required by fibroid grade: 1 procedure: grade 0 = 49, grade I = 34, grade II = 8 2 procedure: grade 0 = 2, grade I = 10, grade II = 4 3 procedure: grade 0 = 0, grade I = 2, grade II = 0 Examination of uterine cavity: 85 of 109 had normal cavity. 8 had small necrotic rest fibroid. 2 lost-to-follow-up. 8 refused hysteroscopy. 6 patients had hysterectomy.	Funding source: Not stated
Marziani 2005 ⁴⁶⁶	case series EL = 3	Hysteroscopic myomectomy	107 women	women with symptomatic submucous leiomyomas (84 abnormal uterine bleeding; 23 infertility) Mean age: 35 years (30–46) A 8 week suppression with GnRH-a was given to women who had myomas larger than 3 cm Country: Italy	No of fibroids resections Control of menorrhagia reproductive outcome	No of fibroids resections: 91 (85%) complete resection 16 (15%) needed 2nd resection Good control of menorrhagia Complete resection: 68 (81%) 2nd resection: 11 (13%) Recurrent menorrhagia: 5 (6%) (2nd resection sig associated with higher number of myomas, $P < 0.05$) Location of myomas: Intra-cavity location positive related to complete resection and resolution of symptoms ($P < 0.05$) 5 (6%) of women underwent laparotomic operation (2 myomectomy and 1 hysterectomy) Intra-operative complications: 0 'overload fluid' 0 uterine perforation 3 post-op haemorrhage Post-op Hgb: Sig. improvement ($P < 0.00$) Reproductive outcome: 8 (35%) achieved pregnancy (7 full term, 1 miscarriage)	Funding source: not stated Study summary: Hysteroscopic myomectomy is effective for control of abnormal uterine bleeding
Olufowobi 2004 ⁴⁶⁷	Retrospective chart review EL = 3	myomectomy	109 records of women who underwent myomectomy (types not specified) over a 5 year period	Mean age: 36 years (24–48) Indications: HMB, pelvic pain, infertility Country: UK	Operative complications fertility	Operative complications: 34% Estimated blood loss of ≥ 500 ml: 31% Hysterectomy due to bleeding: 4% Bowel damage: 1% Pyrexia: 38% Wound infection: 5% Haemoperitoneum: 1%	Funding source: not stated Study summary: Symptomatic improvement and fertility enhancement may be possible in some patients with fibroids. Women should be properly counselled before

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
						Mean post-op stay: 4.8 days IVF treatment: 17 women (2 pregnancy) Natural conception: 28 women (13 pregnancy) No data on live births	embarking on myomectomy
Reilly 1998 ⁴⁶⁸	case series (record review) EL = 3	Abdominal myomectomy (all performed by a single surgeon)	120 case records of women who undergone abdominal myomectomy	Age: 22–54 years Indications: Menorrhagia with anaemia dysmenorrhoea pelvic pain/pressure infertility Country: USA	Operation time Intra- and post-op complications blood loss	Mean operating time: 92.4 minutes, median 91 minutes Mean no of fibroids: 8.3 (25 submucous, 86 intra-myometrial, 64 subserous and 30 pedunculated) Intra-op complications: Mean estimated blood loss: 207 ml, median 150 ml 2 women received blood transfusion Post-op complications: anaemia 5 (4.2%) blood transfusion 1 urinary retention 1 superficial wound separation 1 incisional hernia 14 fever Length of hospital stay: 3.6 days \pm 0.1 No hysterectomy performed	Funding source: not stated Study summary: abdominal myomectomy a safe surgical procedure for uterine myoma
Stringer 1997 ⁴⁶²	retrospective chart review (case series) EL = 3	Open myomectomy and laparoscopic myomectomy	Open myomectomy (OM) ($n = 49$) laparoscopic myomectomy (LM) ($n = 49$)	Indications: symptomatic uterine leiomyoma Country: USA	Surgical outcomes	Mean blood loss (ml): OM: 340; LM: 110 ($P < 0.001$) Post-op blood transfusion: OM: 3; LM: 0 Mean hospital stay (days): OM: 5.6; LM: 0.6 ($P < 0.001$) Frequency of post-op complications: OM: 17; LM: 5 ($P < 0.0068$) No adhesión: OM: 1; LM: 7 Subsequent hysterectomy: OM: 3; LM: 1	Funding source: not stated Study summary: Laparoscopic myomectomy had lower morbidity and fewer complications when compared with open myomectomy

Table 12.1 Indications for hysterectomy – non-comparative studies

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
ACOG 1998 ⁵⁷⁸	Consensus statement EL = 4	Hysterectomy for AUB		Country: USA		<p>Confirmation of Indication:</p> <ol style="list-style-type: none"> Excessive uterine bleeding evidenced by either of the following: <ol style="list-style-type: none"> Profuse bleeding or repetitive periods lasting for more than 8 days Anaemia due to acute or chronic blood loss. Failure to find uterine or cervical pathology that would cause abnormal bleeding Laboratory data <ol style="list-style-type: none"> Endometrial biopsy negative for endometrial neoplasia Cytologic studies of cervix negative for malignancy No documented evidence of pathology following D&C, hysteroscopy, hysteroqram or ultrasonogram. <p>Medical documentation:</p> <ol style="list-style-type: none"> Consideration of patient's medical and psychologic risks concerning hysterectomy. Failure of attempted hormone treatment No history of a bleeding diathesis or use of medications that may cause bleeding Pregnancy ruled out Assessment of surgical risk from anaemia and need for treatment Consideration of alternative therapeutic approaches. <p>Contraindications:</p> <ol style="list-style-type: none"> Desire to maintain fertility Medical or psychological risks that exceed benefits. 	
Bourdrez 2004 ²⁴⁴	Prospective; cohort EL = 3	Patient preferences for treatments	96	<p>Women; DUB; scheduled for either hysterectomy, endometrial ablation and LNG-IUS.</p> <p>No statistical difference between groups for age or symptoms.</p> <p>Country: Netherlands</p>	Importance of symptoms; reasons for treatment choice; patient preference to avoid hysterectomy	<p>HMB was most serious symptom for 74% of IUD group, 77% of ablation group and 84% of hysterectomy group.</p> <p>Main reasons to choose treatment:</p> <p>IUD – Short or no admittance, fast recovery, no general anaesthetics, no hysterectomy, no oral contraceptive.</p> <p>Ablation – No IUD, No hysterectomy, No oral contraceptive, Advice from gynaecologist, Short or no admittance</p> <p>Hysterectomy – no complaints anymore, no oral contraceptive, No IUD, Advice of gynaecologist.</p> <p>Patient preference: 70% of women undergoing ablation preferred this to hysterectomy when success rate was presumed to be 50%. 95% of LNG-IUS patients preferred this to hysterectomy when success was presumed to be 50%</p>	<p>Funding source: Not stated</p> <p>Study summary: Study shows that the majority of women are willing to take a 50:50 chance of treatment success to avoid hysterectomy.</p>
Hurskainen 2004 ⁴⁸³	randomised EL = 3	LNG-IUS; hysterectomy	236: 119 (116 available at 12 months) to LNG-IUS, 117 (112 available at 12 months) to hysterectomy	<p>women; menstruating; subjective menorrhagia; aged 35 to 49; completed families; Excluded if – submucous fibroids, endometrial polyps, urinary or bowel symptoms due to large fibroid, or ovarian pathology.</p> <p>Country: Finland</p>	Predictors of outcome	<p>Presence of fibroids nor age were predictors of outcome at 12 months for LNG-IUS or hysterectomy.</p> <p>Multiple regression analysis showed that MBL was the most significant factor predicting outcome.</p> <p>Comparison of women with and without objective menorrhagia (> 80 ml MBL):</p> <p>For women in LNG-IUS group women without menorrhagia had better QoL outcomes than women with menorrhagia on: anxiety ($P=0.04$), EQ-5D ($P=0.05$). In the hysterectomy group, women without menorrhagia had better outcomes than those with menorrhagia on: anxiety ($P=0.007$), emotional well-being ($P=0.01$) and energy ($P=0.0002$).</p> <p>Women without menorrhagia had better outcomes with LNG-IUS than women with menorrhagia on EQ-5D ($P=0.03$).</p> <p>Women with menorrhagia had better outcomes with hysterectomy than LNG-IUS for: anxiety ($P=0.003$), general health ($P=0.04$), energy ($P=0.05$), and pain relief ($P=0.04$).</p>	<p>Funding source: Not stated</p> <p>Study summary: Success or failure of treatment of menorrhagia is multi-factorial, so difficult to predict in individual cases.</p>

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Lefebvre 2002 ⁴⁸¹	Guidelines EL = 4	Indications for hysterectomy	Society of Obstetricians and Gynaecologists of Canada	Country: Canada		<p>Guidelines outline a number of indications for hysterectomy, but here only those relevant to the HMB guideline are outlined:</p> <p>AUB (III-B; consensus):</p> <p>Investigate to exclude any pathology.</p> <p>One or more medical treatments offered.</p> <p>Health professional performing hysterectomy must be aware of alternatives and offer these to patient.</p> <p>Uterine leiomyomas (I-A; RCT evidence):</p> <p>Treatment based on myoma symptoms, size and growth.</p> <p>No symptomatic patients do not require hysterectomy, unless myoma rapidly expanding.</p> <p>Prophylactic use of hysterectomy where myomas likely to grow beyond 12-week size, due to increased complications.</p> <p>If myomas associated with bleeding the endometrial biopsy required and testing for coagulation disorders.</p> <p>GnRH agonists should be given as pre-treatment.</p> <p>Myomectomy, myoma clips and UAE should be considered as alternatives to hysterectomy, but with associated problems.</p>	Funding source: Not stated
Mingo 2000 ⁴⁸⁵	Focus groups EL = 3	Women's experience of medicine during midlife	23 focus groups	Women; middle-age; various ethnic backgrounds Country: USA		<p>Hysterectomy:</p> <p>Women endure great pain to avoid hysterectomy.</p> <p>Hysterectomy seen as major surgery.</p> <p>Patients want minimally invasive surgery.</p> <p>Patients tried alternative treatments to avoid hysterectomy – CAM.</p> <p>If surgery undertaken then women were generally very satisfied.</p> <p>Women judge hysterectomy using much wider criteria than healthcare providers.</p> <p>Patients did not know that hysterectomy causes menopause.</p>	
Nagele 1998 ⁴⁸⁴	Observational; cohort EL = 3	Patient preference	180 from a 658 cohort	Women; undergone endometrial ablation; surgery for menorrhagia Average age: 42.3 Interval since first ablation = 48.3 months % who had repeat ablation = 9.5 % who had hysterectomy = 6.8 Country: UK	Reasons for rejecting hysterectomy; willingness to change preference	<p>Reasons for rejecting hysterectomy:</p> <p>Hysterectomy is a major operation</p> <p>Wanted to be back to normal quickly</p> <p>Wanted to be out of hospital as quickly as possible</p> <p>Would have more postoperative discomfort after hysterectomy</p> <p>Want to retain uterus</p> <p>Friends had taken a long time to recover from hysterectomy</p> <p>Hysterectomy can ruin sex life</p> <p>Do not want a scar</p> <p>Do not want to put on weight</p> <p>Too young for a hysterectomy</p> <p>Loss of femininity</p> <p>Friend had endometrial ablation and recommended it</p> <p>Change in preference with 50/50 possible adverse outcomes:</p> <p>Period does not stop = approx. 85%</p> <p>Period flow not improved = 80%</p> <p>Period pain not decreased = 80%</p> <p>Repeat ablation needed = 40%</p> <p>Need a hysterectomy = 35%</p> <p>Developing cancer = 65%</p>	<p>Funding source: Not stated</p> <p>Study summary: Women who choose ablation are willing to do so even if chances of success are potentially low.</p>

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Nathorst-Boos 1992 ⁴⁸⁶	Survey EL = 3	Hysterectomy	678	Women; aged < 55; Hysterectomy for benign conditions. Indication: Leiomyoma = 78.9% Endometriosis = 10.8% Symptoms (% before-after surgery): HMB = 67.5 vs 0 Dysmenorrhoea = 43.8 vs 2.2 Pressure = 41.8 vs 6.2 Frequent nocturia = 28.4 vs 2.4 Pain = 17.4 vs 1.8 Dyspareunia = 15.2 vs 3.4 No complaints = 6.8 vs 71.4 Country: Sweden	Patient opinions on positive and negative aspects of hysterectomy	Advantages of hysterectomy: No bleeding = 53% No pain or pressure = 21.2% Feel strong, healthy, fit = 13% No need for contraceptives = 12% No social handicaps = 4.8% No worry about cancer = 4.1% Better blood count = 3.8% Better sexual life = 2.9% Other = 3.5% Disadvantages: Hot flushes = 6.1% Ugly scar = 3.4% Dry sore mucous membranes = 4.0% Weight gain = 3.5% Incontinence = 2.9%	Funding source: Not stated
Schilling 1999 ⁴⁸²	Consensus study EL = 4	Indications for hysterectomy	17 gynaecologists were on panel	Consensus gained via Delphi method Country: Switzerland		Consensus outlines all indications for hysterectomy, but here only those relevant to HMB guideline are described. AUB (no leiomyomata): Investigation and treatment: confirm AUB, If meno / metrorrhagia exclude endometrial or cervical neoplasia, failed or refuse medical treatment. Indications: Pre-menopausal: Hb ≤ 10 g/dl without major impairment = appropriate indication; hysterectomy not necessary Hb ≤ 10 g/dl with major impairment = Appropriate indication; necessary indication Hb > 10 g/dl without major impairment = uncertainty of appropriateness. Hb > 10 g/dl with major impairment = Appropriate indication; not necessary indication Pre-menopausal women with leiomyomata causing bleeding, but no pain or discomfort: Investigations and treatment: Meno- /metrorrhagia = exclude endometrial or cervical neoplasia Estimate uterine weight Confirmation of uterine bleeding Failed or refused medical treatment. Indications: Estimated uterine weight < 300 g, Hb < = 10 g/dl = Appropriate indication; necessary indication. Estimated uterine weight < 300 g, Hb > 10 g/dl = Uncertainty about appropriateness. Estimated uterine weight > 300 g, Hb ≤ 10 g/dl = Appropriate indication; necessary indication. Estimated uterine weight > 300 g, Hb > 10 g/dl = Appropriate indication; Not necessary indication. Pre-menopausal women with leiomyomata causing bleeding and pain or discomfort: Investigations and treatment: Meno-/metrorrhagia = exclude endometrial or cervical neoplasia Estimate uterine weight Confirmation of uterine bleeding Failed or refused medical treatment.	Funding source: Not stated

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
						<p>Indications:</p> <p>Estimated uterine weight < 300 g, Hb < = 10 g/dl, without major impairment = Appropriate indication; necessary indication.</p> <p>Estimated uterine weight < 300 g, Hb > 10 g/dl, without major impairment = Uncertainty about appropriateness.</p> <p>Estimated uterine weight < 300 g, Hb < = 10 g/dl, with major impairment = Appropriate indication; necessary indication.</p> <p>Estimated uterine weight < 300 g, Hb > 10 g/dl, with major impairment = Appropriate indication; not necessary indication.</p> <p>Estimated uterine weight > 300 g, Hb ≤ 10 g/dl, without major impairment = Appropriate indication; necessary indication.</p> <p>Estimated uterine weight > 300 g, Hb > 10 g/dl, without major impairment = Appropriate indication; Not necessary indication.</p> <p>Estimated uterine weight > 300 g, Hb ≤ 10 g/dl, with major impairment = Appropriate indication; necessary indication.</p> <p>Estimated uterine weight > 300 g, Hb > 10 g/dl, with major impairment = Appropriate indication; necessary indication.</p>	
Sculpher 1998 ²⁴⁵	Cohort EL = 3	Patient preferences for surgery	221	<p>Women; referred to specialist care with menorrhagia.</p> <p>Average age: 40.94</p> <p>Duration of menorrhagia = 18 months</p> <p>Country: UK</p>	Importance scores for patient outcomes	<p>Mean importance scores:</p> <p>Stops periods for good = 1.18</p> <p>Not removing womb = 0.71</p> <p>Back to usual activities as soon as possible = 1.07</p> <p>Removing womb = 0.47</p> <p>Least pain and discomfort = 0.68</p> <p>Hospital stay as short as possible = 0.59</p> <p>Reduce periods = 0.42</p> <p>Resume sex life as soon as possible = 0.59</p> <p>No worry about contraception = 0.14</p> <p>Not leaving scar = 0.14</p> <p>Patient preferences based on descriptions of surgery:</p> <p>abdominal hysterectomy = 43%</p> <p>endometrial resection = 41%</p> <p>Neither = 4%</p> <p>Unable to choose = 11%</p>	<p>Funding source: Not stated</p> <p>Study summary: Many women referred for surgery for menorrhagia have conflicting objectives from treatment.</p>

Table 12.2 Hysterectomy for treatment of HMB – comparative studies

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Aka 2004 ⁵¹⁶	randomised; EL = 1–	92 eligible. 30 randomised (15 vaginal hysterectomy, 15 abdominal hysterectomy).	Population characteristics: Inclusion criteria: uterine fibroids, pelvic floor relaxation, uterine prolapse, endometrial hyperplasia. No difference between groups on recent trauma, recent exercise, infections or systemic disease Average age: vaginal = 59.7, abdominal = 56.2 Country: Turkey	Vaginal hysterectomy; abdominal hysterectomy	N/A	Operation duration; hospital stay; tissue damage markers	Mean operation duration (minutes): Vaginal = 85.3, abdominal = 69.1 ($P < 0.0001$) Mean hospital stay (days): Vaginal = 3.1, abdominal = 7.2 ($P < 0.0001$) Tissue damage markers: myoglobin, C-reactive protein, alpha 1-antitrypsin – differences in favour of vaginal	Funding source: Not stated
Benassi 2002 ⁵¹⁷	randomised – computer generated EL = 1+	119 (60 vaginal hysterectomy, 59 abdominal hysterectomy)	Population characteristics: Women; symptomatic voluminous uteri requiring hysterectomy; excluded if – prolapse, uterine or adnexal neoplasm, pelvic inflammation, vaginal stenosis, previous pelvic or vaginal procedures, and hormonal treatment within past 6 – months. Uterus volume range from 200 to 1300 ml Baseline (vaginal vs abdominal): Age: 48 (SD 5.3), 47 (SD 5.1) Weight (kg): 55.7 (SD 5.78), 56.1 (SD 5.48) Parity: 1.38 (SD 0.58), 1.42 (SD 0.69) Uterine weight (g): 380 (SD 165), 436 (SD 171) Country: Italy	Abdominal hysterectomy; vaginal hysterectomy Vaginal vs abdominal	1 month	Operative time (min); operative complications; preoperative haemoglobin levels (g/dl); haemoglobin levels (g/dl); decrease in haemoglobin (g/dl); length of stay (days); postoperative complications; patient satisfaction	Vaginal vs abdominal: Operative time (min): Mean 86 (SD 25.32) vs 102 (SD 31.02) ($P < 0.001$) Operative complications: Major vessel injury – 0 vs 0 Uteral injury – 0 vs 0 Bladder injury – 0 vs 0 Bowel injury – 0 vs 0 Preoperative haemoglobin levels (g/dl): 12.7 (SD 1.6) vs 12.5 (SD 2.02) ($P = 0.840$) Postoperative haemoglobin levels (g/dl): 10.49 (SD 1.8) vs 10.55 (SD 1.6) ($P = 0.897$) Decrease in haemoglobin (g/dl): 2.3 (SD 1.2) vs 2.1 (SD 1) ($P = 0.848$) Length of stay (days): Mean – 3.4 (SD 0.7) vs 4.3 (SD 1.5) ($P < 0.001$) Postoperative complications: Need for analgesics: 40 vs 51 ($P < 0.05$) Vaginal cuff haematoma: 2 vs 0 Pelvic haematoma: 0 vs 3 Wound infection: 0 vs 2 Wound dehiscence: 0 vs 1 Total = 2 vs 6 ($P = 0.136$) Fever ($> 38^{\circ}\text{C}$): 10 vs 18 ($P < 0.05$) Blood transfusions: 2 vs 4 Abdominal infections: 0 vs 0 Other infections: 0 vs 0 Pulmonary embolism: 0 vs 0 Patient satisfaction: Bad or very bad = 2 vs 5	Funding source: Not stated Study summary: These results should lead to the choice of vaginal hysterectomy as a valid alternative to the abdominal hysterectomy, even for enlarged uteri.
Bhattacharya 1996 ³⁶⁰	Groups based on RCT EL = 2+	204: 99 (21 non-responders) in hysterectomy, 105 (23 non-responders) in	Population characteristics: Women; part of previous RCT for ablation vs hysterectomy for HMB Country: UK	Hysterectomy; Endometrial ablation – ELA or TCRE	2 years	Bladder function; ovarian function	Cystometry findings: Total bladder dysfunction – hysterectomy = 14 (31%), Ablation = 17 (35%) Bladder symptoms:	Funding source: Not stated Study summary: Bladder and ovarian symptoms do not differ between

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
		ablation					<p>Stress incontinence – hysterectomy = 32 (44%), ablation = 35 (44%).</p> <p>Urge incontinence – hysterectomy = 15 (21%), ablation = 15 (19%).</p> <p>Ovarian function:</p> <p>FSH level > 40 – hysterectomy = 3 (6%), ablation = 5 (10%)</p> <p>Patients on HRT – hysterectomy = 8 (16%), ablation = 5 (10%).</p> <p>Hot flushes – hysterectomy = 25 (35%), ablation = 35 (44%).</p> <p>Worsening of symptoms from baseline to 2 years:</p> <p>Stress incontinence – hysterectomy = 11 (15%), ablation = 13 (16%).</p> <p>Urge incontinence – hysterectomy = 10 (14%), ablation = 12 (15%).</p> <p>Hot flushes – hysterectomy = 5 (7%), ablation = 14 (18%)</p>	hysterectomy and ablation at 2 years follow-up.
Casey 1994 ⁵⁷⁹	retrospective chart review of comparison of LAVH vs VH vs AH EL = 2-	115 LAVH 220 VH 194 AH	Population characteristics: women undergoing hysterectomy (See 'effect size') Country: USA	LAVH vs VH vs AH LAVH vs VH vs AH	hysterectomies performed during a period of 30 months	case selection analysis (demographics, indications, hospital care) LAVH morbidity (post-op complications)	<p>Mean age:</p> <p>LAVH: 41 years; VH 47 years ($P < 0.001$) LAVH: 41 years; AH: 42 years (NS)</p> <p>Mean weight: range 73–76 kg (NS between groups)</p> <p>Uterine weight:</p> <p>LAVH: 149 g; AH: 280 g ($P < 0.001$) LAVH: 149 g; VH: 138 g (NS)</p> <p>Body weight: NS between groups</p> <p>Indications:</p> <p>LAVH chosen more frequently for abnormal uterine bleeding and CIN, less frequently for endometriosis and leiomyomas than AH</p> <p>Adhesiolysis and adnexectomies more frequently done with AH than LAVH ($P < 0.0001$) vaginal repaired more frequently with VH than LAVH ($P < 0.0001$)</p> <p>Post-op complications:</p> <p>Blood transfusion and leiomyomas sig associated with younger age in all groups ($P < 0.03$)</p> <p>No major complications (cystotomy, enterotomy, laparotomy to control bleeding, transfusion, infection) in LAVH group, 9 in VH, 17 in AH</p> <p>Hospital care:</p> <p>(matched pair control: 28 LAVH/VH; 34 pairs LAVH/AH)</p> <p>Operating time:</p> <p>LAVH 112 min; VH 91 min ($P < 0.04$) LAVH 117 min; AH 115 min (NS)</p> <p>length of stay:</p> <p>LAVH 2.5 days; VH 3.3 days ($P < 0.003$) LAVH 2.2 days; AH 4.3 days ($P < 0.0001$)</p> <p>Accompanied by adnexectomy</p> <p>Fever: sig less with LAVH than AH or VH ($P < 0.05$)</p>	<p>Funding source: not stated</p> <p>Study summary: LAVH can be accomplished with low morbidity, short lengths of stay and little increase in operating time compared with VH and AH</p>

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							Anaemia: sig less with LAVH than with AH length of stay: sig less with LAVH than with VH or AH	
Cheng 2002 ⁴⁸⁸	randomised EL = 1–	167 eligible, 167 randomised (84 LAVH, 83 TLH), 101 assessed (60 LAVH, 41 TLH).	Population characteristics: Women; scheduled for hysterectomy; excluded if – uterine weight > 280 g, previous pelvic surgery, history of pelvic inflammatory disease, need for adnexectomy, lack of uterine descent, limited vessel access. Inclusion criteria were – uterine volume < 16 weeks, uterine fibroids of adenomyosis. baseline characteristic (LAVH vs LTH): Age (years): 45.9 (SD 7.2), 45.5 (SD 4.65) Weight (kg): 59.1 (SD 9.4), 61.0 (SD 10.1) BMI > 25: 35 vs 20 Parity: 2.9, 2.9 Menopausal: 5, 4 Previous abdominal surgery: Tubal ligation: 6 vs 7 Caesarean section: 3 vs 4 Appendectomy: 2 vs 3 Myomectomy: 1 vs 1 Indication for surgery: Uterine fibroids: 42 vs 31 Adenomyosis: 18 vs 10 Country: Taiwan	Laparoscopically assisted vaginal hysterectomy; total laparoscopic hysterectomy LAVH vs TLH	6 to 12 months	Operative duration; blood loss during surgery; Length of stay; Uterine weight; complications; sexual function	LAVH vs TLH: Operative duration (min): 115.1 (SD 38.3) s 140.4 (SD 38.7) ($P=0.002$) Blood loss during surgery (ml): 100 vs 90 Length of stay (days): 3.5 vs 3.5 Uterine weight (g): 220 (50 to 700) vs 200 (60 to 480) Complications: Epigastric injury: 1 vs 1 Transfusion: 4 vs 2 Ureteric injury: 1 vs 2 Bladder rupture: 2 vs 1 Bowel injury: 0 vs 0 Febrile morbidity: 3 vs 3 Cuff cellulitis: 5 vs 1 Conversion to laparotomy: 2 of 62, 1 of 42 (all NS) Sexual function: Dyspareunia: Pre-op: 10 vs 6 post-op: 3 vs 5 Orgasm: pre-op: 19 vs 11 post-op: 29 vs 18	Funding source: Not stated Study summary: LAVH has advantages over TLH with reduced operating time. Although it is a technical challenge, TLH can be effectively performed within reasonable time limits in selected cases. The effects on sexual function, following either LAVH or TLH, are found to be similar.
Darai 2001 ⁴⁸⁹	Randomised – computer generated EL = 1–	80 (40 to LAVH, 40 to vaginal hysterectomy)	Population characteristics: Women; uterine size > 280 g and previous pelvic surgery, history of pelvic inflammatory disease, endometriosis, concomitant adnexal masses or indication for adnexectomy; excluded if – anaesthetic contraindications, suspicion of malignancy. Baseline (vaginal vs LAVH) Age: 49.1 vs 50.2 Parity: 2.7 vs 1.6 Weight (kg): 61.3 vs 63.7 Vaginal delivery: 33 vs 32 Caesarean: 7 vs 0 Previous pelvic surgery: 5 vs 8 Myomectomy: 4 vs 5 Postmenopausal: 9 vs 5 HRT use: 7 vs 5 Indications for surgery: Menorrhagia: 16 vs 14 Uterine fibroids: 40 vs 40 Dysmenorrhoea: 16 vs 15 Adenaxal mass: 2 vs 4	LAVH; vaginal hysterectomy LAVH vs vaginal hysterectomy	6 to 8 weeks	Complications; conversion to laparotomy; operating time (min); hospital stay (days); Haemoglobin decrease	Vaginal hysterectomy vs LAVH: Complications: Excessive haemorrhage: 1 vs 1 Blood transfusion: 1 vs 1 Major vessel injury: 0 vs 0 Conversion to laparotomy: 0 vs 3 Bladder laceration: 0 vs 1 Emphysema: 0 vs 2 Abdominal wall haematoma: 0 vs 2 Vaginal cuff haematoma: 2 vs 1 Pyrexia: 2 vs 3 Vaginal cuff infection: 1 vs 2 Abdominal wall infection: 0 vs 1 Total: 6 vs 16 ($P<0.05$) Operating time (min): 108 vs 160 Hospital stay (days): 5.3 vs 5.7 Haemoglobin decrease: 2.0 vs 2.1	Funding source: Not stated Study summary: Vaginal hysterectomy can be successful even in women with enlarged uteri and other conditions considered by some to contraindicate the operation. Laparoscopically assisted vaginal hysterectomy offered no advantages over the standard vaginal hysterectomy.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			Endometriosis: 3 vs 2 Adnexectomy: 21 vs 15 Uterine weight (g): 424 (SD 211) vs 513 (SD 360) Country: France					
Ellstrom 490	Randomised EL = 1–	150 informed about study, 143 agreed to be included (71 to laparoscopic hysterectomy, 72 to TAH)	Population characteristics: Women; benign disorders; not suitable for vaginal hysterectomy; scheduled for abdominal hysterectomy Baseline (TLH vs TAH) Age: 48.2 vs 48.5 BMI: 23.7 vs 25.2 Uterus weight (g): 157 (SD 83) vs 174.7 (SD 82.2) Country: Sweden	Laparoscopic hysterectomy; abdominal hysterectomy		Operating time (min); Hospital stay (days); Outpatient visits	TLH vs TAH: Operating time (min): 148 vs 93.1 Hospital stay (days): 2.5 vs 5 Outpatient visits: 1.28 vs 1.43	Funding source: Not stated Study summary: A change in surgical technique from abdominal to laparoscopic hysterectomy was possible without compromising the health status of the patients, and it provided substantial financial benefits to society.
Ellstrom 1998 ⁴⁹¹	Randomised EL = 1–	40 (20 LAVH, 20 TAH)	Population characteristics: Women; benign conditions; maximum uterus width of 11 cm. Baseline (LAVH vs TAH): Age: 46 vs 48.6 BMI: 24.3 vs 24.5 Length of uterus (sm): 8.5 vs 8.9 Width of uterus: 7.1 vs 7.2 Country: Sweden	Laparoscopic Hysterectomy; Abdominal Hysterectomy; both mixed total and sub-total		Time of surgery; complications; pulmonary function	LH vs AH: Time of surgery: 138 vs 90 ($P < 0.001$) Complications: Fever: 1 vs 1 Abdominal wall haematoma: 2 vs 0 Vaginal cuff infection: 0 vs 1 Pulmonary function: Post-operatively, the Peak expiratory flow and forced expiratory flow were significantly better in LH compared with AH ($P < 0.05$). Other measures in favour of LH over AH, but not consistent	Funding source: Swedish Medical Council Study summary: Laparoscopic hysterectomy results in less pain and less impairment of respiratory function compared with abdominal hysterectomy.
Ellstrom 2003 ⁴⁹²	randomised; EL = 1+	854 eligible, 248 invited into study; 241 agreed to enter study, 74 randomised (38 to AH, 36 to LH – 4 excluded or converted to AH)	Population characteristics: Women; scheduled for abdominal hysterectomy for benign disorder; not suitable for vaginal hysterectomy Indications for surgery (LH vs AH): Menorrhagia: 20 vs 20 Metrorrhagia: 15 vs 15 Uterine fibroids: 13 vs 16 Endometrial hyperplasia: 9 vs 6 Pelvic pain: 5 vs 9 Mechanical symptoms: 1 vs 1 Endometriosis: 0 vs 2 Age: 50.6 vs 49.7 BMI: 24.4 vs 24.7 Country: Sweden	AH; LH surgery vs surgery	1 year	Psychological well-being; sexual well-being	Psychological general well-being index (LH vs AH): Baseline: Anxiety: 22.5 (SD 5.4) vs 21.3 (SD 4.9) Depression: 14.5 (SD 3.2) vs 14.4 (SD 3.0) Well-being: 15.3 (SD 3.9) vs 14.8 (SD 3.9) Health: 13.8 (SD 3.9) vs 12.7 (SD 3.1) Vitality: 15.5 (SD 4.7) vs 15.1 (SD 4.6) Self-control: 14.3 (SD 3.1) vs 13.9 (3.0) Total: 93.9 (SD 23.7) vs 92.0 (SD 18.7) 1 year: Anxiety: 24.6 (SD 54.1) ($P < 0.05$) vs 23.1 (SD 5.2) ($P < 0.05$) Depression: 15.8 (SD 2.5) vs 14.9 (SD 3.2) ($P < 0.05$) Well-being: 17.4 (SD 3.6) vs 16.1 (SD 3.7) ($P < 0.01$) Health: 15.3 (SD 2.3) ($P < 0.01$) vs 14.6 (SD 2.9) ($P < 0.05$) Vitality: 17.7 (SD 3.3) vs 16.8 (SD 4.1) ($P < 0.05$) Self-control: 15.0 (SD 2.7) vs 14.6 (2.9)	Funding source: Not stated Study summary: This study implies that psychological well-being and sexuality after hysterectomy are not influenced by surgical technique.

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							Total: 102.8 (SD 15.8) vs 97.3 (SD 19.1) No differences between groups for psychological well-being index No differences between groups for McCoy sex scale questionnaire	
Falcone 1999 ⁴⁹³	randomised EL = 1+	218 ineligible and 55 eligible, 48 randomised (24 to LAVH – 1 withdraw, 24 to TAH – 3 withdraw), other 7 declined entry and had TAH.	Population characteristics: Women; scheduled for TAH for benign condition; excluded if – pelvic mass < 2 cm below umbilicus, concomitant incontinence or pelvic reconstruction procedure planned. Baseline: (TAH vs LAVH) Age: 43.8 vs 42.8 BMI: 28.9 vs 28.6 Uterine size: 13.8 (SD 2.6) vs 13.3 (SD 3.7) Any medical illness: 66.7 vs 62.5 Previous surgery: 79.2 vs 58.3 Indication: Fibroids: 87.5 vs 87.5 Adnexal mass: 8.3 vs 4.2 Endometriosis: 8.3 vs 12.5 Uterine weight of ineligible groups: VH = 129 g LAVH = 199 AH = 478 Country: USA	LAVH; TAH Surgery vs surgery	6 weeks	Duration of operation (min); estimated blood loss (ml); Uterine weight (g); postoperative complications; Length of stay; analgesia use	TAH vs LAVH: Duration of operation (min): 130 (97 to 155) vs 180 (139 to 225) ($P < 0.001$) Estimated blood loss (ml): 250 vs 450 ($P = 0.003$) Uterine weight (g): 309 (178 to 635) vs 370 (195 to 561) ($P = 0.78$) Postoperative complications: Fever: 0 vs 3 UTI: 2 vs 3 Wound infection: 3 vs 0 Vaginal cuff infection: 0 vs 1 Lower respiratory tract infection: 0 vs 1 Length of stay: 2.5 vs 1.5 ($P = 0.038$) Analgesia use (hours): 36.7 vs 22.1 ($P < 0.001$) No difference in number of pills used.	Funding source: Not stated Study summary: Laparoscopically assisted vaginal hysterectomy appears to allow patients a more rapid postoperative recovery and an earlier return to work with hospital costs similar to those of abdominal hysterectomy.
Falkeborn 2000 ⁵⁸⁰	Non-comparative epidemiological EL = 2–	17126 available, 1339 records assessed (207 myocardial infarction(MI), 1307 non-MI)	Population characteristics: Women; Uppsala region of Sweden; undergone hysterectomy and/or oophorectomy Country: Sweden	Hysterectomy; Oophorectomy	Up to 18 years	Risk factors for MI	Relative risk of MI by operation (95% CI): BSO with or without hysterectomy, < 50 years: 0 to 5 years = 0.7 (0.2 to 2.7); > 5 years = 0.9 (0.5 to 1.6). BSO with or without hysterectomy, > 50 years: 0 to 5 years = 1.9 (0.6 to 5.6); > 5 years = 1.5 (0.9 to 2.6). Unilateral oophorectomy only: 0 to 5 years = 1.3 (0 to 52); > 5 years = 0.8 (0.4 to 1.9). Hysterectomy alone or with oophorectomy: 0 to 5 years = 0.8 (0.4 to 1.7); > 5 years = 1.1 (0.8 to 1.5)	Funding source: Not stated
Ferrari 2000 ⁴⁹⁴	Randomised; concealed EL = 1+	108 assessed, 65 eligible, 62 agreed to randomisation (31 LAVH, 31 TAH)	Population characteristics: Women; uterine fibroids; between 500 and 1500 ml uterine volume; excluded if – lack of vaginal access. Baseline (LAVH vs TAH): Age: 48 vs 46 Uterine volume: 388 (257 to 570) vs 370 (243 to 463) Adnexal masses: 3 vs 5 Previous pelvic surgery: 5 vs 7 Country: Italy	LAVH; TAH > 500 g vs < 500 g; surgery vs surgery		Operating time (min); Uterine weight (g); Blood transfusions; Hospital stay (days); Post-operative analgesics	LAVH vs TAH: Operating time (min): 135 vs 120 ($P = 0.001$) Uterine weight (g): 400 (263 to 590) vs 400 (255 to 556) Blood transfusions: 0 vs 1 Hospital stay (days): 3.8 vs 5.8 ($P < 0.001$) Post-operative analgesics: 7 vs 24 ($P < 0.001$) No change in pattern between < 500 g and > 500 g uterine weight.	Funding source: Not stated Study summary: Compared with TAH, LAVH has advantages in removing uteri weighing < or = 500 g, with comparable operating time, less post-operative pain and shorter recovery. Among uteri weighing > 500 g LAVH showed a shorter recovery, but longer

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Garry 2004 ⁴⁹⁵	randomised; concealed; ITT EL = 1+	1380 recruited. Abdominal trial = 876 (292 (172 by 12 months) to AH, 584 (418 by 12 months) to Laparoscopic hysterectomy). Vaginal trial = 504 (168 (105 by 12 months) to VH, 336 (198 by 12 months) to LH)	Population characteristics: Women; requiring hysterectomy for benign condition; excluded if – uterine prolapse, uterine mass > 12 weeks gestation; medical condition precluding laparoscopic surgery; requiring bladder or other pelvic surgery; refused consent. Baseline (AH vs LH): Age: 41.2 vs 41.7 BMI: 25.9 vs 26.6 Gravidity: 2 vs 2 Vaginal deliveries (%): 83.4 vs 80.9 Caesarean sections (%): 16.9 vs 19.1 Vaginal capacity narrow: 4.8% vs 5.5% Endometriosis: 3.4% vs 3.3% Current smoker: 48.5% vs 41.3% Previous pelvic surgery: 63.3% vs 63.0% Uterine size (weeks): 6 vs 6 Baseline (VH vs LH): Age: 40.8 vs 40.9 BMI: 26.5 vs 26.4 Gravidity: 2 vs 2 Vaginal deliveries (%): 91.0 vs 94.3 Caesarean sections (%): 9.6 vs 10.2 Vaginal capacity narrow: 4.8% vs 2.1% Endometriosis: 0.6% vs 0% Current smoker: 42.9% vs 39.0% Previous pelvic surgery: 60.7% vs 58.6% Uterine size (weeks): 6 vs 6 Country: UK	Laparoscopic hysterectomy (various); vaginal hysterectomy; abdominal hysterectomy LH vs AH; LH vs VH	6 week, 4 months, 12 months	Complications; QoL (SF-12, EQ-5D); length of stay; duration of surgery (min); Conversions	AH vs LH: Major complications (292 vs 584): Major haemorrhage: 7 vs 27 Bowel injury: 3 vs 1 Ureteric injury: 0 vs 5 Bladder injury: 3 vs 12 Pulmonary embolus: 2 vs 1 Anaesthesia problems: 0 vs 5 Unintended laparotomy: 2 vs 26 Wound dehiscence: 1 vs 1 Other complications: 0 vs 0 Minor complications: Minor haemorrhage: 3 vs 8 Anaesthesia problems: 0 vs 2 Fever: 9 vs 29 Infection: 47 vs 86 Haematoma: 17 vs 25 DVT: 0 vs 2 Other complications 22 vs 40 At least 1 major complication: 18 vs 65 QoL (SF-12, EQ-5D): SF-12 physical component: Baseline (221 vs 447): 45.6 (SD 11.5) vs 44.9 (SD 11.7) 6 weeks (148 vs 301): 41.7 (SD 9.7) vs 46.8 (SD 10.1) ($P < 0.001$) 4 months (134 vs 304): 51.6 (SD 8.6) vs 52.6 (SD 8.6) 12 months (148 vs 330): 52.7 (SD 9.3) vs 53.6 (SD 8.4) SF-12 mental component: Baseline (221 vs 447): 45.3 (SD 11.3) vs 45.8 (SD 11.7) 6 weeks (148 vs 301): 51.9 (SD 10.8) vs 50.0 (SD 11.4) 4 months (134 vs 304): 51.8 (SD 9.5) vs 50.9 (SD 10.5) 12 months (148 vs 330): 51.9 (SD 10.2) vs 50.7 (SD 10.7) Length of stay (days): 5.11 vs 3.95 Duration of surgery (min): 5.0 vs 4.2 VH ($n = 168$) vs LH ($n = 336$): Complications: Major haemorrhage: 5 vs 17 Bowel injury: 0 vs 0 Ureteric injury: 0 vs 1 Bladder injury: 2 vs 3 Pulmonary embolus: 0 vs 2 Anaesthesia problems: 0 vs 2 Unintended laparotomy: 7 vs 10 Wound dehiscence: 2 vs 7	operating time than TAH and a 27% rate of conversion to laparotomy. Funding source: HTA Study summary: Laparoscopic hysterectomy was associated with a significantly higher rate of major complications than abdominal hysterectomy. It also took longer to perform but was associated with less pain, quicker recovery, and better short-term quality of life. The trial comparing vaginal hysterectomy with laparoscopic hysterectomy was underpowered and is inconclusive on the rate of major complications; however, vaginal hysterectomy took less time.

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							<p>Other complications: 1 vs 0</p> <p>Minor complications:</p> <p>Minor haemorrhage: 2 vs 8</p> <p>Anaesthesia problems: 1 vs 3</p> <p>Fever: 12 vs 18</p> <p>Infection: 24 vs 36</p> <p>Haematoma: 10 vs 14</p> <p>DVT: 0 vs 0</p> <p>Other complications 17 vs 24</p> <p>At least 1 major complication: 16 vs 33</p> <p>QoL (SF-12, EQ-5D):</p> <p>SF-12 physical component:</p> <p>Baseline (127 vs 260): 47.0 (SD 11.3) vs 47.4 (SD 11.1)</p> <p>6 weeks (84 vs 150): 46.3 (SD 9.6) vs 46.2 (SD 9.6)</p> <p>4 months (82 vs 152): 53.5 (SD 6.7) vs 53.9 (SD 6.7)</p> <p>12 months (94 vs 173): 53.7 (SD 7.3) vs 54.6 (SD 6.3)</p> <p>SF-12 mental component:</p> <p>Baseline (127 vs 260): 45.1 (SD 12.1) vs 47.9 (SD 10.7)</p> <p>6 weeks (84 vs 150): 53.2 (SD 9.1) vs 52.5 (SD 10.4)</p> <p>4 months (82 vs 152): 53.1 (SD 8.1) vs 51.6 (SD 9.8)</p> <p>12 months (94 vs 173): 51.7 (SD 9.8) vs 52.3 (SD 9.9)</p> <p>Length of stay (days): 4.32 vs 4.29</p> <p>Duration of surgery (min): 39 vs 72</p>	
Gimbel 2005 ⁵¹⁹	RCT EL = 1+	4227 assessed, 2106 eligible, 319 randomised (158 to total hysterectomy – 18 lost to follow-up, 140 in ITT, 15 protocol violations, 125 in per-protocol analysis. 161 to sub-total hysterectomy – 24 lost to follow-up, 137 in ITT, 121 in PP analysis	<p>Population characteristics: Women; scheduled for hysterectomy due to benign condition.</p> <p>Baseline demographics (total vs sub-total)</p> <p>Age (years) = 47.6 vs 46.6</p> <p>Deliveries = 1.7 vs 1.8</p> <p>Indications for surgery:</p> <p>fibroids = 90 vs 93</p> <p>DUB = 53 vs 52</p> <p>Dysmenorrhoea = 6 vs 6</p> <p>Pelvic pain = 5 vs 8</p> <p>Endometriosis = 1 vs 0</p> <p>Other = 2 vs 1</p> <p>Country: Denmark</p>	Total hysterectomy; Sub-total hysterectomy	12 months	<p>Urinary incontinence; Frequency; Double/triple voiding; Incomplete bladder emptying; Nocturia; Dysuria; Urinary tract infection; stress incontinence; urge incontinence; mixed incontinence; all incontinence; risk-factors for incontinence; risk-factors for bother</p>	<p>Lower urinary tract symptoms (total vs sub-total):</p> <p>No difference between groups at 0 or 12 months, except for: urinary incontinence at 12 months – 13 vs 25, $P = 0.03$ double voiding at 0 months, 3 vs 16, $P = 0.002$</p> <p>All urinary incontinences at 12 months – 13 vs 25, OR = 0.46 (0.23 to 0.95), $P = 0.03$.</p> <p>Predictors of urinary incontinence at 12 months:</p> <p>Preoperative incontinence OR = 11.2 (5.1 to 25.9), $P < 0.0001$</p> <p>Operative method OR = 0.43 (0.18 to 0.96), $P = 0.044$</p> <p>Size of uterus OR = 1.56 (1.00 to 2.49), $P = 0.051$</p> <p>Five other factors were not significant</p> <p>Multi-variate analysis of symptoms that cause 'bother':</p> <p>Urinary incontinence OR = 463 (69 to 3109), $P < 0.001$</p> <p>Frequency OR = 29.2 (4.1 to 211), $P = 0.001$</p> <p>Incomplete bladder emptying OR = 20 (5.4 to 74.6), $P < 0.001$.</p> <p>Other urinary symptoms were not significant.</p>	<p>Funding source: Public funded</p> <p>Study summary: Urinary incontinence was found less often among TAH women than among SAH women. This was due to a larger reduction of the number of women with stress and urinary incontinence in the TAH group. No other differences were found between the two operation methods. The number of women with urinary incontinence and frequency was reduced from study entry for follow-up, while double/triple voiding was increased. Incontinent women had significantly lower quality of life scores than continent women</p>

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Gimbel 2003 ⁵¹⁸	randomised; concealed; non-blinded; multicentre EL = 1+	4227 assessed, 2106 eligible, 319 randomised (158 to total hysterectomy – 18 lost to follow-up, 140 in ITT, 15 protocol violations, 125 in per-protocol analysis. 161 to sub-total hysterectomy – 24 lost to follow-up, 137 in ITT, 121 in per-protocol analysis)	Population characteristics: Women; scheduled for hysterectomy due to benign condition. Baseline demographics (total vs sub-total) Age (years) = 47.6 vs 46.6 Deliveries = 1.7 vs 1.8 Indications for surgery: fibroids = 90 vs 93 DUB = 53 vs 52 Dysmenorrhoea = 6 vs 6 Pelvic pain = 5 vs 8 Endometriosis = 1 vs 0 Other = 2 vs 1 Country: Denmark	Total hysterectomy ; subtotal hysterectomy	12 months	Urinary incontinence; Quality of life (SF-36); Constipation; Prolapse; Satisfaction with sexual life; Pelvic pain; Vaginal bleeding; Complications – per and post-operation	Patient outcomes at 0 and 12 months based on ITT analysis (total (<i>n</i> = 140) vs subtotal (<i>n</i> = 136), OR, 95% CI, <i>P</i> value): 0 months: Urinary incontinence: 30 vs 28 Quality of life – physical score: 48.58 (9.04) vs 47.77 (8.69) Quality of life – mental score: 49.67 (9.45) vs 48.76 (10.71) Constipation: 26 vs 30 Prolapse: 0 vs 0 Satisfaction with sexual life: 95 vs 87 Pelvic pain: 109 vs 103 Vaginal bleeding: 135 vs 129 12 months: Urinary incontinence: 13 vs 24, 2.08, 1.01 to 4.29, <i>P</i> = 0.043 Quality of life – physical score: 53.78 (8.81) vs 52.92 (8.81), <i>P</i> = 0.09 Quality of life – mental score: 53.78 (7.73) vs 53.03 (8.74) Constipation: 25 vs 27, 1.13, 0.62 to 2.07, <i>P</i> = 0.69 Prolapse: 0 vs 3, 0.14, 0.01 to 2.67, <i>P</i> = 0.12 Satisfaction with sexual life: 95 vs 85, 0.6, 0.31 to 1.16, <i>P</i> = 0.13 Pelvic pain: 32 vs 31, 1.01, 0.57 to 1.78, <i>P</i> = 0.98 Vaginal bleeding: 0 vs 27 (2 normal, 25 slight). Complications: All = 64 vs 54, 1.02, 0.55 to 1.88, <i>P</i> = 0.95 Serious adverse events (Rupture of wound): 22 vs 21 Severe adverse events (urinary tract infection): 7 vs 8 Moderate adverse events (wound infection): 19 vs 12 Mild adverse events (bleeding from surface of wound): 16 vs 13	Funding source: Public funding – various sources Study summary: A smaller proportion of women suffered from urinary incontinence after total abdominal hysterectomy than after subtotal abdominal hysterectomy one year post-operatively.
Halmesmaki 2004 ²⁶⁴	randomised; prospective EL = 1+	119 LNG-IUS vs 117 hysterectomy. 81 IUDs at 12 months – 24 hysterectomy, 10 removed, 5 used ERT. 107 hysterectomies undertaken at 12 months.	Population characteristics: Women; 35–49; menstruating; completed family. No fibroids, endometrial polyps, urinary or bowel symptoms, ovarian pathology. Hysterectomy: age 43.1, parity = 2.1, BMI = 26.6. LNG-IUS: age = 43.0, parity = 2.1, BMI = 25.1 Country: Finland	LNG-IUS; Hysterectomy Treatment vs baseline; treatment vs treatment	12 months	FSH serum levels; Kupperman index – menopausal symptoms- hot flushes etc	FSH levels increased from 8.4 iu/ml at baseline to 13.8 iu/ml at 12 months vs 8.7 to 9.2 in LNG-IUS groups. (<i>P</i> = 0.005). No difference between or within groups on Kupperman index at 12 months (based on treatment use not intention-to-treat). Hot flushes increased in hysterectomy (<i>P</i> = 0.02) but not IUD; no difference between groups.	Funding source: Not stated Study summary: Hysterectomy may impair ovarian function.
Harkki-Siren 2000 ⁴⁹⁶	Randomised; concealed EL = 1+	50 randomised (25 to LH, 25 to AH), 36 analysed (18 LH, 18 AH)	Population characteristics: Women; Aged 30 to 70; benign conditions; excluded if – major medical disease; BMI > 32; uterus > 14 weeks or width > 10 cm; severe adhesions or endometriosis; prolapse; contraindications to surgery. Baseline (LH vs AH): Age: 47 vs 48 BMI: 25.5 vs 25.6 Nulliparity: 7 vs 9 Prior laparotomy: 12 vs 14	Laparoscopic hysterectomy; Abdominal hysterectomy	28 days	Operating time (min); Estimated blood loss (ml); Haemoglobin drop (g/L); Hospital stay (days); Sick leave (days); Complications	LH vs AH: Operating time (min): 85.3 vs 57.5 (<i>P</i> < 0.001) Estimated blood loss (ml): 156.8 vs 268.0 Haemoglobin drop (g/L): 18.8 vs 27.4 Hospital stay (days): 2.1 vs 3.4 Sick leave (days): 21.4 vs 38.5 Complications: 6 vs 7 Trauma markers: IL-6 at day 0 = 3.7 vs 4.4	Funding source: Clinical Research Institute grant Study summary: Laparoscopic hysterectomy should replace abdominal hysterectomy whenever possible because of a more favourable clinical outcome and less tissue trauma.

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			<p>Prior laparoscopy: 8 vs 8</p> <p>Uterine weight (g): 210.7 (SD 83.0) vs 230 (SD 99.4)</p> <p>Country: Finland</p>				<p>IL-6 at day 1 = 10.4 vs 21.6 ($P < 0.01$)</p> <p>IL-6 at day 2 = .5.5 vs 17.0</p> <p>IL-6 at day 28 = 3.7 vs 3.7</p> <p>CRP at day 0 = 1.4 vs 0.7</p> <p>CRP at day 1 = 12.1 vs 21.8 ($P = 0.03$)</p> <p>CRP at day 2 = 26.5 vs 55.3 ($P < 0.001$)</p> <p>CRP at day 28 = 1.8 vs 1.4</p> <p>Same pattern for tumour-associated trypsin inhibitor (TATI), but not for cancer antigen CA 125.</p>	
Harmanli 2004 ⁵⁸¹	Non-comparative cohort study EL = 2-	288 (200 abdominal hysterectomy, 88 vaginal hysterectomy)	<p>Population characteristics: Women; enlarged uterus > 250 g; undergone hysterectomy for – uterine leiomyomata, endometriosis, uterine prolapse, endometrial hyperplasia, adenomyosis, DUB, cervical dysplasia, pelvic pain, early stage cervical or endometrial carcinoma. Hysterectomy in combination with other surgery excluded.</p> <p>Patient characteristics (vaginal vs abdominal):</p> <p>Mean age: 44 vs 44.1</p> <p>Parity = 2.4 vs 2.3</p> <p>Mean uterine weight: 500.9 (SD 277.2) (250 to 1768) vs 737.4 (SD 637.8) (250 to 5650), $P = 0.0006$</p> <p>Adnexal removal: 19 vs 67, $P = 0.049$</p> <p>Indication for surgery:</p> <p>Uterine fibroids – 84 vs 188</p> <p>Menometrorrhagia – 3 vs 6</p> <p>Other – 1 vs 6</p> <p>Country: USA</p>	<p>Vaginal hysterectomy; abdominal hysterectomy</p> <p>Vaginal hysterectomy vs abdominal hysterectomy</p>	N/A	Complications	<p>Vaginal vs abdominal complications:</p> <p>Post-operative febrile morbidity: 18 vs 28</p> <p>Bleeding requiring transfusion: 8 vs 23</p> <p>Urethral injury: 1 vs 1</p> <p>Bladder injury: 1 vs 3</p> <p>Venous thromboembolism: 0 vs 0</p> <p>Ileus: 1 vs 21 ($P = 0.006$)</p> <p>Haematoma: 2 vs 5</p> <p>Urinary tract infection: 5 vs 13</p> <p>Readmission: 3 vs 6</p>	<p>Funding source: Not stated</p> <p>Study summary: For women with a uterus weighing 250 g or more, vaginal hysterectomy shortens the hospital stay without significantly increasing peri-operative morbidity when compared with the abdominal route.</p>
Hehenkamp 2005 ⁴¹⁸	randomised; multicentre; concealment and blinding not mentioned EL = 1+	349 eligible, 177 randomised (89 in hysterectomy group – 75 received hysterectomy, 14 had not. 88 in UAE group – 81 received UAE, 7 had not)	<p>Population characteristics: Women; uterine fibroids; menorrhagia; pre-menopausal; scheduled for hysterectomy. Women excluded if – future fertility desired, active pelvic infection, allergic to contrast material, uterine malignancy, submucosal fibroids > 50% within uterine cavity.</p> <p>UAE vs hysterectomy:</p> <p>Age = 44.6 vs 45.4</p> <p>Parity ≥ 1 58 vs 69</p> <p>Previous treatment:</p> <p>none = 11 vs 15</p> <p>hormonal = 59 vs 59</p> <p>NSAIDs = 45 vs 41</p> <p>Iron supplement = 50 vs 52</p> <p>Surgery = 17 vs 11</p>	UAE; hysterectomy	2 years	Surgery completed; complications; duration of surgery; length of stay	<p>Completed surgery:</p> <p>72 of 81 completed. 5 with unilateral procedure due to technical failure on one-side, 4 with bilateral failure.</p> <p>8 of 152 (5.3%) of arteries available were not embolised due to technical failure.</p> <p>Complications during hospital stay and at 6 weeks follow-up:</p> <p>At hospital (UAE vs hysterectomy):</p> <p>Nausea = 52 vs 42</p> <p>Pain = 72 vs 71</p> <p>Febrile morbidity = 4 vs 15</p> <p>Minor complications = 23 vs 26</p> <p>Major complications = 1 vs 1</p> <p>At 6 weeks follow-up (UAE vs hysterectomy):</p> <p>Nausea = 25 vs 11 (RR = 2.10 (1.11 to 3.97))</p> <p>Pain = 57 vs 52</p> <p>Febrile morbidity = 17 vs 8</p>	<p>Funding source: ZonMw – Netherlands organisation for health research and development</p> <p>Study summary: UAE is a procedure similar to hysterectomy with a low major complication rate and with reduced length of hospital stay</p>

Heavy menstrual bleeding

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			<p>Symptoms:</p> <p>Menorrhagia = 88 vs 89</p> <p>Dysmenorrhoea = 47 vs 50</p> <p>Duration of symptoms = 24 vs 24</p> <p>Number of fibroids (median) = 2 vs 2</p> <p>Uterine volume (median, cm³) = 321 vs 313</p> <p>Fibroid volume (median, cm³) = 59 vs 89</p> <p>Country: Netherlands</p>				<p>Minor complications = 68 vs 34 (RR = 1.45 (1.04 to 2.02), <i>P</i> = 0.024)</p> <p>Major complications = 3 vs 1 (RR = 2.78 (0.3 to 26.13), <i>P</i> = 0.62)</p> <p>Unscheduled visits to health professionals: UAE = 45 vs hysterectomy = 24</p> <p>Readmission after UAE up to 6 weeks = 9</p> <p>Duration of procedure (median): UAE = 75 min vs hysterectomy = 90 min</p> <p>(<i>P</i> = 0.007 for comparison of means)</p> <p>Blood loss (median, ml): UAE = 20 vs hysterectomy = 300</p> <p>(<i>P</i> < 0.01 for comparison of means)</p> <p>Length of stay (days): UAE = 2 vs hysterectomy = 5.1</p>	
Hehenkamp 2006 ⁴¹⁹	randomised; multicentre; concealment and blinding not mentioned EL = 1+	349 eligible, 177 randomised (89 in hysterectomy group – 75 received hysterectomy, 14 had not. 88 in UAE group – 81 received UAE, 7 had not)	<p>Population characteristics: Women; uterine fibroids; menorrhagia; pre-menopausal; scheduled for hysterectomy. Women excluded if – future fertility desired, active pelvic infection, allergic to contrast material, uterine malignancy, submucosal fibroids > 50% within uterine cavity.</p> <p>UAE vs hysterectomy:</p> <p>Age = 44.6 vs 45.4</p> <p>Parity ≥ 1 58 vs 69</p> <p>Previous treatment:</p> <p>none = 11 vs 15</p> <p>hormonal = 59 vs 59</p> <p>NSAIDs = 45 vs 41</p> <p>Iron supplement = 50 vs 52</p> <p>Surgery = 17 vs 11</p> <p>Symptoms:</p> <p>Menorrhagia = 88 vs 89</p> <p>Dysmenorrhoea = 47 vs 50</p> <p>Duration of symptoms = 24 vs 24</p> <p>Number of fibroids (median) = 2 vs 2</p> <p>Uterine volume (median, cm³) = 471.9 vs 483.5</p> <p>Fibroid volume (median, cm³) = 121.5 vs 159.0</p> <p>Country: Netherlands</p>	UAE; Hysterectomy		Pain; Return to daily activities	<p>UAE (<i>n</i> = 72) vs Hysterectomy (<i>n</i> = 68):</p> <p>Analgesia use:</p> <p>Tablets only = 15 vs 5</p> <p>Opiates = 46 vs 43</p> <p>Epidural anaesthesia = 8 vs 20</p> <p>Secondary epidural = 3 vs 0</p> <p>Time to return to activity (days, SD):</p> <p>Paid work = 28.1 (25.7) vs 63.4 (33.2), <i>P</i> < 0.001</p> <p>Voluntary work = 16.6 (8.9) vs 46.6 (30.1), <i>P</i> = 0.016</p> <p>Usual household activities = 12.0 (12.4) vs 29.0 (30.1), <i>P</i> < 0.001</p> <p>Heavy household activities = 20.7 (15.4) vs 53.7 (30.8), <i>P</i> < 0.001</p> <p>Buying groceries = 14.0 (12.1) vs 35.0 (30.2), <i>P</i> < 0.001</p> <p>Doing things around the house = 18.9 (14.4) vs 39.8 (24.7), <i>P</i> < 0.001</p> <p>Leisure time activities = 14.8 (13.3) vs 40.4 (40.1), <i>P</i> < 0.001</p> <p>Activities with children = 17.4 (14.2) vs 30.3 (20.6), <i>P</i> = 0.001</p>	
Hurskainen 2004 ¹⁰⁴	randomised; allocation concealed; controlled EL = 1++	236: 119 LNG-IUS (57 had IUS; 10 nothing; 50 had hysterectomy by 5 years); 117 hysterectomy (109 had hysterectomy by 5 years), 5 LNG-	<p>Population characteristics: women; menorrhagia; no pathology</p> <p>Country: Finland</p>	LNG-IUS; hysterectomy treatment vs baseline; treatment vs treatment	5 years	QoL – EQ-5D, SF-36	<p>QoL at 5 years: change in EQ-5D was 0.08 for IUS vs 0.1 for hysterectomy from baseline of 0.76 (0.7, 0.8) and 0.78 (0.7, 0.8). No difference between groups (<i>P</i> = 0.6). SF-36: change in general health = 3.6 vs 4.4 from baseline of 64 vs 65; physical functioning = -1.4 vs -2 from baseline of 83 vs 84; social functioning = 8.7 vs 9.0 from baseline of 72 vs 76. No difference between groups (<i>P</i> = 0.8, 0.9, 0.9).</p> <p>At 5 years: 50 LNG-IUS users had hysterectomy. Another 10</p>	<p>Funding source: Government grant</p> <p>Study summary: Study shows that at 5 years LNG-IUS offered effective alternative to hysterectomy.</p>

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
		IUS, 7 hysterectomy lost to follow-up.					women were without LNG-IUS <i>in situ</i> . 7 Hysterectomy group had cancelled operation or had IUD fitted. Baseline figures: EQ-5D (LNG-IUS, Hysterectomy) – 0.76, 0.78; SF-36 general health – 64, 65; physical functioning – 83, 84; emotional well-being – 67, 70; social functioning – 72, 76; energy – 55, 57; pain 63, 62; role functioning – emotional – 65, 66; emotional – 61, 66. No data for entire population average.	
Hurskainen 2001 ¹⁰⁵	randomised; allocation concealed EL = 1++	236: 117 LNG-IUS (24 had hysterectomy); 119 hysterectomy (107 underwent operation). 3 LNG-IUS and 5 hysterectomy patients were lost to follow-up.	Population characteristics: women; menorrhagia; no pathology – fibroids, cancer etc.; no previous failure with LNG-IUS; no acne Country: Finland	LNG-IUS; hysterectomy treatment vs baseline; treatment vs treatment	12 months	QoL – EQ-5D, SF-36	Baseline QoL: EQ-5D – IUS = 0.76 (0.7 to 0.80), Hysterectomy = 0.78 (0.70 to 0.80) SF-36 scores: General health – IUS = 64 (60.6 to 67.4), Hysterectomy = 65 (61.0 to 69.0) Physical functioning – IUS = 83 (79.4 to 86.6), Hysterectomy = 84 (80.8 to 87.2) Emotional functioning – IUS = 67 (63.2 to 70.8), Hysterectomy = 70 (66.6 to 73.4) Social functioning – IUS = 72 (67.6 to 76.4), Hysterectomy = 76 (72.2 to 79.8) Energy – IUS = 55 (50.6 to 59.4), Hysterectomy = 57 (53.0 to 61.0) Pain – IUS = 63 (58.4 to 67.4), Hysterectomy = 62 (57.6 to 66.4) Role functioning – physical – IUS = 65 (57.5 to 72.3), Hysterectomy = 66 (58.9 to 73.1) Role functioning – emotional – IUS = 61 (53.5 to 68.5), Hysterectomy = 66 (58.7 to 73.3) General Health questionnaire – IUS = 73 (69.4 to 76.6), Hysterectomy = 75 (71.8 to 78.2) Anxiety – IUS = 32 (30.8 to 33.2), Hysterectomy = 31 (30.0 to 32.0) Depression – IUS = 5.2 (4.2 to 6.2), Hysterectomy = 4.2 (3.4 to 5.0) Sexual satisfaction – IUS = 23.6 (22.4 to 24.8), Hysterectomy = 23.7 (22.9 to 24.5) Sexual problems – IUS = 4.4 (4.0 to 4.8), Hysterectomy = 4.5 (4.1 to 4.9) Partner satisfaction – IUS = 11.2 (10.6 to 11.8), Hysterectomy = 11.6 (11.2 to 12.0) QoL at 12 months (intention-to-treat): all measured improved for both groups. EQ-5D by 0.1 in both groups ($P = 0.0001$) from baseline of 0.76 (0.7, 0.8) for LNG-IUS and 0.78 (0.7, 0.8) for hysterectomy. SF-36 General health – 5.5 for IUS and 6.2 for hysterectomy from baseline of 64 vs 65; physical functioning 4.8 vs 7.1 from baseline of 83 vs 84; social functioning 11.8 vs 12.4 from baseline of 72 vs 76. No difference between groups, except pain 11.8 vs 21.2 ($P = 0.01$). At 12 months: 24 LNG-IUS group had undergone hysterectomy. Another 10 women had had LNG-IUS removed. 5 hysterectomy group cancelled operation.	Funding source: Government funded. IUD provided free by Leiras. Study summary: Study shows LNG-IUS was effective alternative to hysterectomy at 12 months.

Heavy menstrual bleeding

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Hwang 2002 ⁴⁹⁷	Randomised; blinding not mentioned; envelope concealed EL = 1+	90 (30 LAVH, 30 TAH, 30 VTH)	Population characteristics: Women; myoma > 6 cm, Less than 3 in total; excluded if – adenomyosis, uterine prolapse, chronic pelvic pain, DUB, cervical dysplasia, pelvic inflammatory disease. Mean average age: LAVH = 44, TAH = 45, VTH = 46 No difference between groups on: college education, previous caesarean section, > 3 pregnancies, BMI Country: Taiwan	LAVH, Total Abdominal Hysterectomy, Vaginal Total Hysterectomy	6 weeks	Complications; duration of operation; blood loss; length of hospital stay; return to work; use of antibiotics; post-operative tenderness score; uterine weight (g)	Total complications: LAVH = 6, TAH = 9, VTH = 5 ($P < 0.05$) Duration of operation (minutes): LAVH = 119 (± 20), TAH = 117 (± 32 , VTH = 93 (± 15). ($P = 0.12$) Blood loss (cm ³): LAVH = 343 (± 218), TAH = 293 (± 182), VTH = 215 (± 134). ($P = 0.04$) Length of hospital stay: LAVH = 4.7, TAH = 5, VTH = 4.7. ($P = 0.003$) Return to work: LAVH = 30 (± 16), TAH = 41 (± 10), VTH = 29 (± 11). ($P = 0.001$) Use of antibiotics: LAVH = 1.3, TAH = 1.7, VTH = 1.3. ($P = 0.001$) Post-operative tenderness score: LAVH = 4, TAH = 6, VTH = 3. ($P = 0.001$) Uterine weight (g): LAVH = 748 (± 255), TAH = 1020 (± 383), VTH = 835 (± 330). ($P = 0.02$)	Funding source: Not stated Study summary: The study shows vaginal hysterectomy and laparoscopically assisted vaginal hysterectomy can be performed in women with uterine weight of at least 450 g. Preoperative ultrasonographic examination can provide the surgeon with valuable information on the size of the fibroid and the estimated weight of the enlarged uterus before implementing a suitable surgical method.
Iversen 2005 ⁵⁸²	Comparative cohort EL = 2+	7410 (3705 with hysterectomy, 3705 without hysterectomy)	Population characteristics: Women; either had hysterectomy or not Country: UK	hysterectomy	Average of 240 months	Risk of mortality; risk of mortality from cardiovascular disease; risk of mortality from cancer	Adjusted hazard ratios (95% CI) for hysterectomy causing mortality (adjusted for cigarette use, oral contraceptive use, history of hypertension, cardiovascular events, gynaecological malignancy, other malignancies) divided by median age of whole group: All-cause mortality: Aged < 43.7: 0.82 (0.65 to 1.03) Aged > 43.7: 0.94 (0.75 to 1.18) Cardiovascular mortality: Aged < 43.7: 0.85 (0.54 to 1.33) Aged > 43.7: 0.80 (0.52 to 1.23) Cancer mortality: Aged < 43.7: 0.81 (0.55 to 1.19) Aged > 43.7: 1.02 (0.69 to 1.49)	Funding source: Mixed public, private and charitable Study summary: Hysterectomy did not increase the risk of death in the medium to long term.
Johnson 2005 ⁴⁸⁷	Systematic review – meta-analysis EL = 1++	27 RCTs involving 3643 women undergoing abdominal hysterectomy (AH), vaginal hysterectomy (VH), laparoscopic hysterectomy (LH) for benign diseases	Population characteristics: MDSG Specialised registered for controlled trials, CENTRAL, MEDLINE, EMBASE, Biological Abstracts, National Research Register Country: NA	Different surgical approaches to hysterectomy AH vs LH, vs VH, vs LH(a), vs LAVH	Varied: till discharge from hospital, or till participants return to work/normal activities (6 days, 2–8 weeks after	Operation time Intra-operative complications Short-term: Bladder, ureteric, bowel and vascular injuries blood loss infections/febrile episodes Hospital stay	Operation time: 1) AH operation significantly shorter than LH (WMD 10.6 min, 95% CI 7.4 to 13.8). 2) LAVH operation significantly shorter than AH (WMD 7.6 min, 95% CI 3.0 to 12.2). 3) VH operation significantly shorter than LH (WMD 41.5 min, 95% CI 33.7 to 49.4). 4) LAVH operation significantly shorter than LH(a) (WMD 25.3 min, 95% CI 10.0 to 40.6). Intra- and post-operative complications: No significant difference between VH vs AH; LH vs AH; LH vs VH; LH(a) vs LAVH in bladder, ureteric and bowel injuries.	Funding source: NA Study summary: Significantly improved outcomes suggest that VH should be performed in preference to AH where possible. Where VH is not possible, LH may avoid the need for AH. However, the length of surgery for LH needs to be considered. Surgical approach to

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
		including fibroids			surgery) or 6– 12 months after surgery	Long-term: fistula formation urinary and sexual dysfunction patient satisfaction – QOL (SF12)	<p>No significant difference between LH vs AH, LH vs VH or LH(a) vs LAVH in vascular injury.</p> <p>No significant difference between VH vs AH in mean blood loss.</p> <p>No significant difference between the no of women with substantial bleeding between LH vs AH and LH vs VH.</p> <p>No significant difference between LH vs VH, or LH(a) vs LAVH in unintended laparotomy.</p> <p>Significant fewer unspecified infections/febrile episodes between VH vs AH (OR 0.42, 95% CI 0.21 to 0.83).</p> <p>Significant fewer wound/abdominal infections (OR 0.32, 95% CI 0.12 to 0.85) unspecified infections or febrile illness (OR 0.65, 95% CI 0.49 to 0.87) between LH vs AH.</p> <p>8) No significant differences in: Need for blood transfusion for VH vs AH, LH vs VH, LH(a) vs LAVH; (LH associated with significantly lower mean blood loss (WMD 45.3 ml, 95% CI 17.9 to 72.7) and smaller drop in Hgb (WMD 0.55 g/L, 95% CI 0.28 to 0.82)); Occurrence of pelvic haematoma for VH vs AH, LH vs AH, or LH(a) vs LAVH; UTI for VH vs AH, LH vs AH, LH vs VH; Other unspecified infection or pyrexial illness for LH vs VH, or LH(a) vs LAVH; Thrombo-embolic events for LH vs AH, LH vs VH</p> <p>Hospital stay: Shorter hospital stay (WMD 1.0 day, 95% CI 0.7 to 1.2) and return to normal activities (WMD 9.5 days, 95% CI 6.4 to 12.6) for VH vs AH. Shorter hospital stay (WMD 2.0 days, 95% CI 1.9 to 2.2) and return to normal activities (WMD 13.6 days, 95% CI 11.8 to 15.4) for LH vs AH. No significant differences in hospital stay and return to normal activities for LH vs VH. No significant differences in hospital stay for LH(a) vs LAVH</p> <p>Long-term outcomes – No significant differences in: Fistula formation for LH vs AH, LH vs VH. Urinary dysfunction for VH vs AH, LH vs VH. Sexual dysfunction (dyspareunia od failure to orgasm) for LH(a) vs LAVH. Patient satisfaction for LH vs AH</p> <p>Exclusion of 3 trials in which the surgeons for on intervention were different to those performing the other intervention did not alter the statistical significance of any meta-analysis results.</p> <p>Data expressed as medians were not included in the meta-analysis results.</p>	hysterectomy should be decided by the woman after discussing the relative benefits and hazards with her surgeon.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Kung 1996 ⁵⁸³	Prospective cohort EL = 2+	291 women (144 in LAVH group, and 157 in TAH)	Population characteristics: Women; hysterectomy; u LAVH group: Age = 44.2 Gravidity = 4.2 Parity = 3 BMI = 24 Indication for surgery: Leiomyoma = 71 Adenomyosis = 42 Combination = 13 Normal sized uterus = 12 Pre-operative haemoglobin = 119 g/l TAH group: Age = 44.5 Gravidity = 4.1 Parity = 3 BMI = 24.9 Indication for surgery: Leiomyoma = 86 Adenomyosis = 38 Combination = 13 Normal sized uterus = 20 Pre-operative haemoglobin = 117 g/l Country: Taiwan	LAVH; TAH	No follow-up	Completed surgery; Operative time; Blood loss; complications; Length of stay; post-operative haemoglobin	Comparison of LAVH vs TAH: Completed surgery: LAVH = 138 of 144, TAH = 157 of 157 (NS) Operative time = 134.5 (SD 31.2) vs 112 (SD 21.7) ($P < 0.001$) Estimated blood loss (ml) = 260 vs 259 Uterine weight: 272 (SD 131) vs 309 (SD 186) Complications: Transfusion = 2 vs 6 UTI = 2 vs 1 Intestinal injury = 1 vs 0 Subcutaneous emphysema = 2 vs 0 Abdominal wall ecchymosis = 2 vs 0 Total = 8 vs 7 (NS) Post-operative complications: Total = 13 vs 21 (NS) Length of stay = 4.9 vs 5.2 days Post-operative haemoglobin = 107 vs 109 (NS)	Funding source: Not stated
Kupperman 2004 ³²⁶	RCT EL = 1+	63 in total, 31 (2 lost to follow-up) to hysterectomy and 32 (2 lost to follow-up) to medical treatment	Population characteristics: Women; failed medical treatment – medroxyprogesterone; 30 to 50 years of age; minimum of 2 months AUB; no hyperplasia on biopsy; excluded if – wanted future fertility desired, pregnant, or coagulopathy; long-acting treatments within 6 months; COC or IUD within 3 months; pelvic pathology for which surgery was indicated. Average age: hysterectomy = 42, medicine = 40 Health insurance = 65%, 81% < high school education = 39%, 38% <\$25,000 income = 42%, 53% Uterine fibroids = 65%, 63% Pervious treatment: hysterectomy = COC 39%, Prostaglandin inhibitors 13%, GnRH-a 10%, D&C 19%, myomectomy 6%, endometrial ablation 3% Medicine = COC 50%, Prostaglandin	Hysterectomy; expanded medical treatment treatment vs treatment; treatment vs baseline	24 months	SF-36; Body image and sexual functioning; Mental health; General health	Baseline QoL scores (all on 0 to 100 scale, with 100 being optimal health): SF-36 MCS score: hysterectomy = 45 (SD 11), Medicine = 45 (SD 10). SF-36 PCS score: hysterectomy = 43 (SD 8), Medicine = 42 (SD 9). Body image score: hysterectomy = 59 (SD 28), Medicine = 62 (SD 22). Satisfaction with sex: hysterectomy = 45 (SD 31), Medicine = 56 (SD 32). Psychological well-being score: hysterectomy = 73 (SD 17), Medicine = 71 (SD 18). Overall health score: hysterectomy = 58 (SD 19), Medicine = 59 (SD 18). Satisfaction with health: hysterectomy = 38 (SD 22), Medicine = 39 (SD 24). Change in QoL scores from baseline to 6 months using intention to treat (hysterectomy, medicine, P value for difference between groups): SF-36 MCS score: hysterectomy = 8, Medicine = 2, $P = 0.04$. SF-36 PCS score: hysterectomy = 6, Medicine = 3, $P = 0.21$. Body image score: hysterectomy = 15, Medicine = 5, $P = 0.07$. Satisfaction with sex: hysterectomy = 20, Medicine = 10, $P = 0.19$.	Funding source: Agency for Healthcare Research and Quality grant Study summary: Hysterectomy was superior to expanded medical treatment at 6 months in study population, at 24 months there was no difference by half of women in medical group had had hysterectomy.

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			inhibitors 19%, GnRH-a 6%, D&C 38%, myomectomy 0%, endometrial ablation 0% Country: USA				<p>Psychological well-being score: hysterectomy = 8, Medicine = 0.2, $P = 0.07$.</p> <p>Overall health score: hysterectomy = 12, Medicine = 2, $P = 0.006$.</p> <p>Satisfaction with health: hysterectomy = 31, Medicine = 14, $P = 0.01$.</p> <p>Symptom resolution: hysterectomy = 75, medicine = 29, $P < 0.001$.</p> <p>Satisfaction with symptom level: hysterectomy = 44, medicine = 7, $P < 0.001$.</p> <p>By 24 months 17 (53%) of medical group had undergone hysterectomy</p> <p>Change in QoL scores from baseline to 24 months using intention to treat (hysterectomy, medicine, P value for difference between groups):</p> <p>SF-36 MCS score: hysterectomy = 7, Medicine = 4, $P = 0.25$.</p> <p>SF-36 PCS score: hysterectomy = 7, Medicine = 9, $P = 0.19$.</p> <p>Body image score: hysterectomy = 11, Medicine = 12, $P = 0.97$.</p> <p>Satisfaction with sex: hysterectomy = 17, Medicine = 18, $P = 0.89$.</p> <p>Psychological well-being score: hysterectomy = 7, Medicine = 3, $P = 0.24$.</p> <p>Overall health score: hysterectomy = 11, Medicine = 9, $P = 0.64$.</p> <p>Satisfaction with health: hysterectomy = 27, Medicine = 25, $P = 0.68$.</p> <p>Symptom resolution: hysterectomy = 70, medicine = 256, $P = 0.09$.</p> <p>Satisfaction with symptom level: hysterectomy = 46, medicine = 40, $P = 0.36$.</p> <p>Change in QoL scores from baseline to 24 months using as treated (hysterectomy, medicine, P value for difference between groups):</p> <p>SF-36 MCS score: hysterectomy = 7, Medicine = 2.</p> <p>SF-36 PCS score: hysterectomy = 7, Medicine = 11.</p> <p>Body image score: hysterectomy = 12, Medicine = 8.</p> <p>Satisfaction with sex: hysterectomy = 17, Medicine = 13.</p> <p>Psychological well-being score: hysterectomy = 7, Medicine = 0.6.</p> <p>Overall health score: hysterectomy = 11, Medicine = 5.</p> <p>Satisfaction with health: hysterectomy = 27, Medicine = 20.</p> <p>Symptom resolution: hysterectomy = 71, medicine = 35.</p> <p>Satisfaction with symptom level: hysterectomy = 47, medicine = 31.</p>	
Kupfermann 2005 ⁵²¹	RCT EL = 1+	135 undergoing total abdominal hysterectomy (TAH) or supra-cervical hysterectomy (SCH)	<p>Population characteristics: Premenstrual women > 30 years old, with abnormal uterine bleeding, or fibroids (confirmed by ultrasound)</p> <p>Exclusion criteria:</p> <ul style="list-style-type: none"> > 50 years old positive pregnancy test Desire for future childbearing Known cervical or genital tract cancer Complex endometrial hyperplasia 	SCH vs TAH SCH ($n = 68$) vs TAH ($n = 67$)	up to 2 years (data available for 96% of TAH and 90% of SCH at 2 years)	Sexual functioning using the Medical Outcomes Study (MOS) Sexual Problems Scale and Body Attitudes Questionnaire, and modified to assess health-related quality of life	<p>Sexual functioning:</p> <p>SCH: higher mean score the TAH group on orgasm frequency at 6 months (likely due to better sexual functioning at baseline)</p> <p>Reported problems with sexual functioning (on a 0–100 scale with 100 indicating the absence of problems)</p> <p>SCH: 82</p> <p>TAH: 80 (Mean difference 2, 95% CI –8 to 11) (but no significant differences in both groups at 2 years (mean</p>	<p>Funding source: funded by a grant from the Agency for Health Care Research and Quality</p> <p>Study summary: SCH and TAH resulted in similar sexual functioning and health-related quality of life at 2 years follow-up</p>

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
		(TOSH) study	Candidates for vaginal hysterectomy Sig higher scores on Sexual Problems Scale in the SCH group (indicating fewer problem; 69 vs 55, $P = 0.03$), all other demographic variables were comparable Country: USA				scores above 90)	
Langebrekke 1996 ⁴⁹⁸	Randomised; concealed EL = 1+	100 (46 LH, 54 TAH)	Population characteristics: Women; women excluded if – malignancy found, intra-abdominal adhesions, Uterus > 12 weeks in size; serious cardiopulmonary disease or previous colporrhaphy Country: Norway	LAVH; TAH	N/A	Operation time (min); Hospital stay (days); Resumption of work (days); Postoperative pain; Estimated blood loss (ml); Complications	LAVH vs TAH: Median operation time (min): 100 vs 60.5 Hospital stay (days): 2 vs 5 ($P < 0.001$) Resumption of work (days): 19.5 vs 36.5 ($P < 0.001$) Estimated blood loss fall in haemoglobin (g/l): 2 vs 1.9 Complications: Hgb fall < 3 g/l: 2 vs 6 Haematoma: 3 vs 1 Wound infection: 1 vs 0 Bladder injury: 1 vs 1 Urinary infection: 1 vs 2 Ureteral injury: 2 vs 0 Nerve lesion: 0 vs 1 Abscess: 0 vs 1 Pneumonia: 0 vs 1 Bundle branch block: 0 vs 1	Funding source: Not stated Study summary: In expert hands, LH as a primary method for uterine removal is superior to TAH.
Learman 2004 ¹¹⁹	randomised – block; non-blinded; concealment EL = 1+	63 in total, 31 (2 lost to follow-up) to hysterectomy and 32 (2 lost to follow-up) to medical treatment	Population characteristics: Women; failed medical treatment – medroxyprogesterone; 30 to 50 years of age; minimum of 2 months AUB; no hyperplasia on biopsy; excluded if – wanted future fertility desired, pregnant, or coagulopathy; long-acting treatments within 6 months; COC or IUD within 3 months; pelvic pathology for which surgery was indicated. Average age: hysterectomy = 42, medicine = 40 Health insurance = 65%, 81% < high school education = 39%, 38% <\$25000 income = 42%, 53% Uterine fibroids = 65%, 63% Previous treatment: hysterectomy = COC 39%, Prostaglandin inhibitors 13%, GnRH-a 10%, D&C 19%, myomectomy 6%, endometrial ablation 3% Medicine = COC 50%, Prostaglandin inhibitors 19%, GnRH-a 6%, D&C 38%, myomectomy 0%, endometrial ablation	medical treatment; hysterectomy treatments vs baseline	2 years	Menstrual bleeding; Pelvic discomfort; urinary symptoms; menopausal symptoms	Baseline symptomology figures: Hysterectomy group = pelvic pain 74%, pelvic or bladder pressure 55%, low back pain 68%, Hot flushes 19%, Urinary symptoms – urgency 26%, frequent urination 26%, stress incontinence 29%. Continued vaginal bleeding at 6 months was 87% for medicine and 11% for hysterectomy ($P < 0.001$). Continued vaginal bleeding at 24 months was 37% for medicine and 7% for hysterectomy ($P < 0.001$). Continued bleeding in hysterectomy group due to cross-over between treatments. Medicine group = pelvic pain 88%, pelvic or bladder pressure 84%, low back pain 72%, Hot flushes 41%, Urinary symptoms – urgency 44%, frequent urination 41%, stress incontinence 25%. Change in symptom frequency fro baseline at 6 months (intention-to-treat): Pelvic pain: hysterectomy = -2.3, medicine = -0.7, $P < 0.01$. Urinary urgency: hysterectomy = -0.7, medicine = 0.0, $P = 0.03$. Urinary incomplete emptying: hysterectomy = -0.6, medicine = +0.1, $P = 0.03$. Breast pain: hysterectomy = -1.3, medicine = -0.5, $P = 0.02$. No difference for other pelvic, urinary or menopausal symptoms. Change in symptom frequency fro baseline at 2 years (intention-to-treat): Urinary incomplete emptying: hysterectomy = -0.8, medicine = -0.3, $P = 0.04$. Hot flushes: hysterectomy = -0.6, medicine = 0.5, $P < 0.01$.	Funding source: Agency of HealthCare Research and Quality grant Study summary: Hysterectomy was more effective treatment than additional medical treatment in this selected patient group.

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			0% Country: USA				No difference for other pelvic, urinary or menopausal symptoms. Change in symptoms for groups as treated: Hysterectomy only groups produced significant reduction in symptoms, except for stress incontinence ($P = 0.34$) and urge incontinence ($P = 0.74$). Medicine then hysterectomy group produced same results, except hot flushes not significant ($P = 0.13$). Medicine only group produced significant reductions in symptoms for pelvic pain, pelvic pressure, and stress incontinence ($P < 0.05$), all other changes were non-significant.	
Learman 2003 ⁴⁹⁹	RCT EL = 1+	135 undergoing total abdominal hysterectomy (TAH) or supra-cervical hysterectomy (SCH) Total or supra-cervical hysterectomy (TOSH) study	Population characteristics: Premenstrual women > 30 years old, with abnormal uterine bleeding, or fibroids (confirmed by ultrasound) Exclusion criteria: > 50 years old positive pregnancy test Desire for future childbearing Known cervical or genital tract cancer Complex endometrial hyperplasia Candidates for vaginal hysterectomy No sig differences between the 2 groups in demographic variables Country: USA	TAH or SCH TAH ($n = 67$) vs SCH ($n = 68$) TAH group ($n = 67$) 3 had SCH, 2 had no hysterectomy SCH group ($n = 68$) 4 had TAH, 1 had no hysterectomy	up to 2 years (data available for 96% of TAH and 90% of SCH at 2 years)	Symptoms relief Surgical characteristics Operative findings Complications	Symptoms relief: 48–97% reduction in pelvic symptoms and back pain: NS Menopausal symptoms: NS 41–88% reduction in urinary symptomatology and incontinence: NS Surgical characteristics and operative findings (concomitant procedures, antibiotic prophylaxis, ovarian removal, uterine weight and histopathologic diagnosis): NS Narcotic use of analgesia: SCH – 42% at 3 months, 5% at 24 months TAH – 51% at 3 months, 3% at 24 months (NS) Complications: Mean estimated blood loss: SCH – 382 ± 355 ml TAH – 418 ± 306 ml (RR -36.3, 95% CI -153 to 80) (NS) Febrile morbidity: SCH: 15% TAH: 25% (RR 0.75, 95% CI 0.52 to 1.08) (NS) Urinary tract injury: SCH: 0% TAH: 3% (NS) Intra-operative blood transfusion: SCH: 3% TAH: 3% (RR 0.98, 95% CI 0.36 to 2.64) (NS) Postoperative blood transfusion: SCH: 3% TAH: 3% (RR 1.49, 95% CI 0.30 to 7.44) (NS) Procedure time: SCH: 113 ± 35 min TAH: 123 ± 46 min (RR -10.1, 95% CI -27.3 to 7.20) Length of stay in hospital: SCH: 3.3 ± 1.1 days TAH: 3.5 ± 1.2 days (RR -0.25, 95% CI -0.65 to 0.14) Missed days of work: SCH: 29.2 ± 18.5 days	Funding source: funded by a grant from the Agency for Health Care Research and Quality Study summary: No significant differences between SCH and TAH in surgical complications and clinical outcomes at 2 years' follow-up.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							<p>TAH: 8.8 ± 18.8 days (NS)</p> <p>Cut down on activities:</p> <p>SCH: 9.3 ± 15.7 days</p> <p>TAH: 6.0 ± 14.6 days (NS)</p> <p>Rate of patients hospital admission (0–2 years):</p> <p>SCH: 31%</p> <p>TAH: 16% (Relative hazard 2.05, 95% CI 0.99 to 4.2) (NS)</p> <p>During 1st year:</p> <p>SCH: 7.4%</p> <p>TAH: 6%</p> <p>Baseline body weight > 100 kg associated with hospital re-admission (by multivariate analysis)</p> <p>for all cause (RR 2.18, 95% CI 1.06 to 4.48)</p> <p>for readmission related to hysterectomy (RR 2.83, 95% CI 0.86 to 9.36)</p> <p>2 deaths (1 from stroke and 1 from breast cancer)</p>	
Lethaby 2004 ³³⁰	systematic review; meta-analysis EL = 1++	5 RCTs included with 752 patients	<p>Population characteristics: Searches undertaken on Cochrane library, MEDLINE, EMBASE, PsychLIT; Web of Science; CINAHL. Searches of bibliographies.</p> <p>Search designed to identify studies comparing ablation and hysterectomy.</p> <p>Free-text and MeSH headings used as search terms.</p> <p>Search date 1999</p> <p>Country:</p>	<p>Transcervical Resection of the Endometrium (TCRE); Laser ablation; electrocautery ablation; radiofrequency ablation; hysterectomy – any route.</p> <p>Resection/Ablation vs hysterectomy</p>		<p>MBL – subjective and objective; QoL; Length of stay; Duration of procedure; Patient satisfaction; Adverse events; mortality; further surgery</p>	<p>Comparison of improvement in MBL between ablation/resection and hysterectomy: At 12 months (3 studies, $n = 440$) Peto OR = 0.12 (0.06 to 0.25)</p> <p>Comparison of satisfaction between ablation/resection and hysterectomy:</p> <p>At 12 months (3 studies, $n = 519$) Peto OR = 0.46 (0.24 to 0.88).</p> <p>At 24 months (3 studies, $n = 354$) Peto OR = 0.31 (0.16 to 0.59).</p> <p>Comparison of QoL between ablation/resection and hysterectomy: SF-36 – no difference between groups, except for general health ($P = 0.02$), pain ($P = 0.007$), and social functioning ($P = 0.007$) that were all in favour of hysterectomy.</p> <p>Comparison of duration of procedure between ablation/resection and hysterectomy: 5 studies, $n = 706$, WMD = -23.06 [-23.80, -22.32] in favour of ablation/resection.</p> <p>Comparison of duration of hospital stay between ablation/resection and hysterectomy: 5 studies, $n = 706$, WMD = -4.91 [-4.95, -4.87] days in favour of ablation/resection.</p> <p>13 types of adverse events reported. Results favour ablation/resection over hysterectomy for 8 of these, 5 were no different.</p> <p>Proportion requiring further surgery at 12 months: 5 studies, $n = 706$, Peto OR = 7.33 (4.18 to 12.86).</p>	<p>Funding source: Not stated – Cochrane review usually unfunded.</p> <p>Study summary: Study shows that ablation/resection is an alternative to hysterectomy, but is less effective at reducing MBL and improving satisfaction. However, ablation/resection does lead to better QoL, shorter surgery and fewer complications.</p>
Lumsden 2000 ³⁰⁰	Randomised EL = 1–	200 (100 LAVH – 5 lost to follow-up, 100 TAH – 5 lost to follow-up)	<p>Population characteristics: Women; scheduled for hysterectomy for benign conditions; uterine size > 14 weeks included, Need oophorectomy included; HRT inappropriate excluded.</p> <p>TAH vs LAVH:</p> <p>Age: 42.7 vs 41.1</p> <p>BMI: 26.6 vs 26.3</p>	TAH; LAVH	12 months	<p>Length of operation (min); total length of stay (days); Admission to ITU; Additional surgery; Readmissions; Blood transfusions; Complications; QoL (euroQoL)</p>	<p>TAH vs LAVH:</p> <p>Length of operation (min): 45 vs 80</p> <p>Total length of stay (days): 6 vs 4</p> <p>Admission to ITU: 0 vs 2</p> <p>Additional surgery: 2 vs 3</p> <p>Readmissions: 8 vs 6</p> <p>Blood transfusions: 2 vs 1</p>	<p>Funding source: Not stated</p> <p>Study summary: This study demonstrates that despite the decreased length of hospital stay, LAVH is more expensive than TAH. In addition, recovery following</p>

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			<p>Previous significant vaginal surgery: 3 vs 6</p> <p>Previous abdominal surgery: 29 vs 21</p> <p>Significant adhesions: 8 vs 12</p> <p>Uterine fibroids: 25 vs 24</p> <p>Severe endometriosis: 3 vs 2</p> <p>Immobile uterus: 1 vs 1</p> <p>Indication for surgery:</p> <p>Menstrual problems – 55% vs 59%</p> <p>Pelvic pain – 17% vs 22%</p> <p>Country: UK</p>				<p>Complications:</p> <p>Haemorrhage: 0 vs 2</p> <p>UT damage: 1 vs 2</p> <p>Pulmonary embolus: 0 vs 1</p> <p>Bowel damage: 0 vs 0</p> <p>Severe infection: 0 vs 1</p> <p>Pyrexia: 3 vs 4</p> <p>Positive urine culture: 6 vs 4</p> <p>Chest infection: 4 vs 0</p> <p>Wound infection: 4 vs 1</p> <p>Erythema wound: 9 vs 3</p> <p>Patient reported outcomes:</p> <p>Oral analgesic use: 68 vs 75</p> <p>Number of visits to GP: 1.71 vs 1.75</p> <p>Discharging wounds: 12 vs 12</p> <p>Fever: 15 vs 15</p> <p>Antibiotics prescribed: 23 vs 35</p> <p>Urinary symptoms: 12 vs 18</p> <p>Difficulty with micturition: 22 vs 21</p> <p>QoL (Mean EuroQoL):</p> <p>1 month – 6.8 (SD 19.2) vs 7 (SD 24.1)</p> <p>6 months – 14.9 (16.7) vs 11.3 (SD 23.9)</p> <p>12 months – 15.9 (21) vs 12.6 (25)</p>	operation and patient satisfaction were not affected by the route chosen. It is unlikely that LAVH represents an efficient use of NHS resources.
Marana 1999 ⁵⁰¹	Randomised; multicentre EL = 1–	116 (58 in LAVH group, 58 in Abdominal Hysterectomy)	<p>Population characteristics: Women; contraindications to vaginal surgery – uterine size > 280 g, previous pelvic surgery, history of inflammatory pelvic surgery, endometriosis, concomitant adnexal mass, nulliparity with lack of uterine descent or limited vaginal access. Excluded if – uterus size > 16 weeks or 700 g.</p> <p>Baseline (LAVH vs AH):</p> <p>Age: 49.2 vs 49.1</p> <p>Parity: 1.67 vs 1.78</p> <p>Uterine weight: 326.4 (SD 125.8) vs 352.3 (SD 165.9)</p> <p>Country: Italy</p>	Laparoscopically assisted vaginal hysterectomy; abdominal hysterectomy LAVH vs AH	3 days	<p>Operating time (min); Estimated blood loss; postoperative haemoglobin drop (g/100 ml); Complications; Postoperative pain levels; Length of stay (days)</p>	<p>LAVH vs AH:</p> <p>Operating time (min): 91.1 vs 01.8</p> <p>Estimated blood loss: 264.7 (SD 194.4) vs 353.9 (SD 254.6)</p> <p>Postoperative haemoglobin drop (g/100 ml): 1.09 vs 1.55</p> <p>Complications:</p> <p>Conversions to AH from LAVH = 0</p> <p>Bladder laceration: 1 vs 0</p> <p>Febrile morbidity: 2 vs 0</p> <p>Vaginal cuff haematoma: 0 vs 1</p> <p>Pelvic bleeding: 0 vs 1</p> <p>Post-operative fever: 0 vs 5</p> <p>Length of stay (days): 4 vs 5.9 ($P < 0.001$)</p> <p>Postoperative pain levels:</p> <p>day 1 = 5.2 vs 6.3 ($P < 0.05$)</p> <p>day 2 = 2.3 vs 4.4 ($P < 0.001$)</p> <p>day 3 = 1.3 vs 2.8 ($P < 0.005$)</p>	<p>Funding source: Not stated</p> <p>Study summary: The present study demonstrates that, given adequate training in laparoscopic surgery, laparoscopically assisted vaginal hysterectomy may replace abdominal hysterectomy in most patients who require a hysterectomy and have contraindications to vaginal hysterectomy, with all the benefits associated with the vaginal route.</p>
Martel 1995 ⁵⁸⁴	Matched case–control study EL = 2–	212 (106 had LAVH, 106 had TAH)	<p>Population characteristics: Women; matched for age and uterine weight</p> <p>Country: Canada</p>	LAVH; TAH	No follow-up	<p>Operative time; Length of stay; Narcotic use; Complications</p>	<p>Operative time (minutes): LAVH = 146 vs TAH = 61.9 ($P = 0.00001$)</p> <p>Length of stay: 3.5 vs 6.4 days ($P = 0.00001$)</p> <p>Narcotic use (mg): 527 vs 983 ($P = 0.00001$)</p> <p>Complications (LAVH vs TAH): 24 vs 15</p>	<p>Funding source: Not stated</p> <p>Study summary: There was no difference in the complication rate between the two groups.</p>

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							No difference between groups None: 89 vs 94 UTI: 4 vs 3 UT injury: 1 vs 0 Bowel injury: 0 vs 2 Abdominal wall haematoma: 5 vs 1 Haemorrhage: 3 vs 3 Transfusion: 2 vs 2 Vault cellulitis: 3 vs 1 Wound infection: 2 vs 2 Respiratory: 0 vs 1 Abdominal pain: 2 vs 2 Vaginal cuff bleeding: 2 vs 0 TAH: 2 vs 0	
Mehra 1999 ⁵⁸⁵	Case series EL = 2-	663 (312 had TAH, 174 had LAVH, 177 had VH)	Population characteristics: Women; Decision for surgical method based on uterine size. Patient characteristics (VH, TAH, LAVH): Age: 47.2, 44.7, 43.8 Uterine size (weeks): 6.95, 9.18, 9.94 Indication for surgery: Fibroids: 42, 153, 94 Prolapse: 71, 1, 0 DUB: 24, 42, 27 Multiple pathology: 15, 30, 26 Other: 9, 64, 10 Country: India	VH; TAH; LAVH	N/A	Operating time (min); Recovery time (days); Length of stay (days); complications	VH vs TAH vs LAVH: Operating time (min): 82.9, 94.8, 130.8 ($P=0.001$) Recovery time (days): 18, 30, 16.4 ($P=0.001$) Length of stay (days): 6.4, 7.6, 4.3 Complications: Bladder trauma: 1, 0, 2 Haemorrhage: 0, 0, 1 Febrile illness: 6, 21, 7 Paralytic ilcus: 0, 16, 3 Uterovaginal fistula: 0, 0, 1 Wound haematoma: 0, 2, 1 Wound infection: 0, 33, 0 UTI: 14, 26, 5 Vault granulation: 1, 0, 2 Abdominal wall ecchymosis: 0, 0, 3	Funding source: Not stated
Meikle 1997 ⁵²⁵	Systematic review EL = 2+	5420 hysterectomies (3112 LAVH, 1618 TAH, 690 VH) from 34 studies (28 retrospective, 6 others)	Population characteristics: Medline search from 1989 to 1995. Any study on LAVH. English language only Country: USA	LAVH	No follow-up	Complication and recovery rates	Complication rates for LAVH ($n=2273$): Bladder trauma = 39 (1.8%) Bowel trauma = 10 (0.4%) Fistula = 1 (0.04%) Ureter trauma = 6 (0.3%) Pulmonary embolus = 4 (0.2%) Sepsis = 0 Transfusion = 43 (1.4%) Complications rates for TAH ($n=434$): Bladder trauma = 0 Bowel trauma = 0 Fistula = 0 Ureter trauma = 0 Pulmonary embolus = 0 Sepsis = 2 (0.5%) Transfusion = 43 (2.65%)	Funding source: Not stated Study summary: Although laparoscopy-assisted vaginal hysterectomy involves a shorter hospital stay, speedier postoperative recovery, and less analgesia use, there is also a higher rate of bladder injury and lengthier surgery. These outcomes must be weighed when choosing an intervention.
Miskry 2003 ⁵⁰²	randomised – sealed envelopes; blinded;	120 assessed, 57 eligible, 36 randomised (AH = 18,	Population characteristics: Women; scheduled for hysterectomy; excluded if – genital tract malignancy, adnexal pathology, uterine size > 14 weeks	Abdominal hysterectomy; Vaginal	6 months	QoL – SF-36; Recovery; Complications	Outcomes for AH ($n=18$) vs VH ($n=18$): SF-36 at 6 weeks – no differences between groups. However, trend towards AH group having lower scores than VH group.	Funding source: Not stated Study summary: Vaginal

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
	concealed EL = 1+	VH = 18). All completed trial.	pregnancy, need for concurrent procedure, reduced uterine mobility, inadequate vaginal access. Baseline characteristics (AH vs VH): Age: 42.0 vs 41.4 BMI: 27.4 vs 29.0 Uterine size (weeks): 6.9 vs 7.8 Nulliparous: 11.8% vs 27.7% Uterine weight (g): 150 vs 218 Indications for surgery: DUB: 12 vs 9 Leiomyomas: 3 vs 6 Pelvic pain: 3 vs 3 Planned oophorectomy: 8 vs 5 Country: UK	hysterectomy AH vs VH			SF-36 at 6 months – no differences between groups Change in SF-36 – significant improvements for AH on physical functioning ($P = 0.05$), Physical role ($P = 0.009$), Bodily pain ($P = 0.04$), social functioning ($P = 0.02$). And for VH on physical role ($P = 0.008$). VAS diary scores for 2 weeks after surgery = no difference between groups for energy, appetite, pain, mobility, overall well-being. However, trend towards AH group having lower scores than VH group. Postoperative recovery (mean, SD): Intravenous infusion = 32.7 (9.8) vs 25.3 (7.6), $P = 0.05$ Analgesia use (mg) = 131.4 (58.2) vs 75.4 (29.7), $P = 0.002$ Bowels open (days): 3.7 vs 2.6, $P = 0.002$ Postoperative stay (days) = 5.0 (1.49) vs 3.6 (1.42), $P = 0.01$ Time to domestic activity (weeks): 8.5 (4.1) vs 4.6 (1.9), $P = 0.01$ Time to fitness to work = 13.9 (9.5) vs 7.0 (2.9), $P = 0.005$ Time to full recovery (weeks) = 16.9 (10.1) vs 7.9 (4.5), $P = 0.02$. Complications (AH vs VH): Febrile morbidity = 5 vs 2 Vault haematoma = 1 vs 2 Abdominal wound infection = 1 vs - UTI = 1 vs 0 Unidentified = 2 vs 0 Haemorrhage requiring transfusion = 0 vs 3 Intra-operative = - vs 2 Postoperative = - vs 1 Unintended surgical procedure = 0 vs 1 Re-hospitalisation = 0 vs 1	hysterectomy was associated with significant benefits in terms of reduced hospital stay and improved patient recovery. Vaginal hysterectomy should be the route of choice not only for women with genital tract prolapse but also those without.
Mousa 2001 ³⁶³	Matched case-control EL = 2+	169: 91 rollerball ablation, 78 abdominal hysterectomy	Population characteristics: Women; surgery for menorrhagia Average age: ablation = 43, hysterectomy = 41 Duration of problem = 20 months, 24 months Menorrhagia = 25%, 25% Menorrhagia and dysmenorrhoea = 75%, 75% Country: UK	Rollerball ablation; hysterectomy	At least 18 months	Procedure outcomes; Patient outcomes	Operative complications: ablation = 4, hysterectomy = 0 Post-operative complications: ablation = 0, hysterectomy = 5 Bleeding pattern: ablation – 35 amenorrhoea, 32 improved, 6 same, 7 had hysterectomy. Hysterectomy – all amenorrhoea. Patient satisfaction: ablation: 63 (79%) satisfied, hysterectomy: 40 (100%) satisfied Would recommend to friend: ablation: 73 (91%), hysterectomy: 40 (100%).	Funding source: Not stated Study summary: Both treatments are effective, but hysterectomy is associated with better patient outcomes.
Neumann 2004 ⁵⁸⁶	Comparative case series EL = 2-	451 women who had had a hysterectomy for reasons of menometrorrhagia or dysmenorrhoea/dyspareunia Control	Population characteristics: No previous surgery 53 supra-cervical H 151 total AH 247 VH Country: Denmark	supra-cervical H total AH VH vs control supra-cervical H total AH VH vs control	during a period of 9–45 months	Duration of operation Blood loss Hospital stay Bladder injury de novo urinary symptoms based on subjective report by postal questionnaire	Supra-cervical H vs AH vs VH: Mean duration of operation: 63 vs 71 vs 57 min ($P = 0.01$) Blood loss: 252 vs 303 vs 137 ml ($P = 0.01$) Sig longer hospital stay in AH group Bladder injury: 1 in supra-cervical H, 0 in AH, 7 in VH Urinary symptoms: Pre-op: Women in supra-cervical H group experienced sig more	Funding source: not stated Study summary: supra-cervical H is related to more urinary symptoms than VH and AH. De novo urinary symptoms and cure are common, hence need to be

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
		110 women who had had a laparoscopic cholecystectomy, excluding nulliparous					bothersome incontinence than AH, VH and cholecystectomy <i>De novo</i> urinary symptoms post-op: Women in supra-cervical H group experienced sig urge, urgency and feeling of hygienic problem than AH, VH and cholecystectomy <i>De novo</i> cure sig more common than in cholecystectomy group Use of devices and feeling of having a hygiene problem more associated with women after supra-cervical H than AH	reviewed over time
Olsson 1996 ⁵⁰³	randomised; concealed EL = 1+	150 eligible, 143 agreed to enter study (71 laparoscopic hysterectomy, 72 abdominal hysterectomy)	Population characteristics: Women; benign disorders; uterine width < 11 cm; not suitable for vaginal hysterectomy (which are undertaken on: normal size uterus, no endometriosis, no prolapse, no post-inflammatory disorders). Baseline (LH vs AH): Age (years): 47 vs 47 BMI: 23.1 vs 23.8 Parity: 2 vs 2 Prior laparotomies: 1 vs 1 Uterus width (cm): 7 vs 7 Uterus length (cm): 9 vs 9 Uterus weight (g): 149 (range 60 to 540) vs 159 (57 to 394) Indications for surgery: Menorrhagia: 44 vs 37 Metrorrhagia: 26 vs 30 Uterine fibroids: 22 vs 20 Endometrial hyperplasia: 21 vs 25 Dysmenorrhoea: 13 vs 23 Mechanical symptoms: 4 vs 6 Endometriosis: 2 vs 7 Adnexal mass: 0 vs 4 Country: Sweden	Laparoscopic hysterectomy; abdominal hysterectomy		Anaesthesia (min); Duration of surgery (min); Hospital stay (days); Convalescence (days); Complications	LH vs AH: Anaesthesia (min): 190 (range 125 to 305) vs 125 (range 65 to 275) Duration of surgery (min): 148 (range 70 to 240) vs 85 (45 to 225) Hospital stay (days): 2.0 vs 4.0 Convalescence (days): 16.0 (o to 74) vs 35.0 (7 to 125) Complications: Haematoma of vaginal cuff: 6 vs 5 Haematoma of abdominal wall: 5 vs 12 Pyrexia: 5 vs 8 Vaginal cuff infection: 6 vs 4 Abdominal wall infection: 1 vs 6 Pyelonephritis: 2 vs 0 Cystitis: 3 vs 3 Bladder laceration: 1 vs 1 Vesicovaginal fistula: 1 vs 0 Patients with at least one complication: 19 vs 24 Blood transfusions: 5 vs 9 Blood units given: 11 vs 23 ($P < 0.001$)	Funding source: Swedish Medical Research Council Study summary: Laparoscopic hysterectomy is a safe procedure for selected patients scheduled for abdominal hysterectomy, and offers benefits to the patients in the form of less operative bleeding, less post-operative pain, shorter time in hospital and shorter convalescence time.
Ottosen 2000 ⁵⁰⁴	Randomised; concealed; ITT EL = 1+	120 (40 VH, 40 AH, 40 LAVH)	Population characteristics: Women; indications of menorrhagia, uterine fibroids < 15 cm in diameter, dysplasia, endometrial atypia, pain; excluded if – uterus > 16 weeks, known dense adhesions, narrow vagina or inaccessible uterus. Baseline (TAH vs VH vs LAVH) Age: 47 vs 49 vs 48 BMI: 165 vs 165 vs 166 Previous caesarean section: 6 vs 2 vs 3 Nulliparity: 4 vs 7 vs 2 Uterine weight (g): 258 (43 to 1025) vs 266 (86 to 1175) vs 263 (61 to 671) Indications: Uterine fibroids: 18 vs 21 vs 21	LAVH; abdominal hysterectomy; vaginal hysterectomy LAVH vs AH vs VH		Duration of surgery; Length of stay; Recovery (days); Peri-operative blood loss (ml); Complications	TAH vs VH vs LAVH: Duration of surgery: 68 ($P < 0.05$) vs 81 ($P < 0.05$) vs 102 ($P < 0.05$) Length of stay: 3.7 ($P < 0.05$) vs 2.8 vs 3.1 Recovery (days): 28.1 ($P < 0.05$) vs 21.3 vs 19.7 Peri-operative blood loss (ml): 225 vs 287 vs 311 Complications: Re-operation and transfusion: 0 vs 2 vs 1 Transfusions: 1 vs 0 vs 0 Bladder tear: 0 vs 1 vs 0 Paralytic ileus: 1 vs 0 vs 0 Pyrexia: 1 vs 1 vs 1 UTI: 1 vs 1 vs 0 UTI and vaginal cuff infection: 0 vs 1 vs 1 Vaginal cuff haematoma: 1 vs 1 vs 0	Funding source: Funded by charitable foundations Study summary: Traditional vaginal hysterectomy proved to be feasible and the faster operative technique compared with vaginal hysterectomy with laparoscopic assistance. The abdominal technique was somewhat faster, but time spent in theatre

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			Menorrhagia pain: 17 vs 15 vs 13 Pre-malignant conditions: 5 vs 4 vs 6 Histopathology: Uterine fibroids: 21 vs 31 vs 23 Adenomyosis 8 vs 2 vs 8 Uterine malignancy: 3 vs 5 vs 5 Normal: 8 vs 2 vs 4 Country: Sweden				Abdominal wall infection: 1 vs 0 vs 0 Prolonged catheter time: 0 vs 0 vs 1 Converted to TAH: 0 vs 1 vs 4	was not significantly shorter. Abdominal hysterectomy required on average a longer hospital stay of one day and one additional week of convalescence compared with traditional vaginal hysterectomy. Vaginal hysterectomy should be a primary method for uterine removal.
Perino 1999 ⁵⁰⁵	Randomised EL = 1-	108 – 51 laparoscopic hysterectomies, 57 abdominal hysterectomies	Population characteristics: Women; scheduled for hysterectomy; not > 16 weeks gestation Laparoscopic groups: age = 47.8, parity = 2.3, uterine weight = 368 g (SD 125.3) abdominal group: age = 47.6, parity = 2.4, uterine weight = 389 g (SD 143.9) Each surgeon had undertaken 100 major laparoscopic procedures prior to study. Country: Italy	Laparoscopic hysterectomy; abdominal hysterectomy	No follow-up period	Operating time (min)	Operating time (min): Laparoscopic – first 15 = 129.2 min (SD 22.3), last 36 = 93.6 (SD = 21.4) Abdominal – first 15 = 87.9 min (SD = 20.3), last 36 = 87.8 min (SD = 20.7) Blood loss (ml): Laparoscopic = 140 ml (SD = 41.5) Abdominal = 406 ml (SD = 103.9) ($P < 0.001$) Postoperative stay: Laparoscopic = 2.4 days Abdominal = 6.2 days ($P < 0.001$) Postoperative pain (LH vs AH, VAS): Day 1 = 4.1 vs 6.9 Day 2 = 2.3 vs 5.4 Day 3 = 1.0 vs 3.1 All $P < 0.001$)	Funding source: Not stated Study summary: Study shows the learning curve involved in laparoscopic surgery, but after this it is equivalent to abdominal hysterectomy in terms of operating time, but with less blood loss and shorter stay.
Pinto 2003 ⁴²⁰	randomised; concealed – sealed envelopes; blinding not mentioned EL = 1+	64 eligible. 57 randomised (38 in UAE group – 1 refused assignment and had hysterectomy, 19 in hysterectomy group – 3 refused assignment and had UAE, 1 of whom later had hysterectomy)	Population characteristics: Women; bleeding associated with uterine fibroids; patient with fibroid > 10 cm; contraindications to surgery; desire to maintain fertility and/or sensitivity to iodine were excluded from study. Baseline characteristics (UAE vs hysterectomy): Age (years) 46.4 vs 44.6 No pregnancies = 2.6 vs 3.2 Births = 2.2 vs 2.5 Previous treatment: None = 23 vs 9 Hormonal = 14 vs 10 Myomectomy = 1 vs 0 Number of fibroids = 1.6 vs 1.6 Fibroid type:	UAE; hysterectomy	2 years	ER visits after surgery; complications; success on bleeding patterns; length of stay	Success of treatment on bleeding patterns: UAE = 31 of 36 (86%) had cessation of bleeding. Hysterectomy bleeding not measured. Visits to ER after surgery: UAE = 13, Hysterectomy = 4 Intra-operative complications: Minor – UAE = 11 vs 0 Major – UAE = 0 vs hysterectomy = 4 Post-operative complications: Minor – UAE = 20 vs hysterectomy = 3 Moderate – UAE = 19 vs hysterectomy = 2 Major – UAE = 1 vs hysterectomy = 7 Length of stay (based on intention to treat) – UAE = 1.71 days (SD 1.59), hysterectomy = 5.85 day (SD 2.52)	Funding source: Not stated Study summary: Compared with hysterectomy, UAE is safe and effective treatment for bleeding fibroids, necessitates a shorter hospital stay, and results in fewer major complications.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			<p>mural = 16 vs 13 Submucosal = 15 vs 2 Subserous = 7 vs 4 Fibroid volume (cm³) = 72 vs 113</p> <p>Symptoms: Menorrhagia = 37 vs 17 Metrorrhagia = 19 vs 9 Country: Spain</p>					
Raju 1994 ⁵⁰⁶	randomised; concealed EL = 1+	80 (40 abdominal hysterectomy; 40 LAVH)	<p>Population characteristics: Women; scheduled for hysterectomy and bilateral oophorectomy for benign condition; excluded if – uterus > 14 weeks in size, morbidly obese, uterine prolapse.</p> <p>Baseline characteristics (LAVH vs TAH):</p> <p>Indication:</p> <p>Menorrhagia – 28 vs 28 Dysmenorrhoea – 18 vs 15 Pelvic pain – 8 vs 4 Post-menopausal bleeding – 2 vs 1 Failed TCRE – 2 vs 4 Mean age – 45.5 vs 45.9 BMI – 25.7 vs 24.9 endometriosis – 5 vs 4 Adhesions – 5 vs 6 Fibroids – 11 vs 6</p> <p>Maximum uterus size: 12 weeks vs 14 weeks. Country: UK</p>	Laparoscopic-assisted bilateral salpingo-oophorectomy and vaginal hysterectomy; total abdominal hysterectomy with bilateral salpingo-oophorectomy Surgery vs surgery	6 weeks	<p>Operating time (min); estimated blood loss (ml); Length of stay; duration of post-operation analgesia (days); recovery from pain (days); time for recovery (days)</p>	<p>LAVH vs TAH:</p> <p>Operating time (min): 100 (61 to 180) vs 57 (25 to 151) ($P < 0.0001$)</p> <p>Estimated blood loss (ml): 260 (70 to 700) vs 220 (50 to 500)</p> <p>Length of stay: 3.5 (1 to 6) vs 6 (3 to 13) ($P < 0.0001$)</p> <p>Duration of post-operation analgesia (days): 6.6 vs 13.3 ($P < 0.0001$)</p> <p>Recovery from pain (days): 13 vs 26 ($P < 0.0001$)</p> <p>Time for recovery (days): restricted physical activity – 16 (6 to 35) vs 27 (5 to 47) ($P < 0.001$)</p>	<p>Funding source:</p> <p>Study summary: The study shows laparoscopic-assisted bilateral salpingo-oophorectomy and vaginal hysterectomy is a safe and cost-effective procedure for women requiring a hysterectomy and bilateral salpingo-oophorectomy.</p>
Ribeiro 2003 ⁵⁰⁷	randomised EL = 1–	60 consecutive patients (20 AH, 20 VH, 20 LAVH)	<p>Population characteristics: Women; suitable for hysterectomy; excluded if – uterine volume > 400 cm³, use of anti-inflammatory drugs in past 3 months; diabetes mellitus; coagulation disorders; autoimmune diseases.</p> <p>Average uterine weight: TAH = 189.50, VH = 155.65, LH = 154.50</p> <p>Patient age: range 34 to 76 (mean average = 42.33)</p> <p>HMB = 57 Myoma = 41 Adenomyosis = 19 Country: Brazil</p>	Abdominal hysterectomy; vaginal hysterectomy; LAVH	2 days	<p>Operative time; complications; blood loss; C-reactive protein levels; interleukin 6 levels</p>	<p>Operative time (min): TAH = 109, VH = 78, LH = 119</p> <p>Blood loss: VH had lower levels of haemoglobin than TAH and LH ($P < 0.05$)</p> <p>Inflammatory response: TAH different from VH and LH ($P < 0.05$)</p>	<p>Funding source: Not stated</p> <p>Study summary: Vaginal hysterectomy presents superior results in terms of operative time and inflammatory response when compared with total abdominal and laparoscopic hysterectomy and it should be the first option for hysterectomy. Laparoscopic hysterectomy should be considered when the vaginal approach is unfeasible, showing clear advantages over abdominal</p>

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
								hysterectomy.
Richardson 1995 ⁵⁰⁸	randomised EL = 1+	45 randomised (22 LH, 23 VH)	Population characteristics: Women; contraindications to vaginal surgery – endometriosis, need for oophorectomy, uterine enlargement. Baseline (LH vs VH): Age: 41 vs 45 Uterine size (weeks): 9 (4 to 15) vs 8 (4 to 16) Previous pelvic surgery: 6 vs 4 Nulliparous: 6 vs 4 Oophorectomy: 9 vs 9 Previous caesarean section: 4 vs 2 Indications for surgery (LH vs VH): Fibroids/menorrhagia: 16 vs 16 Pelvic pain/endometriosis: 4 vs 3 Dysmenorrhoea: 2 vs 4 Country: UK	Laparoscopic hysterectomy(LAVH) ; Vaginal hysterectomy	6 weeks	Operating time; Opioid injections; analgesia required (days); inpatient stay (days); discomfort (days); Normal activities (days); Work (weeks)	LH (<i>n</i> = 22) vs VH (<i>n</i> = 23): Operating time: 131.4 vs 76.7 Opiod injections:2.3 vs 2.6 Analgesia required (days): 2.9 vs 2.6 Inpatient stay (days): 3.2 vs 3.3 Discomfort (days):10.2 vs 9.5 Normal activities (days): 23.1 vs 22.2 Work (weeks): 6.4 vs 5.7	Funding source: Not stated Study summary: Our study confirms that most hysterectomies could be performed vaginally, and that LH is a much slower procedure. If LH is done, it should be converted to a vaginal procedure as early as possible to reduce the overall operating time. LH does seem to be a waste of time for most patients.
Sawin 2000 ⁴⁵⁷	Prospective comparative cohort study EL = 2+	394 women Abdominal myomectomy (AM): <i>n</i> = 197 Abdominal hysterectomy (AH): <i>n</i> = 197	Population characteristics: Mean age AM: 36 years AH: 44 years (<i>P</i> < 0.0001) Mean weight: AM: 156 lbs AH: 174 lbs (<i>P</i> < 0.0001) Mean parity: AM: 0.5 AH: 1.6 (<i>P</i> < 0.0001) Pre-op uterus size (weeks equivalent): AM:14 AH: 16 (<i>P</i> < 0.0001) Indications: AM: vaginal bleeding (37%) or pain (39%), recurrent miscarriage, infertility. AH: vaginal bleeding (62%) or pain (31%). Country: USA	AM vs AH AM vs AH	Chart review over a period of 2 years	Morbidity Post op care	Morbidity: Overall morbidity: AM: 39%, AH: 40% (OR 0.93, 95% CI 0.63 to 1.40) Febrile morbidity: AM: 33%, AH: 26% (OR 1.41, 95% CI 0.91 to 2.17) Haemorrhage: AM: 10%, AH: 14% (OR 0.46, 95% CI 0.26 to 0.83) Unintended procedure: AM: 4.5%, AH: 0.6% (OR 0.45, 95% CI 0.20 to 0.99) Life-threatening event: AM: 1.5%, AH: 1% (OR 1.51, 95% CI 0.17 to 18.00) Readmission: AM: 1.5%, AH: 2.5% (OR 0.59, 95% CI 0.09 to 3.10) Post-op care: Mean operative time (min): AM: 201, AH: 176 (<i>P</i> < 0.00002) Estimated blood loss (ml): AM: 227, AH: 484 (<i>P</i> < 0.00001) Length of hospital stay (days): AM: 4, AH: 4.4 (<i>P</i> < 0.048) Max drop in Hgb: AM: 2.5, AH: 4 (NS) Transfusion (no.): AM: 9%, AH: 13% (NS)	Funding source: Not stated Study summary: No clinical difference in peri-operative morbidity between myomectomy and hysterectomy. Myomectomy should be considered a safe alternative to hysterectomy
Schutz 2002 ⁵⁰⁹	Randomised; concealed EL = 1+	48 (28 LAVH, 20 AH)	Population characteristics: Women; Uterine weight > 200 g; no preference for surgical method. Baseline (LAVH vs AH; median (25 to 75 percentiles)): Age: 47.5 vs 48 Gravidity: 2 vs 2 Parity: 2 vs 2 Estimated uterine weight: 283 (234 to 435)	Laparoscopically assisted vaginal hysterectomy; Abdominal hysterectomy LAVH vs AH	12 months	Duration of operation (min); Estimated blood loss (ml); number of blood transfusions; Additional procedures; uterine weight (g); complications; Haemoglobin levels;	LAVH vs AH (median, 25 to 75 percentile): Duration of operation (min): 133 to 132 Estimated blood loss (ml): 200 (150 to 280) vs 600 (400 to 1225) Number of blood transfusions: 3 vs 10 Additional procedures: 5 vs 3 Actual uterine weight (g): 334 (244 to 500) vs 428 (263 to 675) Complications: UTI = 2 vs 2	Funding source: Not stated Study summary: For the treatment of uteri > 200 g, LAVH has several advantages over AH: lower postoperative morbidity, quicker short-term recuperation, and better patient

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			vs 369 (254 to 595) Country: Germany			pain index (WHO); length of stay (days); Recovery time (days)	Anaemia = 1 vs 4 Lymph node swelling = 1 vs 0 Haemoglobin levels day 3: -0.6 vs -1.55 Pain index (WHO): 0 vs 5 Length of stay (days): 6.5 (5 to 7) vs 10 (8.25 to 11) Recovery time (days): 42 vs 42	acceptance.
Seracchioli 2003 ⁵⁸⁷	Randomised EL = 1+	62 (31 GnRH, 31 no treatment)	Population characteristics: Women; Uterine fibroids; Uterine volume between 16 and 20 weeks; absence of pelvic pathologies; no therapy with GnRH or progestational agents within 6 months; no condition requiring hospital monitoring (diabetes etc), previous abdominal surgery requiring laparotomy; contraindications to surgery. Baseline (GnRH vs No treatment) Age: 47.6 vs 48.4 BMI: 23.1 vs 24.4 Pre-treatment uterine volume (ml): 528 (SD 275) vs 579 (SD 337) Country: Italy	GnRH pre-treatment (depot Decapeptyl 11.25 mg) for 3 month; no treatment	3 months prior to surgery and 2 months after surgery	Preoperative haemoglobin (g/dl); Preoperative uterine volume (ml); Uterine weight (g); operating time (min); Drop in haemoglobin; number of transfusions; Mean hospital stay (hours)	GnRH vs no treatment: Pre-treatment uterine volume (ml): 528 (SD 275) vs 579 (SD 337) Preoperative haemoglobin (g/dl): 12.3 vs 11.4 ($P < 0.02$) Preoperative uterine volume (ml): 388 (SD 193) vs 587 (SD 341) ($P < 0.005$) Uterine weight (g): 328 (SD 165) vs 462 (SD 226) ($P < 0.02$) Operating time (min): 85.3 vs 115.3 ($P < 0.001$) Drop in haemoglobin: 1.2 vs 1.9 ($P < 0.005$) Number of transfusions: 0 vs 3 Mean hospital stay (hours): 76.2 vs 80.4 7 in GnRH and 8 in no treatment group had BSO. 3 women in no treatment group converted to TAH due to fibroid size.	Funding source: Not stated Study summary: In women with a large uterus, a 3 month preoperative course of GnRH may facilitate laparoscopic hysterectomy, decreasing uterine size, operating time, and blood loss.
Seracchioli 2002 ⁵¹⁰	Randomised; concealed EL = 1+	122 enrolled (60 TLH, 62 TAH)	Population characteristics: Women; uterine fibroid > 14 weeks Baseline (TLH vs TAH): Age: 46.3 vs 47.4 BMI: 24.7 vs 23.1 Previous pelvic surgery: 31.6 vs 24.1 Mean number of myomas: 3.3 vs 2.9 Mean diameter of myomas (cm): 4.2 vs 4.9 Mean longitudinal diameter of myomas: 14.1 vs 14.7 Mean uterine weight (g): 411.8 (SD 175) vs 429.6 (SD 125) Country: Italy	TLH; TAH Surgery vs surgery	2 months	Operating time (min); Estimated blood loss (ml); number of transfusions; Number of with fever; Lapro-conversions; Length of stay (hours); length of recovery (days)	TLH vs TAH: Operating time (min): 95.2 vs 88.6 Estimated blood loss (ml): 311.6 vs 376.9 Number of transfusions: 0 vs 1 Number of with fever: 8 vs 18 ($P < 0.05$) Laparo-conversions: 1 vs 0 Length of stay (hours): 76.4 vs 121.8 Length of recovery (days): 22 vs 36 Complications: TAH = 1 cystotomy TLH = 0	Funding source: Study summary: Laparoscopic hysterectomy is safe and feasible even in the presence of large uterus, and is a valid alternative to abdominal hysterectomy when the vaginal route is contraindicated.
Soriano 2001 ⁵¹¹	Randomised EL = 1-	80 (LAVH = 40 - 3 had AH, VH = 40)	Population characteristics: Women; Inclusion criteria - uterine size > 280 mg and one of following - previous pelvic surgery, history of pelvic disease, endometriosis, concomitant adnexal masses. Exclusion criteria were - suspicious adnexal mass, anaesthetic contraindications, contraindications to pain relief. Baseline (VH vs LAVH): Age: 49.1 vs 49.3 Gravidity: 3.7 vs 2.4	Vaginal hysterectomy; Laparoscopic assisted vaginal hysterectomy	1 day	Operative time (min); haemoglobin drop in day 1; NSAID (g); Paracetamol (g); Opioid (mg); Gas and stool (day); Length of stay (day); Conversion to abdominal hysterectomy	VH vs LAVH: Operative time (min): 108 (SD 35) vs 160 (SD 50) ($P < 0.001$) Haemoglobin drop in day 1: 2.0 vs 2.2 NSAID (g): 137 vs 137 Paracetamol (g): 10.1 vs 11.1 Opioid (mg): 8.7 vs 6.8 Gas and stool (day): 1.3 vs 1.5 Length of stay (day): 5.3 vs 5.7 Conversion to abdominal hysterectomy: 0 vs 3	Funding source: Not stated Study summary: In contrast with earlier reports, there was no difference in short-term recovery between patients undergoing vaginal or laparoscopic hysterectomy. No advantage was found performing laparoscopic assisted vaginal

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			Parity: 2.7 vs 1.6 Vaginal delivery: 33 vs 32 Previous caesarean: 7 vs 0 Previous pelvic surgery: 5 vs 8 Indication for surgery: Menorrhagia: 16 vs 13 Uterine fibroids: 40 vs 37 Pelvic pain: 16 vs 12 Adnexal mass: 2 vs 4 Endometriosis: 3 vs 2 Adnexectomy: 21 vs 15 Uterine weight (g): 424 (SD 211) vs 481 (SD 329) Country: France					hysterectomy in comparison with the standard vaginal hysterectomy.
Spies 2004 ⁴³³	Prospective; cohort EL = 2+	102 in UAE, 50 in hysterectomy	Population characteristics: Women; symptomatic leiomyomas; aged between 30 and 50; For UAE > 50% of leiomyomas within uterine cavity or dominant pedunculated serosal leiomyoma excluded. Average age: UAE = 42.6, Hysterectomy = 41.6 Number of leiomyoma: 1 = 26%, 40% 2 = 32%, 38% > 3 = 41%, 20% Largest leiomyoma volume (ml): 146.8, 90.6 Previous treatment: None = 52%, 70% Hormonal = 39%, 24% Surgery = 53%, 20% Country: USA	UAE; hysterectomy UAE vs Baseline UAE vs hysterectomy	12 months	PBAC score; Menorrhagia questionnaire; SF-12; complications	Baseline symptoms: Menstrual flow: Heavy: UAE = 96%, Hysterectomy = 84% Normal = 2%, 8% Menstrual bleeding score: UAE = 467.4, Hysterectomy = N/A SF-12 physical score: UAE = 44.4 (SD 8.3), Hysterectomy = 42.0 (SD 10.1). SF-12 mental score: UAE = 44.7 (SD 11.8), Hysterectomy = 40.3 (SD 10.8) UAE baseline vs 6 month follow-up results: PBAC score at baseline = 435.6 (SD 286.5), 6 months = 140.6 (SD 110.1), -58.1% (SD 36.6) Menorrhagia questionnaire score at baseline = 47.2 (SD 13.8), 6 months = 19.2 (SD 8.3), -56.6% (SD 20.3) Comparison of UAE and hysterectomy for SF-12 scores: SF-12 physical for UAE at baseline = 45.1 (SD 8.2), 12 months = 53.6 (SD 6.1), +22.6% (SD 27.1), $P < 0.001$. SF-12 physical for hysterectomy at baseline = 43.0 (SD 9.9), 12 months = 51.4 (SD 6.9), +25.4 (SD 32.7), $P < 0.001$. SF-12 mental for UAE at baseline = 45.4 (SD 11.5), 12 months = 52.6 (SD 7.9), +23.4% (SD 37.7), $P < 0.001$. SF-12 mental for hysterectomy at baseline = 40.6 (SD 11.1), 12 months = 51.1 (SD 11.2), $P < 0.001$ Complications: On SCVIR: UAE = 4 (3.9%), hysterectomy = 6 (12.0%) On ACOG: UAE = 15 (14.7%), Hysterectomy = 17 (34%)	Funding source: Biosphere Medical Study summary: Both procedures substantially improved symptoms for most patients, with an advantage for hysterectomy at 12 months for pelvic pain. Serious complications were infrequent in both groups.
Summitt 1992 ⁵¹²	randomised; EL = 1+	70 eligible, 56 included (27 for VH, 29 for LAVH)	Population characteristics: Women; Included if – aged 18 to 65, no significant medical condition, a telephone, a support person, understanding of postoperative instructions, uterine size < 16 weeks, presence of uterine mobility, pubic arch of at least 90 degrees. Excluded if –	Vaginal hysterectomy; LAVH Surgery vs surgery	6 weeks	Duration of operation (min); Uterine weight; Intra-operative complications; postoperative complications; surgery completed;	LAVH vs VH: Duration of operation (min): 120.1 (SD 28.5) vs 64.7 (SD 27.0), ($P < 0.001$) Uterine weight: 162.6 (SD 89.5) (range 41 to 390) vs 203.7 (SD 143) (range 60 to 650) Intra-operative complications:	Funding source: Not stated Study summary: Other than cost, laparoscopy-assisted vaginal hysterectomy and standard vaginal

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
			<p>concomitant anterior or posterior colporrhaphy required, cervical conisation performed, antibiotic prophylaxis used for heart disease, patient could not tolerate anaesthesia, severe bleeding disorders, acute peritonitis of upper abdomen; uterine fibroid or pelvic mass > 16 weeks.</p> <p>Baseline (VH vs LAVH):</p> <p>Age: 37.5 vs 37.7</p> <p>Parity: 2.5 vs 2.4</p> <p>Indication:</p> <p>Leiomyomata uteri: 18 vs 16</p> <p>Recurrent CIN: 2 vs 1</p> <p>Abdominal bleeding 3 vs 4</p> <p>Adenomatous hyperplasia: 1 vs 2</p> <p>Chronic pelvic pain: 3 vs 6</p> <p>Country: USA</p>			<p>post-operative pain relief use.</p>	<p>LAVH = 1 laceration, 1 cystotomy</p> <p>VH = none</p> <p>5 (2 VH and 3 LAVH) patients underwent oophorectomy</p> <p>Postoperative complications:</p> <p>LAVH = 1 readmitted for pain control</p> <p>VH = 1 vaginal cuff infection, 1 vesticovaginal fistula.</p> <p>Post-operative pain relief use:</p> <p>Day of surgery: 3.13 vs 3.82</p> <p>Day 1: 3.67 vs 3.61</p> <p>Day 2: 2.71 vs 1.57 ($P = 0.027$)</p>	<p>hysterectomy appear comparable in patients who could otherwise undergo a vaginal hysterectomy.</p>
Summitt 1998 ⁵¹³	Randomised; concealed EL = 1–	65 (34 LAVH, 31 TAH)	<p>Population characteristics: Women; not suitable for vaginal hysterectomy; Had TAH if – pelvic endometriosis, pelvic adhesions, > 3 laparotomies, Uterine fibroid between 12 to 18 weeks, previous tubo-ovarian abscess or pelvic inflammatory disease, adnexal mass, hysterectomy in presence of mobility and unfavourable vaginal introitus. Inclusion criteria were – > 18 years old, a working telephone in the home, support person, understanding of post-operative instructions. Excluded from study if – concomitant colporrhaphy, urethropexy, vaginal vault suspension, or nongynaecologic major operation, major medical condition requiring monitoring, Fibroid or pelvic mass > 18 weeks, intolerant to anaesthesia, severe bleeding disorder, acute peritonitis of the upper abdomen, midline abdominal hernia.</p> <p>Baseline (TAH vs LAVH):</p> <p>Age: 41.5 vs 38.3</p> <p>Gravidity: 2.4 vs 3.1</p> <p>Parity: 1.7 vs 2.3</p> <p>Weight (lbs): 178.1 vs 168.8</p> <p>Indications for surgery:</p> <p>Endometriosis: 1 vs 1</p> <p>Adhesions: 2 vs 0</p> <p>Uterine fibroids: 23 vs 23</p>	Laparoscopic-assisted vaginal hysterectomy; total abdominal hysterectomy LAVH vs TAH	6 weeks	<p>Operating time (min); Estimated blood loss (ml); Uterine weight (g); Haematocrit levels; Length of stay (days); Convalescent (days); complications</p>	<p>TAH vs LAVH:</p> <p>Operating time (min): 146 (SD 69.9) vs 179.8 (SD 56.4)</p> <p>Estimated blood loss (ml): 660.5 (SD 610.0) vs 568 (SD 394.0)</p> <p>Uterine weight (g): 383.9 (SD 227.8) vs 336.8 (SD 276.0)</p> <p>Haematocrit levels:</p> <p>Pre-surgery – 35.8 vs 36.9</p> <p>Day 2 – 29.3 vs 29.3</p> <p>Length of stay (days): 4.13 vs 2.12 ($P < 0.001$)</p> <p>Convalescent (days): 38 vs 28 ($P = 0.002$)</p> <p>Complications:</p> <p>Cystotomies: 0 vs 2</p> <p>Artery damage: 0 vs 1</p> <p>Intra-operative haemorrhage > 100 ml: 2 vs 2</p> <p>Need for IM narcotics: 26 of 34 vs 30 of 31 ($P = 0.018$)</p>	<p>Funding source: US surgical corporation</p> <p>Study summary: Except for operating time, there are no differences between laparoscopically assisted vaginal hysterectomy and abdominal hysterectomy regarding intra-operative characteristics among abdominal hysterectomy candidates.</p> <p>Postoperatively, laparoscopically assisted vaginal hysterectomy requires a shorter hospital stay and convalescence. Hospital charges are similar between the procedures. A larger number of cases will help determine the indications for laparoscopically assisted vaginal hysterectomy.</p>

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Thakar 2002 ⁵²⁰	double-blind EL = 1+	<i>n</i> = 279 Subtotal hysterectomy STH (<i>n</i> = 133) Total hysterectomy TH (<i>n</i> = 146) BSO as concomitant procedure: 81 in TH group; 61 in STH group	Population characteristics: Women undergoing hysterectomy for benign disease Mean age: 44 years (29–59) > 88% pre-menopausal Indications: STH and TH: Menorrhagia 67% vs 54% (<i>P</i> < 0.03) Menorrhagia and dysmenorrhoea NS dysmenorrhoea only NS Pelvic pain NS irregular bleeding NS Abdominal mass NS PMT NS Ovarian cyst NS urine retention NS No sig differences in base-line characteristics between groups Country: UK	Subtotal hysterectomy and total hysterectomy Subtotal hysterectomy vs total hysterectomy	12 months	Urinary, bowel and sexual functions Recovery and complications	At 12 months post-op: Urinary functions: Frequency (> 7 times/day): Pre-op: STH 33%; TH 31% Post-op: STH 24%; TH 20% at 12 months (<i>P</i> = 0.03 for the change over time within each group; <i>P</i> = 0.84 for the interaction between treatment assignment and time) Reduction in nocturia and improvement in bladder capacity: NS between groups Bowel functions: Frequency of symptoms (report of constipation, urgency, flatus and use of laxatives): NS between both groups Sexual functions: Frequency of and desire for intercourse pre- and post-op: NS between the 2 groups Sig increase in frequency of intercourse in both groups combined after surgery (<i>P</i> < 0.01) Frequency of orgasm, and sexual relationship: NS between both groups post-op Deep dyspareunia: Pre-op: STH 46%; TH 39% Post-op: STH 7%; TH 14% (<i>P</i> < 0.001 for change over time in each group) Intra- and post-operative complications: Operating time (min): STH 59.5 ± 20.6, TH 71.1 ± 23.4 (difference -11.6, 95% CI -16.9 to -0.6) Blood loss (ml): STH 320 ± 271, TH 422 ± 302 (difference -102.4, 95% CI -172 to -32.8) Blood transfusion: (NS) Hospital stay (days): STH 5.2 ± 1.1, TH 6.0 ± 4.7 (difference -0.8, 95% CI -1.6 to -0.04) Pain score: NS Intra-op complications: STH 11 (8%), TH 21 (14%) NS Post-op complications: Before discharge: STH 13 (10%), TH 40 (27%) (<i>P</i> < 0.001) Pyrexia (STH 8; TH 28) Urine retention (STH 0; TH 2) vault haematoma (STH 0; TH 1) wound haematoma ((STH 3; TH 4) wound infection (STH 2; TH 3) Ileus (STH 0; TH 1) vaginal bleeding (STH 0; TH 1) At 12 months: STH 14 (11%), TH 9 (6%) (<i>P</i> < 0.001)	Funding source: NHS R&D Study summary: Neither STH nor TH adversely affects pelvic organ functions at 12 months. STH results in more rapid recovery and fewer short-term complications but infrequently cause cyclical bleeding or cervical prolapse

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							bowel obstruction (STH 0; TH 2) cyclical vaginal bleeding (STH 9; TH N/A) cervical prolapse (STH 2; TH -N/A) persistent pain (STH 3; TH 7)	
Tsai 2003 ⁵¹⁴	randomised EL = 1+	222 assessed. 200 eligible and randomised (100 to LAVH plus LETS, 100 to TAH)	Population characteristics: Women; estimated uterine upper margin is not beyond the midpoint between umbilicus and pubic symphysis; no pre-existing cardiopulmonary dysfunction or poor control of systemic diseases; bimanual pelvic examination confirmed good mobility of an enlarged uterus; no cervical malignancy; no indication for conventional vaginal hysterectomy; very large myoma; uterine prolapse; combined surgery. Baseline (LAVH vs TAH): Age: 46.7 vs 46.9 Parity: 2.8 vs 2.7 BMI: 23.2 vs 24.1 Indication for surgery: Myomas: 78 vs 73 Chronic pelvic pain: 2 vs 3 Endometriosis: 8 vs 10 DUB: 4 vs 5 Cervix carcinoma <i>in situ</i> : 5 vs 8 Endometrial atypia: 3 vs 1 Country: Taiwan	Laparoscopic assisted vaginal hysterectomy plus light-endorsed transvaginal section; total abdominal hysterectomy	1 day	Estimated blood loss (ml); Operating time (min); Weight of uterus (g); Complications; Length of stay (day); Number of meperidine ampules	Estimated blood loss (ml): 202 vs 238 Operating time (min): 77 vs 102 ($P < 0.05$) Weight of uterus (g): 375 (SD 206) vs 380 (SD 203) Complications: Febrile – 0 vs 5 Blood transfusions – 1 vs 3 Bladder injury – 0 vs 1 Dysuria – 0 vs 1 GI dysfunction – 1 vs 3 Vaginal stump infection – 1 vs 2 Total – 3 vs 15 ($P < 0.05$) Length of stay (day): 3.2 vs 5.5 ($P < 0.05$) Number of meperidine ampules: 1.2 (SD 0.7) vs 3.7 (SD 1.3) ($P < 0.05$)	Funding source: Not stated
Unger 2002 ⁵⁸⁸	Comparative case series; retrospective EL = 2–	318 (group 1 uteri < 500 g = 208, group 2 uteri between 500 = 63 and 999 g, group 3 uteri > 1000 g = 47)	Population characteristics: Women; undergone abdominal hysterectomy. Baseline (group 1, group 2, group 3): Age: 41, 42.8, 45.1 Parity: 2.5, 2.6, 2.2 Black: 63%, 93.6%, 93.6% ($P < 0.001$) Uterine weight: 227.7, 729.3, 1658.8 ($P < 0.001$) Presence of PID: 5.9%, 8.2%, 2.4% Prior surgery: 38.05%, 50.8%, 36.2% Adhesions: 43.3%, 54%, 42.6% Country: USA	Abdominal hysterectomy Surgical outcomes by uterine size	N/A	Estimated blood loss (ml); EBL > 500 (ml); Operative time (min); Blood transfusions; At least one complication – blood loss > 500 ml, blood transfusion, pelvic organ injury, antibiotic use, hospital readmission, major systemic complication; Hospital stay (days)	Group 1 ($n = 208$) vs group 2 ($n = 63$) vs group 3 ($n = 47$): Estimated blood loss (ml): 387.6 vs 464.3 vs 555.86 ($P = 0.032$) EBL > 500 (ml): 25.5 vs 41.3 vs 55.3 ($P = 0.004$) Operative time (min): 122.6 vs 129.5 vs 124 Blood transfusions: 6 vs 4 vs 4 At least one complication: 32.7% vs 41.3% vs 61.7% ($P = 0.006$) Hospital stay (days): 2.9 vs 2.8 vs 2.9	Funding source: Not stated Study summary: The complication rate from hysterectomy increases with increasing uterine weight, due mainly to an increased blood loss associated with surgery for larger uteri.
Wattiez 2002 ⁵⁸⁹	Matched case–control EL = 2+	283 admitted for hysterectomy for benign conditions. 240 were appropriate for TLH. 34 had uteri 500 g>, and 68 matched	Population characteristics: Women; hysterectomy for benign conditions; Excluded if – aesthetic contraindications or malignancy; No upper limit on uteri size; High BMI, previous pelvic surgery, history of pelvic disease, or endometriosis were not contraindications. Baseline (> 500 g vs < 300 g):	Total laparoscopic hysterectomy with or without Burch operation and/or adnexectomy.	6 to 6 weeks	Operating time (min); oral analgesia use (mg); Opioid administration (mg); Hospital stay (days); Complications	Operating time (min): 159.8 vs 107.9 ($P < 0.0001$) Oral analgesia use (mg): 57.7 (SD 18.4) vs 62.5 (SD 37.2) Opioid administration (mg): 23.2 (SD 4.9) vs 25.8 (SD 12.9) Hospital stay (days): 3.6 vs 3.5 Complications: Haemorrhage: 1 vs 1 Blood transfusions: 0 vs 0	Funding source: Not stated Study summary: A very enlarged uterus should not be considered a contraindication for TLH. However, it may be necessary to undertake

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
		controls had uteri < 300 g	Age: 47.6 vs 47.6 Parity: 1.8 vs 1.5 Nulliparity: 3 vs 15 Previous caesarean section: 1 vs 11 Previous pelvic surgery: 16 vs 41 Preoperative GnRH agonist: 20 vs 14 Adnexectomy: 18 vs 36 Uterine weight (g): 617 (SD 177.8) vs 178.9 (SD 66.7) Country: France				Conversion to laparotomy: 0 vs 0 Bladder laceration: 0 vs 1 Ureter injury: 1 vs 1 Vaginal cuff haematoma: 2 vs 0 Pyrexia: 2 vs 4 Vaginal cuff infection: 0 vs 1	certain surgical steps to ensure optimal exposure of the operative field and more effective and safer excision of the uterine vascular pedicle.
Weeks 2000 ⁵²⁹	Randomised; Double-blind; concealment EL = 1–	51: 26 (2 withdrawals due to side effects) in Leuporelin group, 25 (no withdrawals to side effects) in control group	Population characteristics: Women; menorrhagia requiring hysterectomy; failed medical treatment; Excluded if treated with gonadotrophin agonist within 6 months; Exclude if leiomyomas > 2.5 cm present; excluded if malignancy present. Average age: leuporelin = 39, placebo = 40 No pathology: 15, 13 Abdominal hysterectomy: 14, 20 Country: UK	Leuporelin acetate or placebo pre-treatment; hysterectomy	120 days	Operative outcome4s; complications; patient outcomes – return to normal activity	Operative blood loss: Leuporelin = 183, placebo = 285, $P = 0.27$ Operative difficulty: Leuporelin = 2.4, placebo = 3.2, $P = 0.09$ Length of operation: Leuporelin = 39, placebo = 49, $P = 0.64$ No statistically significant differences for post-operative outcomes between groups – analgesia use, day of discharge, transfusions. Complications: Leuporelin = 11, placebo = 14 Patient return to normal health: Leuporelin = 37 days, placebo = 64 days, $P = 0.06$	Funding source: Wyeth-Lederle UK Study summary: Leuporelin pre-treatment before hysterectomy in non-fibroid patients had no operative or post-operative benefits.
Ylikorkala 1995 ⁵²⁸	randomised; double-blind EL = 1–	188 of which 125 were in nafarelin group, and 63 were in placebo group	Population characteristics: Women; scheduled for hysterectomy for benign conditions. 111 had uterine fibroids, 58 had menometrorrhagia, 19 had pelvic pain. Average age: Nafarelin = 43, placebo = 44.5 Uterine volume: 301 ml, 336 ml Country: Finland	Nafarelin 200 µg as nasal spray or placebo for 3 months prior to surgery; hysterectomy Treatment vs placebo	Up to surgery	Change in uterine volume; adverse events	Change in uterine volume (ml) at 3 months: Nafarelin = -84.1 (SD 10.7), - 23.7% Placebo = +6.6 (SD 18.3), +14.2% $P, < 0.001$ from baseline, $P < 0.05$ between groups. Adverse events: nafarelin = 107, placebo = 59. Mainly hot flushes and headaches.	Funding source: Syntex, Palo Alto, USA
Yuen 1998 ⁵¹⁵	randomised EL = 1+	44 (laparoscopic hysterectomy = 20, TAH = 24)	Population characteristics: Women; no major medical condition; benign gynaecological condition; excluded if – uterus > 16 weeks; suitable for vaginal hysterectomy Baseline (LH vs TAH): Age: 44 vs 43 BMI: 23.8 vs 25.0 Median uterine weight (g): 225 (164 to 473) vs 328 (168 to 420) Country: Hong Kong	Laparoscopic hysterectomy; abdominal hysterectomy LH vs AH	3 days	Trauma response (IL-6, C-reactive protein, cortisol) Operating time (min); Anaesthetic time (min); Estimated blood loss (ml); Decline in haemoglobin level (g/dl); Postoperative stay (days); complications	LH vs AH: Trauma response (IL-6, C-reactive protein, cortisol): IL-6: 50.6 vs 73.9 ($P = 0.01$) Serum C-reactive protein: 28.1 vs 44.7 ($P = 0.005$) Serum cortisol: 23.4 vs 27.2 ($P = 0.04$) Plasma glucose: 41.5 vs 45.6 Urinary epinephrine: 32.2 vs 34.1 Urinary norepinephrine: 80.8 vs 132.4 ($P = 0.001$) Urinary cortisol: 34.8 vs 44.2 ($P = 0.02$) White blood cell: 59.5 vs 69.8 ($P = 0.009$) Operating time (min): 95 vs 105 Anaesthetic time (min): 135 vs 120 Estimated blood loss (ml): 200 (150 to 350) vs 450 (300 to 800) Decline in haemoglobin level (g/dl): 1.2 vs 1.7 Postoperative stay (days): 4 vs 6 Complications:	Funding source: Not stated Study summary: Laparoscopic hysterectomy is associated with a lower morbidity and a less intense stress response than abdominal hysterectomy for benign diseases.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
							Febrile: 3 vs 11 UTI: 2 vs 3 Vault haematoma: 4 vs 1 Wound infection: 1 vs 0	
Zupi 2003 ³³³	Randomised; concealment and blinding not mentioned EL = 1+	203 entered study. 13 from HER and 9 from LSH withdraw from study prior to treatment. 89 had HER and 92 had LSH. No difference between those that withdraw and those that underwent treatment.	Population characteristics: Women; referred with menometrorrhagia; younger than 50 years; less than 100 kg; finished families; clear pap test; uterus size < 12 weeks equivalent; no adnexal masses or endometriosis. Average age: HER = 43.2, LSH = 42.6 Parity: = HER = 1.8, LSH = 1.9 Irregular bleeding: HER = 62.9%, LSH = 59.7% Country: Italy	Hysteroscopic endometrial resection (HER), Laparoscopic supra-cervical hysterectomy (LSH) and GnRH-a (3.75 mg) 1 month prior to surgery. Ablation vs hysterectomy	2 year	Peri-operative outcomes; complications; QoL – SF-36; Additional treatment; Haemoglobin levels	Operating times: HER = 41.7 min, LSH = 71.5 min, $P < 0.01$ Operative complications: HER = 13, LSH = 9 Long-term complications: HER = 3, LSH = 6 Additional surgery by 2 years: HER = 12, LSH = 1 SF-36 outcome (HER pre-operatively scores, HER post-operative score, LSH pre-operative score, LSH post-operative score): General health – 51.9 (SD 12.7), 59.6 (SD 13.7), 52.1 (SD 12.2), 69.4 (SD 14.2). Physical function – 62.6 (SD 14.4), 66.4 (SD 15.1), 62.8 (SD 10.9), 67.6 (SD 13.2). Role (physical) – 58.3 (SD 13.0), 61.3 (14.8), 59.2 (SD 15.4), 62.1 (SD 13.9). Role (emotional) – 60.8 (SD 12.0), 64.2 (SD 14.4), 60.3 (SD 11.9), 68.1 (SD 15.2). Mental Health – 58.1 (SD 12.3), 60.5 (SD 14.8), 59.8 (SD 12.9), 63.2 (SD 13.6). Social function – 56.4 (SD 11.0), 67.3 (SD 12.7), 53.6 (SD 9.7), 88.5 (SD 11.5). Vitality 56.7 (SD 11.0), 61.0 (SD 12.8), 55.4 (SD 10.3), 72.3 (SD 11.3). Pain – 57.1 (SD 19.2), 58.6 (SD 17.0), 56.4 (SD 18.5), 60.1 (SD 14.0). $P < 0.01$ for change in general health score for both treatments, and for difference after treatment between groups in favour of hysterectomy. $P < 0.01$ for change in emotional role in hysterectomy group. $P < 0.01$ for change in social function score for both treatments, and for difference after treatment between groups in favour of hysterectomy. $P < 0.01$ for change in vitality score for hysterectomy treatments, and for difference after treatment between groups in favour of hysterectomy.	Funding source: Not stated Study summary: Laparoscopic hysterectomy may offer curative advantages of hysterectomy with operative advantages of ablation.

Table 12.3 Hysterectomy for treatment of HMB – non-comparative studies

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Clarke 2005 ³⁶⁴	Cohort EL = 3	Hysterectomy; TCRE	5294 of 15280 in hysterectomy group and 4032 of 11478 in the TCR group responded to 5 year follow-up	Women; underwent hysterectomy or TCRE; Surgery for DUB Part of VALUE/MISTLETOE cohorts Country: UK	Readmission rates to hospital	Readmission rates by 5 years: Any type of readmission – 2754 (44.6%) of TCRE, 3477 (41.7%) of hysterectomy. Hazard ratio = 0.87 [CI 0.80 to 0.95], $P = 0.038$ Gynaecological readmission – TCRE = 837, hysterectomy = 440. Hazard ratio = 0.40 [CI 0.33 to 0.48], $P < 0.0001$ Operation-related readmission – TCRE = 1026, Hysterectomy = 721. Hazard ratio = 0.53 [CI 0.45 to 0.61], $P < 0.001$.	Funding source: Department of Health, UK Study summary: Differences in readmission patterns for hysterectomy and ablation. Women undergoing hysterectomy are less likely to be readmitted to hospital.
Cravello 1999 ⁴⁶³	case series EL = 3	hysteroscopic myomectomy	196 women undergoing hysteroscopic myomectomy	haemorrhagic submucous fibroids Country: France	Failure rate (women who underwent hysterectomy after the resection, or with recurrent/uncontrolled haemorrhagic symptoms Success rate (complete absence of symptoms, no repeat surgical procedures, taking HRT)	Death: 1 due to malignant lymphoma Failure: 18% (13% subsequent hysterectomy, 5% recurrent bleeding) Satisfaction: 68% 13% loss to follow-up	Funding source: not stated Study summary: Hysteroscopic myomectomy appears to be satisfactory over the long term with low complication rates
De Meeus 1997 ⁵⁹⁰	retrospective study EL = 3	AH and VH	171 women undergoing hysterectomy 109 (60.4%) VH 62 (39.6%) AH 146 (85.4%) menometrorrhagia 19 (11%) chronic pelvic pain 6 (3.5%) ovarian tumour	VH: Mean age: 45 years Mean parity: 1.95 5.5% menopausal 63% previous surgery 10% previous laparoscopy AH: Mean age: 47 years Mean parity: 1.59 6.5% menopausal 40% previous surgery 5% previous laparoscopy Country: France	Uterine weight Intra-operative events	Uterine weight: Mean weight: VH: 236 ± 137 g, H: 608 ± 432 g ($P < 0.0001$) Weight > 280 g: VH: 32%, H: 77% ($P < 0.01$) weight+myomas: VH: 267 g, AH: 879 g ($P < 0.0001$) Intra-operative events: Bleeding (mean vol.): VH: 140 ± 119 ml, AH: 384 ± 283 ml ($P < 0.0001$) Duration of procedure: VH: 50.6 ± 16 min, AH: 90 ± 34.4 min ($P < 0.0001$) Hospital stay: VH: 6 ± 1.6 days, AH: 8 ± 2.3 days ($P < 0.0001$) Bladder injury: VH: 1, AH: 1 (NS) Conversion to abdominal route: VH: 1	Funding source: Not stated Study summary: Uterine volume limits VH. Duration of procedure, blood loss and recovery time lower in VH than AH group
Erian 2005 ⁵⁹¹	case series, prospective EL = 3	laparoscopic subtotal hysterectomy with Plasma Kinetic (PK) and Lap Loop system	100 women undergoing laparoscopic subtotal hysterectomy for menorrhagia	Mean age: 44.6 years (28–56) Mean parity: 2 (0–4) Mean BMI: 26.8 (20–42) 64 had previous abdominal/pelvic surgery Concomitant surgery: 39 oophorectomy	Post-op complications Operating time Hospital stay satisfaction	Post-op complications: Mean blood loss: 114 ml (20–600) 2 haemorrhage requiring blood transfusion 0 bowel injury 0 bladder injury 0 ureteric injury 0 unintended laparotomy 0 haematoma 0 thrombosis	Funding source: not stated Study summary: Laparoscopic subtotal hysterectomy for menorrhagia using the PK and Lap loop system is safe and can be performed as an outpatient procedure,

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
				7 pelvic adhesiolysis 2 excision of implants 2 ovarian cystectomy 1 cystoscopy 59% of laparoscopic subtotal hysterectomy performed on an outpatient basis Country: UK		0 anaesthetic complications Operating time: 45.5 min (15–90) Hospital stay: median 3 days (2–5) Satisfaction: 100% satisfaction with operation and would recommend to friends	reduced operating time and high patient satisfaction
Gath 1982 ¹⁰⁶	Cohort; prospective EL = 3	hysterectomy	174 invited: 18 refused, 156 entered study.	women; menorrhagia – benign origin; scheduled for hysterectomy Country: UK	psychiatric state – present state examination (PSE); Eysenck Personality Inventory; Profile of Mood States.	Baseline PSE: 1–4 = 66 (42.3%), 5a = 37 (23.7%), 5b = 22 (14.1%), 6–8 = 31 (19.9%). (5 or > = case). Patients had higher PSE scores than general population ($P < 0.001$). Patients vs general population: Worry = 45% vs 89% ($P < 0.001$), Somatic features of depression = 9% vs 85% ($P < 0.001$), tension = 33% vs 77% ($P < 0.001$), irritability = 17% vs 62% ($P < 0.001$), situational anxiety = 28% vs 55% ($P < 0.001$), lack of energy = 8% vs 53% ($P < 0.001$), simple depression = 16% vs 47% ($P < 0.001$), social unease = 23% vs 43% ($P < 0.001$), anxiety = 6% vs 40% ($P < 0.001$), loss of concentration = 12% vs 31% ($P < 0.001$). Patients after vs patients before surgery (P values for after surgery figures vs general population figures: Worry = 61% vs 89% ($P < 0.01$), Somatic features of depression = 37% vs 85%, ($P < 0.001$), tension = 64% vs 77% ($P < 0.001$); irritability = 22% vs 62% (NS), situational anxiety = 48% vs 55% ($P < 0.001$), lack of energy = 27% vs 53% ($P < 0.001$), simple depression = 24% vs 47% (NS), social unease = 28% vs 43% (NS), anxiety = 22% vs 40% ($P < 0.001$), loss of concentration = 22% vs 31% ($P < 0.05$).	Funding source: Not stated Study summary: Hysterectomy reduces level of psychiatric morbidity. Hysterectomy did not cause psychiatric morbidity. Psychiatric morbidity higher in patient group than general population.
Gath 1995 ⁵⁹²	case series (last of a series of 3 studies by the same authors) EL = 3	hysterectomy	239 women undergoing hysterectomy for menorrhagia of benign origin	Study 1 – mean age: 42 years Study 2 – mean age: 38 years Study 3 – mean age: 39 years Country: UK	Levels of psychiatric morbidity Association between psychiatric morbidity and demographic factors psychotropic medication past psychiatric illness women's understanding and expectation of the operation	Levels of psychiatric morbidity@ Pre-op level of PSE drop: Study 1: 58%, Study 2: 28%, Study 3: 9% ($P < 0.001$) Post-op level of PSE drop: Study 1: 26%, Study 2: 7%, Study 3: 4% ($P < 0.001$) Demographic factors: Study 1 women sig older than women in Study 2 and 3. No significant differences between the 3 groups in social class, marital status and menstrual symptoms Medication: Anti-menorrhagic drugs: prescribed more frequently in Study 3 than in Study 1 and 2 ($P < 0.001$) Psychotropic medication: prescribed more frequently in Study 1 than in Study 2 and 3 ($P < 0.001$) Past psychiatric illness: significant fall in 'neuroticism' across the 3 studies ($P < 0.001$) Women's understanding and expectation of the operation: Satisfaction with GP's explanation: Study 1: 65%, Study 3: 49% NS Satisfaction with gynaecologists' explanation: Study 1: 64%, Study 3: 60% NS Books and magazines as source of information for women: Study 1: 51%, Study 3: 42% NS Limited information in 10% of women in Study 1 and Study 3. Women expressing concern about side effects of hysterectomy: Study 1: 56%, Study 3: 41% NS	Funding source: MRC Study summary: Clinicians may have changed referral practice for emotional symptoms, less inclined to refer women with psychological problems for hysterectomy. GP treating more women with explanation and reassurance

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Harkki-Siren 1997 ⁵⁹³	Survey EL = 3	Laparoscopic hysterectomy	1165	Women; Undergone laparoscopic hysterectomy. Age = 45.3 BMI = 24.2 Weight of uterus = 185 Indication for surgery: Uterine fibroids = 627 Menorrhagia = 319 Dysmenorrhoea = 96 Endometriosis = 22 Other = 101 Country: Finland	Duration of operation (min); Estimated blood loss (ml); Hospital stay; Recovery time; Complications	Duration of operation (min): 132 Estimated blood loss (ml): 295 Hospital stay: 3.3 Recovery time (days): 17.9 Complications: Bleeding = 14 (1.2%) Urinary tract = 32 (2.7%) Bowel = 5 (0.4%) Infections = 65 (5.6%) Other = 3 (0.3%) Additional surgery: Blood transfusion = 44 (3.8%) Laparotomy = 47 Laparoscopy = 6 Vaginal surgery = 14 Ureteral stenting = 2	Funding source: Not stated Study summary: Laparoscopic hysterectomy offers a short hospital stay and convalescence time to the patient, but effective teaching is imperative to minimize, in particular, the risk of urinary tract injuries.
Hur 1995 ⁵⁹⁴	Case series EL = 3	LAVH Concomitant procedures: 67 appendectomy 64 posterior repair 39 adhesiolysis 40 SO 10 vaporisation of endometriosis 1 salpingectomy	176	Women undergoing LAVH Mean age: 40.3 years (27–59) Indications: 139 myoma 11 dysmenorrhoea 7 PID 6 DUB 11 cancer/tumour 2 TV abscess Country: Korea	Operating time duration of operation recovery period post-op hgb intra and post-op complications	Mean operating time: 110 min (55–380) Duration of operation: 4–7 days Mean recovery period: 3 weeks Mean post-op Hgb: 1.2 g/dl Intra-op complications: 1 bladder perforation 1 massive haemorrhage, requiring 3 units of blood transfusion 1 inferior epigastric injury Post-op complications: 7 (infection, high fever, perineal palsy, voiding problems, vaginal vault bleeding, incisional hernia, pelvic abscess)	Funding source: Not stated Study summary: LAVH can be safely performed by well-trained laparoscopists with reduced surgical morbidity, blood loss, post-op discomfort, recovery time and hospitalisation
Hurskainen 2004 ⁴⁸³	randomised EL = 3	LNG-IUS; hysterectomy	236 – 119 (116 available at 12 months) to LNG-IUS, 117 (112 available at 12 months) to hysterectomy	women; menstruating; subjective menorrhagia; aged 35 to 49; completed families; Excluded if – submucous fibroids, endometrial polyps, urinary or bowel symptoms due to large fibroid, or ovarian pathology. Country: Finland	Predictors of outcome	Neither presence of fibroids nor age were predictors of outcome at 12 months for LNG-IUS or hysterectomy. Multiple regression analysis showed that MBL was the most significant factor predicting outcome. Comparison of women with and without objective menorrhagia (> 80 ml MBL). For women in LNG-IUS group women without menorrhagia had better QoL outcomes than women with menorrhagia on: anxiety ($P=0.04$), EQ-5D ($P=0.05$). In the hysterectomy group, women without menorrhagia had better outcomes than those with menorrhagia on: anxiety ($P=0.007$), emotional well-being ($P=0.01$) and energy ($P=0.0002$). Women without menorrhagia had better outcomes with LNG-IUS than women with menorrhagia on EQ-5D ($P=0.03$). Women with menorrhagia had better outcomes with hysterectomy than LNG-IUS for: anxiety ($P=0.003$), general health ($P=0.04$), energy ($P=0.05$), and pain relief ($P=0.04$).	Funding source: Not stated Study summary: Success or failure of treatment of menorrhagia is multifactorial, so difficult to predict in individual cases.

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Johns 1994 ⁵⁹⁵	case series EL = 3	LAVH	119 women undergoing LAVH 82 concomitant oophorectomy	Mean age: 39.2 ± 0.7 years Parity: 1.7 ± 0.1 Previous abdominal operations: 0.9 ± 0.1 Indications: 67 pelvic pain 40 DUB 34 pelvic mass 11 myoma 9 cervical dysplasia 8 pelvic relaxation 8 endometriosis 3 adenomyosis 3 pelvic adhesion/pressure Country: USA	Operation time blood loss length of hospital stay Intra- and post-op complications Association between experience of LAVH and blood loss and hospital stay	Mean operation time: 79 ± 3 min Mean blood loss: 135 ± 10 ml (25–500) Mean length of hospital stay: 59 hours (1–5 days) Intra- and post-op complications: 1 bladder laceration 1 elective bladder entry to resect endometriosis 4 others (voiding problems, sinus infection, upper resp infection) Significant association between experience of LAVH and blood loss ($P < 0.01$) and hospital stay ($P < 0.001$) Association between operating time and blood loss: NS Association between no of previous operations and operating time blood loss or length of hospitalisation: NS	Funding source: not stated Study summary: The potential advantages of LAVH were suggested
Kjerulff 2000 ⁵²⁶	Prospective case series study, EL = 3	hysterectomy 30% had concomitant surgery for urinary incontinence	1299	Women undergoing hysterectomy for benign conditions, enrolled in the Maryland Women's Health Study 1992–1993 (28 hospitals) Age range: < 30–70+ years Parity: 0–3+ Diagnosis: 48% uterine leiomyomas 17% menstrual disorders 13% prolapse 9% endometriosis 3% cancer 3% adnexal condition 2% infectious condition Country: USA	In-hospital complications Symptoms relief (vaginal bleeding, pelvic pain, back pain, activity limitation, sleep disturbance, fatigue, abdominal bloating, urinary incontinence) Psychological functions (depressed, anxious) and limitations in QoL (physical, social functions, poor health perception) Problems relieved and new problems Predictors of lack of symptom relief	In-hospital complications: 21% had no complications 67% had ≥ 1 mild complications 11% had ≥ 1 moderate complications 0.7% had ≥ 1 serious complications 4% readmission related to hysterectomy during 1st year, 5% in 2nd year (common reasons: infection, adhesions, intestinal blockage and UTI) Symptoms relief: Mean no of symptoms at problematic-severe levels (adjusted): 4.0 pre-op 0.9 at 2 years post-op ($P < 0.001$) 8% women had same no of symptoms at problematic-severe levels post-hysterectomy as before Psychological functions and limitations in QoL: Significant improvement post-op ($P < 0.001$) 73% depression relieved 68% anxiety relieved 89% no longer reported limited social function Predictors of lack of symptom relief by logistic regression: Baseline depression and therapy sig associated with poor outcomes (OR 3.46, 95%CI 1.84 to 6.51) BSO sig. associated with symptom relief at 2 year (OR 2.01, 95%CI 1.14 to 3.53), but not at 1 year (OR 1.48, 95%CI 0.82 to 2.75) Household income of ≤ \$35,000 sig. associated with lack of symptom relief (OR 0.37, 95% CI 0.24 to 0.59) at 2 years	Funding source: Agency of Health Care Policy and Research, USA Study summary: Significant improvement after hysterectomy for symptoms relief, psychological function and quality of life up to 2 years post-op. Hysterectomy did not relieve symptoms for those in therapy at time of operation and those who had low incomes
Malzoni 2004 ⁵⁹⁶	Case series; retrospective EL = 3	LAVH	1020 (series 1 = 396, series 2 = 624)	Women; symptomatic myomas or uterine fibroatosis; not suitable for vaginal hysterectomy. Baseline (Series 1, Series 2): Age: 50.1, 49.8 BMI: 25.2, 24.8	Operating time (min); Hospital stay (days); Recovery time (days); complications; Postoperative haemoglobin drop	Series 1 (1997 to 1999) vs series 2 (2000 to 2002): Operating time (min): 105 vs 80 Hospital stay (days): 2.4 vs 2.3 Recovery time (days): 19 vs 20 Postoperative haemoglobin drop (g/dl): 1.44 vs 1.39	Funding source: Not stated Study summary: Laparoscopic hysterectomy is a safe, effective, and reproducible

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
				Indication: Uterine size > 12 weeks: 171, 398 Adnexal pathologies: 43, 61 History of chronic pelvic pain: 34, 55 Endometriosis: 71, 111 Limited vaginal access: 6 vs 9 Previous laparotomy: 58, 96 Previous laparoscopy: 42, 68 Country: Italy	(g/dl)	Complications: Bowel injury – 0 vs 1 Bladder rupture – 5 vs 1 Ureteral injury – 2 vs 0 Vascular damage – 1 vs 1 Febrile morbidity from infection – 22 vs 32 Vaginal cuff haematoma – 2 vs 0 Vault prolapse – 4 vs 0 Vaginal cuff granulation – 4 vs 3 Hernia complication – 0 vs 0 Re-operation: 2 vs 1 Blood transfusions: 2 vs 1	technique after completion of a period of training necessary to standardize the procedure. The results support the importance of optimizing some steps of the surgical technique to reduce severe complications.
Maresh 2002 ⁵²³	Clinical audit of a group of hysterectomy cases in a multicentre cohort study EL = 3	Hysterectomy	37048 cases of hysterectomy	Median age: 45 years (12–91) (70% < 50 years) 46% had dysfunctional uterine bleeding with no gynae pathology 67% treated by AH Indications: 46% DUB (7% fibroids) 35% fibroids (12% clinically relevant) 4% previous treatment with endometrial resection/ablation Country: UK	Length of stay (LOS) deaths Peri-operative complications	LOS: Median 5 days (1–205, mode 5 days) AH: mode 5 days VH: mode 4 days LH: mode 3 days Deaths: 14 deaths (8 AH; 6 VH; 0 LH) reported 6 weeks post-op (Mortality rate 0.38/1000, 95% CI 0.25 to 0.64) Median age at death: 58 years Peri-operative complications: Respiratory/CVS complications@ Significantly less risk with VH (Age adjusted – OR 0.51, 95% CI 0.33 to 0.79) Significantly less bleeding with VH in older women (age dichotomised to ≥ 50 years) Significantly higher rate of complications with LH vs AH and VH (visceral damage, haemorrhage, return to theatre) (crude OR 1.75, 95% CI 1.36 to 2.24) Bladder damage : 0.5–0.6% for all methods	Funding source: DH BUPA Foundation
McPherson 2005 ³⁸⁰	Cohort EL = 3	TCRE; hysterectomy with or without BSO	Numbers responding at 5 year follow-up: TCRE = 3845, hysterectomy = 3397, hysterectomy and BSO = 2305	Women; undergone TCRE or hysterectomy. Average age at 5 year follow-up: TCRE= 47.9, hysterectomy = 54.1, BSO = 50.6 Country: UK	Libido loss, difficult sexual arousal; vaginal dryness.	Adjusted OR for loss of libido against TCRE (adjusted for age and HRT use): Some – Hysterectomy = 1.25 (1.13 to 1.39), BSO = 1.32 (1.16 to 1.51), $P = 0.254$ Severe – Hysterectomy = 1.29 (1.16 to 1.44), BSO = 1.68 (1.48 to 1.92), $P < 0.001$ Extreme – hysterectomy = 1.42 (1.22 to 1.65), BSO = 1.80 (1.51 to 2.14), $P < 0.001$ Adjusted OR for difficulty of sexual arousal against TCRE (adjusted for age and HRT use): Some – Hysterectomy = 1.16 (1.05 to 1.29), BSO = 1.27 (1.11 to 1.44), $P = 0.068$ Severe – Hysterectomy = 1.28 (1.15 to 1.44), BSO = 1.79 (1.56 to 2.05), $P < 0.001$ Extreme – hysterectomy = 1.35 (1.15 to 1.58), BSO = 1.82 (1.52 to 2.19), $P < 0.001$. Adjusted OR for vaginal dryness against TCRE (adjusted for age and HRT use): Some – Hysterectomy = 1.28 (1.15 to 1.41), BSO = 1.17 (1.03 to 1.33), $P = 0.057$ Severe – Hysterectomy = 1.55 (1.36 to 1.78), BSO = 1.43 (1.22 to 1.69), $P = 0.170$ Extreme – hysterectomy = 1.50 (1.19 to 1.88), BSO = 1.69 (1.29 to 2.22), $P = 0.195$.	Funding source: Department of Health and BUPA foundation Study summary: At 5 years follow up women who had undergone hysterectomy reported increase psychosexual problems than those who had undergone TCRE, and these figures were higher for women who had had BSO at the time of hysterectomy.
McPherson 2004 ⁵²²	Case series EL = 3	Women undergoing abdominal hysterectomy (67% AH, 30%	37295 cases of hysterectomies	Median age: 45 years (12–95) 46% DUB 19% fibroids 19% prolapse 5% endometriosis/adenomyosis	Peri- and post-op complications, association between these complications and	14 deaths (0.38/1000) (No death in LH group) Operative complications in: 3% overall Age:	Funding source: DOH BUPA Study summary: Younger women, with more

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
		VH, 3% LAVH) 72% received antibiotic prophylactic 58% carried by consultants Hysterectomies by non-consultants (34% supervised) < 2% by unsupervised SHO 152/194 consultants performed LHs 11% LH by non-consultants (65% unsupervised, 3% supervised)		3% pelvic mass 8% misc Country: UK	age, comorbidity, indications, pre-op use of antibiotics, grade of surgeon, grade of supervisors and types of hysterectomy	<p>20–39 (NS) 40–49 (Reference category) 50 – ≥ 60 (NS)</p> <p>Operator: Consultants vs non-consultants (NS) Supervisor: Non-supervised vs consultant (Adjusted OR 1.27, 95% CI 1.06 to 1.52) Non-supervised vs non-consultant (NS)</p> <p>Indications: DUB (Reference category) Fibroids (4.4% vs 3.6%, adjusted OR 1.34, 95%CI 1.14 to 1.56) Endometriosis/prolapse, pelvic mass and others (NS)</p> <p>History of serious illness: No (ref category) Yes (4.8% vs 3.4%, adjusted OR 1.47, 95%CI 1.18 to 1.82)</p> <p>Method: AH (ref category) VH (NS) LAVH (6.1% vs 3.6%, adjusted OR 1.92, 95%CI 1.48 to 2.50)</p> <p>Reduction in risk associated with increasing age in women with fibroids but not DUB</p> <p>Post-op complications: 1% overall</p> <p>Age: 20–39 (NS) 40–49 (Reference category) 50 – ≥ 60 (NS)</p> <p>Operator: Consultants vs non-consultants (NS) Supervisor: Non-supervised vs consultant (NS) Non-supervised vs non-consultant (NS)</p> <p>Indications: DUB (Reference category) Fibroids (1.2% vs 1.0%, adjusted OR 1.34, 95%CI 1.10 to 1.95) Endometriosis/prolapse, pelvic mass and others (NS)</p> <p>History of serious illness: No (ref category) Yes (NS)</p> <p>Method: AH (ref category) VH (1.2% vs 0.9%, adjusted OR 1.39, 95% CI 1.01 to 1.90) LAVH (1.7% vs 0.9%, adjusted OR 1.92, 95%CI 1.00 to 2.68)</p> <p>Prophylactic antibiotics: No (ref category)</p>	vascular pelvises, undergoing hysterectomy, especially LAVH for fibroids, are at most risk of experiencing severe peri- and post-operative complications. A less invasive approach for fibroids for this group will be beneficial. A less invasive approach for DUB needs further evaluation

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
						Yes (NS) Operative complications: No (ref category) Yes (adjusted OR 8.39, 95% CI 6.53 to 10.77)	
McPherson 2005 ³⁸¹	Prospective cohort EL = 3	TCRE; Hysterectomy	11323 (5592 with TCRE, 5731 with hysterectomy – 1240 vaginal, 4227 abdominal, 251 LAVH)	Women; undergone hysterectomy or TCRE for DUB. Mean average age: TCRE = 42.17, Hysterectomy = 42.21 Presence of fibroids: TCRE = 924 of 3740 (24.71%), hysterectomy = 424 (7.44%) of 5701 Country: UK	Risk of urinary incontinence	OR of Urinary symptoms for hysterectomy compared with TCRE (adjusted for age, BMI, number of pregnancies, caesarean sections, fibroids, co-morbidities, age of first pregnancy): Urinary incontinence – mild: OR = 1.28 (1.12 to 1.45) Urinary incontinence – severe: OR = 1.54 (1.29 to 1.85) Urinary frequency – mild: OR = 1.17 (1.04 to 1.33) Urinary frequency – severe: OR = 1.36 (1.14 to 1.62) Nocturia – mild: OR 1.23 (1.04 to 1.46) Nocturia – severe: OR 1.28 (1.09 to 1.50) Vaginal: Urinary incontinence – mild: OR = 1.19 (1.00 to 1.41) Urinary incontinence – severe: OR = 1.52 (1.20 to 1.93) Urinary frequency – mild: OR = 1.28 (1.08 to 1.52) Urinary frequency – severe: OR = 1.51 (1.20 to 1.90) Nocturia – mild: OR 1.34 (1.06 to 1.69) Nocturia – severe: OR 1.33 (1.08 to 1.64) Abdominal: Urinary incontinence – mild: OR = 1.30 (1.15 to 1.46) Urinary incontinence – severe: OR = 1.59 (1.34 to 1.89) Urinary frequency – mild: OR = 1.10 (0.97 to 1.23) Urinary frequency – severe: OR = 1.15 (.96 to 1.37) Nocturia – mild: OR 1.19 (1.01 to 1.39) Nocturia – severe: OR 1.17 (1.00 to 1.36) LAVH: Urinary incontinence – mild: OR = 1.82 (1.28 to 2.59) Urinary incontinence – severe: OR = 2.02 (1.32 to 3.07) Urinary frequency – mild: OR = 1.03 (0.74 to 1.43) Urinary frequency – severe: OR = 1.33 (0.85 to 2.07) Nocturia – mild: OR 1.03 (0.68 to 1.57) Nocturia – severe: OR 0.90 (0.57 to 1.41)	Funding source: DoH and BUPA
Nathorst-Boos 1992 ⁴⁸⁶	Survey EL = 3	Hysterectomy	678	Women; aged < 55; Hysterectomy for benign conditions. Indication: Leiomyoma = 78.9% Endometriosis = 10.8% Symptoms (% before-after surgery): HMB = 67.5 vs 0 Dysmenorrhoea = 43.8 vs 2.2 Pressure = 41.8 vs 6.2 Frequent nocturia = 28.4 vs 2.4 Pain = 17.4 vs 1.8 Dyspareunia = 15.2 vs 3.4 No complaints = 6.8 vs 71.4 Country: Sweden	Patient opinions on positive and negative aspects of hysterectomy	Advantages of hysterectomy: No bleeding = 53% No pain or pressure = 21.2% Feel strong, healthy, fit = 13% No need for contraceptives = 12% No social handicaps = 4.8% No worry about cancer = 4.1% Better blood count = 3.8% Better sexual life = 2.9% Other = 3.5% Disadvantages: Hot flushes = 6.1% Ugly scar = 3.4% Dry sore mucous membranes = 4.0% Weight gain = 3.5% Incontinence = 2.9%	Funding source: Not stated

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Panici 2005 ⁵⁹⁷	case series EL = 3	minilaparotomy hysterectomy	148 women undergoing AH (118 minilaparotomy hysterectomy) for benign gynae disease Reasons for hysterectomy: 115 (78%) fibroids with HMB 20 (13%) fibroids with adnexal pathology 7 (5%) stress incontinence 6 (4%) DUB	All women: Median age: 47 years (37–85) Median BMI: 25 (18–45) Median parity: 2 (0–4) 27 (18%) menopausal women 18 (12%) hypertension 1 (1%) diabetes 1 (1%) myasthenia Country: Italy	Operating time intra- and post-op complications Post-op stay	Operating time: 50 min (34–88) 0 intra-operative complications 0 needed blood transfusion 16 (14%) minor post-op complications (not specified) Median bladder drainage: 1 day (1–2) Median post-op stay: 3 days (2–5)	Funding source: not stated Study summary: Minilaparotomy hysterectomy is feasible for women undergoing hysterectomy for benign disease because of the excellent outcomes achieved
Parkar 2004 ⁵⁹⁸	Retrospective case analysis EL = 3	LAVH	149 LAVH	Women undergoing LAVH 86 Menorrhagia 27 dysmenorrhoea 21 intermenstrual bleeding 9 post-coital bleeding 3 asymptomatic fibroids 3 renal changes on IVP 84 previous surgery Age: 35-> 56 (51% between 46–50 years) Country: Kenya	Operation time Hospital stay Intra- and post-op complications	Operation time: 45–245 min (58% between 91–120 min) Hospital stay: 2–29 days (95% 2 nights) Intra-op complications: 5 bladder injury 1 ventricular fibrillation 2 bowel injury Post-op complications: 1 intra-abdominal haemorrhage 2 omental evisceration 1 intestinal obstruction 1 bladder injury (delayed recognition) Laparotomy conversion: Intra-op: 5 due to bladder/rectal injury Post-op: 3 due to bladder tear and bleeding	Funding source: Not stated Study summary: LAVH gaining popularity
Riza 1997 ⁵⁹⁹	Case series EL = 3	LAVH	209 (1090 records available for review)	Women; LAVH for benign condition Endometriosis = 52.2% Leiomyomas = 30.2% Endometriosis and Leiomyomas = 8.8% Menorrhagia = 5% Adenocarcinoma = 1.1% Squamous = 1.1% Cancer <i>in situ</i> and menorrhagia = 0.5% Other = 1.1% Average age = 41.3 Gravidity = 2.7 Weight (lbs) = 159.6 Uterine weight (g) = 178.6 Country: USA	Operative time; operative blood loss; complications; Length of stay	Average operative time = 117.3 minutes Post-operative length of stay = 0.7 days Average intra-operative blood loss = 242.3 ml Complications: fever = 6, transfusion = 3, UTI = 2, Vaginal cuff cellulitis = 1	Funding source: Not stated

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Schofield 1991 ⁶⁰⁰	retrospective survey by telephone interview and postal questionnaire EL = 3	Hysterectomy	236	Women who had had a hysterectomy between 2–10 years ago (50% between 2–5 years, 50% between 6–20 years) 51% hysterectomy only 13% hysterectomy + 1 ovary 36% hysterectomy + BSO Mean age at time of hysterectomy: 44.2 years (28–68) Country: Australia	Hysterectomy characteristics Perceived benefits and problems Satisfaction with hysterectomy	Hysterectomy characteristics: Perceived reasons: 50% for bleeding and pain 20% fibroids 16% prolapse 17% endometriosis Perceived benefits: 57% relief from heavy periods Overall 66% of all symptoms experienced before hysterectomy have improved 28% no different 59% had symptoms made worse by hysterectomy (22% required visit to GPs and 7% to gynaecologist in previous 12 months) Satisfaction with hysterectomy: 96% women satisfied 95% would make same decision again 4% said hysterectomy caused more problems 7% would not have agreed to have op Women with fewer than 3 children significantly more satisfied with their recovery Women aged < 50 years more likely to be satisfied with hysterectomy outcome	Funding source: NH and MRC Public Health Grant Study summary: High levels of satisfaction with hysterectomy. Problems after hysterectomy also high enough to warrant consideration for trials of hysterectomy vs conservative treatment
Takamizawa 1999 ⁶⁰¹	Case series EL = 3	Total hysterectomy	923	Women; undergone hysterectomy for uterine fibroids Country: Japan	Complications	Complications: Bladder laceration = 5 Ureteric injury = 5 Bowel injury = 2 Haemorrhage requiring transfusion = 41 Pulmonary embolism = 1 Re-operation = 1 Prolonged paralytic ileus = 6 Vaginal vault problem = 7 Abdominal wound dehiscence = 3	Funding source: Not stated Study summary: The incidences of complications and unrecognized uterine malignancies were similar to the results of previous studies. Of patients undergoing hysterectomy for presumed benign leiomyomas, the risk of major complications was 6.0% (55/923) and the risk of preoperatively undiagnosed uterine malignancies was 0.4%.
Toma 2004 ⁶⁰²	Retrospective chart audit EL = 3	Hysterectomy	chart audit of 372 hysterectomies	Mean age: 48.5 ± 11.5 years Mean BMI: 28.6 ± 7.3 (29.6% BMI 25 – 29.9; 36.6% BMI ≥ 30) Mean Parity: 2.1 ± 1.5 78% AH 14% VH 5.9% LAVH 2.2% VH converted to AH 79.8% total hysterectomies 16.1% subtotal 4% radical/modified radical hysterectomies	Factors associated with: length of stay (LOS) length of surgery indication for surgery and approach readmissions complications infections repeat laparotomies	26 visited emergency room within 30 days of discharge 19 readmission 15.3% infections (UTI, wound and pelvic) (significantly higher BMI and longer LOS length of surgery in this group) 4% repeat/unplanned laparotomy 24.5% other complications (11.3% excessive bleeding, 5.4% post-op ileus) < 2% bladder, bowel, pulmonary function, cardiac function or drug reactions Removal of both or last ovary: 65% (57% of the 257 pre-menopausal women; 84% of the 113 post-menopausal women). 35% in women with dysfunctional uterine bleeding. 71.4% in women with leiomyomas.	Funding source: not stated Study summary: Significant reduction in LOS with the VH when compared with AH

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
				<p>Indications:</p> <p>26.4% abnormal uterine bleeding</p> <p>16% leiomyomas</p> <p>11.4% pelvic mass, neoplasm or cyst</p> <p>11% endometrial/ovarian/cervical cancer</p> <p>10.6% Chronic dysmenorrhoea</p> <p>8.9% endometrial hyperplasia, dysplasia or family history of cancer</p> <p>7.6% pelvic prolapse/incontinence</p> <p>5.1% endometriosis</p> <p>2.9% chronic salpingitis, hydro- and pyo-salpinx</p> <p>16% had diagnosis of cancer pre-op</p> <p>20% had diagnosis of cancer post-op</p> <p>Country: Canada</p>	Rate of concurrent oophorectomy	<p>AH vs VH:</p> <p>Age – NS</p> <p>BMI – 29.2 (7.8) vs 25.8 (4.6) ($P < 0.01$)</p> <p>LOS in days – 5.2 (4.8) vs 3.0 (1.6) ($P < 0.01$)</p> <p>Length of surgery in minutes – 106.3 (48.7) vs 84.7 (34.6)</p> <p>Infection – NS</p> <p>Readmission – NS</p> <p>Excessive bleeding or complication – NS</p> <p>Logistic regression:</p> <p>Patient 1.1 times more likely to have AH for each one-point increase in BMI ($P = 0.003$); 47.6 times more likely to have AH if concurrent unilateral/bilateral oophorectomy ($P < 0.001$); 1.7 times more likely to have VH with each additional child</p>	
Varol 2001 ⁵²⁴	retrospective review of medical records EL = 3	VH, AH and LAVH Prophylactic antibiotics received: 45% AH 84% VH 80% LAVH	1940 women undergoing hysterectomy for benign non-obstetric indications 1986–1995: 462 (24%) VH 1440 (74%) AH 36 (2%) LAVH	<p>VH:</p> <p>Mean age: 57 years</p> <p>Mean parity: 3.1</p> <p>6.5% Leiomyomas</p> <p>19.5% DUB</p> <p>0% endometriosis</p> <p>1.7% adenomyosis</p> <p>67.3% uterovaginal prolapse</p> <p>2.6% cervical dysplasia</p> <p>0% adenal mass</p> <p>0% PID</p> <p>0.2% endometrial hyperplasia</p> <p>0.9% pelvic pain</p> <p>1.3% others</p> <p>AH:</p> <p>Mean age: 45.3 years</p> <p>Mean parity: 2.5</p> <p>34% Leiomyomas</p> <p>26.5% DUB</p> <p>5.4% endometriosis</p> <p>11% adenomyosis</p> <p>0.4% uterovaginal prolapse</p> <p>4.9% cervical dysplasia</p> <p>7.6% adenal mass</p> <p>1.7% PID</p> <p>4.3% endometrial hyperplasia</p> <p>2.6% pelvic pain</p> <p>1.5% others</p> <p>LAVH:</p> <p>Mean age: 44.4 years</p> <p>Mean parity: 1.8</p> <p>25% leiomyomas</p>	Post-op complications and injuries to adjacent organs	<p>Post-op complications:</p> <p>Mortality rate: 1.5/1000 women</p> <p>VH:</p> <p>27.3% overall complication rates</p> <p>10.2% febrile morbidity</p> <p>9.7% infections</p> <p>5% haemorrhage requiring transfusion</p> <p>1% unintended major surgical procedure</p> <p>0% life-threatening event</p> <p>2.4% re-hospitalisation</p> <p>3.4% minor complications (retention, incontinence, ileus etc)</p> <p>Injuries to adjacent organs (0.5–1.5% bladder, 0.05–0.1% ureter, 0.1–0.8% bowel, 0.1–0.2% vesicovaginal fistula)</p> <p>AH:</p> <p>44% overall complication rates</p> <p>15.9% febrile morbidity</p> <p>12.6% infections</p> <p>6.5% haemorrhage requiring transfusion</p> <p>3% unintended major surgical procedure</p> <p>0.4% life-threatening event</p> <p>2% re-hospitalisation</p> <p>14.4% minor complications (retention, incontinence, ileus etc)</p> <p>Injuries to adjacent organs (1–2% bladder, 0.1–0.5% ureter, 0.1–0.5% bowel, 0.1–0.2% vesicovaginal fistula)</p> <p>LAVH:</p> <p>22.2% overall complication rates</p> <p>5.5% febrile morbidity</p> <p>0% infections</p> <p>5.5% haemorrhage requiring transfusion</p> <p>2.8% unintended major surgical procedure</p> <p>0% life-threatening event</p>	<p>Funding source: Victoria Medical Foundation</p> <p>Study summary: Higher complication in AH than VH</p>

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
				50% DUB 11% endometriosis 0% adenomyosis 2.8% uterovaginal prolapse 0% cervical dysplasia 0% adenal mass 0% PID 0% endometrial hyperplasia 5.6% pelvic pain 5.6% others Concurrent surgical procedures: VH:91.5% 84.8% colporrhaphy 2.2% adnexectomy 0% adhesiolysis 1.3% Burch colposuspension 0% appendicectomy 0% lipectomy 3.2% other AH: 65.7% 1.9% colporrhaphy 50.8% adnexectomy 4.5% adhesiolysis 2.3% Burch colposuspension 3.7% appendicectomy		8.3% re-hospitalisation 2.8% minor complications (retention, incontinence, ileus etc) Injuries to adjacent organs (1.1% bladder, 0.3% ureter, 0.5% bowel, 0.3% vesicovaginal fistula)	
Walker 2006 ⁶⁰³	Cross-sectional survey EL = 3	UAE	258 questionnaires sent out, 172 replied	Women; undergone UAE Country: UK	Amenorrhoea/menopause rate; vaginal discharge; sexual function; subsequent treatment for fibroids; Satisfaction with UAE	Amenorrhoea/menopause rate: Amenorrhoea = 8 Normal flow = 96 Reduced flow but heavier than normal = 32 No change = 4 Heavier = 1 Longer = 3 Reduction only temporary = 32 164 women were pre-menopausal at time of treatment Vaginal discharge: 83 women complained of vaginal discharge post-treatment. Sexual function: Improved = 31 Same = 64 Worse = 12 Subsequent treatment for fibroids: 28 (16%) had further treatment. Satisfaction with UAE: Very satisfied = 104 Satisfied = 48 Dissatisfied = 5 Very dissatisfied = 2	Funding source: Not stated

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
						Quality of life: Better = 146 Not improved = 8	

Table 13.1 Oophorectomy undertaken at the time of hysterectomy – comparative studies

Bibliographic information	Study type and evidence level	No. of patients	Patient characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Ballard 1996 ⁵⁴¹	Chart review EL = 2-	151 (90 ovaries removed, 61 ovaries not removed)	Population characteristics: Women; > 50 years old; vaginal hysterectomy Country: USA	Removal of ovaries and fallopian tubes	No follow-up	Success of operation (ovary removal); operating time; estimated blood loss; length of stay; complications	There was no statistical difference between groups on any of the outcome measures. Only difference was age of groups (66.4 for BSO vs 71.1 or non-BSO) Of the 61 women where ovaries were not removed: In 48 cases women wanted BSO, but ovaries were found to be normal or could not be removed vaginal. In 12 cases women opted not to have BSO. In 1 case women had already had BSO.	Funding source: Not stated
Davies 1996 ⁵⁴²	Prospective cohort EL = 2+	88 (40 oophorectomy, 48 no oophorectomy)	Population characteristics: Women; undergone hysterectomy with oophorectomy or not. Oophorectomy vs no oophorectomy Age = 48.6 vs 43.1 Indications: DUB = 18 vs 19 Fibroids = 15 vs 20 Country: UK	Hysterectomy with or without oophorectomy	No follow-up	Duration of surgery; uterine weight; estimated blood loss; blood transfusions; overall complications; major complications; post-operative stay	Comparison of oophorectomy vs no oophorectomy: Duration of surgery(min) 88.3 vs 64.9 ($P < 0.001$) Uterine weight – 243 vs 275.7 Estimated blood loss (ml) 262 vs 227 Blood transfusions – 3 vs 4 Overall complications – 16 vs 14 Major complications – 1 vs 4 Post-operative stay – 3.9 vs 3.8	Funding source: Not stated

Table 13.2 Oophorectomy undertaken at the time of hysterectomy – non-comparative studies

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Bhavnani 2003 ⁵⁴³	Qualitative interviews EL = 3	Oophorectomy	16	Women; waiting for hysterectomy for benign conditions. Average age = 45 Country: UK	Patient opinions on oophorectomy	<p>Women who want to retain ovaries view them as a healthy organ that does not need removing.</p> <p>Women who wanted oophorectomy viewed ovaries as source of problems, and needed to be removed.</p> <p>Women often expressed views that ovaries were 'worn out' so should be removed.</p> <p>Few women talked about long-term impact of oophorectomy for preventing ovarian cancer.</p> <p>Women who wanted oophorectomy highlighted potential of ovarian cancer.</p> <p>Women who wanted to retain ovaries often expressed concern about menopause, and want to postpone it as long as possible.</p> <p>For all women, the health professional played a key role in the evolution of patient preferences.</p> <p>Women highlighted that it was them who had to raise the issue of oophorectomy.</p> <p>Women had a variety of sources of information about oophorectomy – books, newspapers, internet and people.</p>	Funding source: NHS R&D programme
Fry 2001 ²⁵³	Survey EL = 3	Factors influencing decision to have oophorectomy	58: 30 having oophorectomy, 28 ovarian screening	women Country: UK	Factors related to oophorectomy	<p>Frequency of item being rated high or extremely important:</p> <p>Reducing risk of ovarian cancer, reducing cancer worry, Age, worries about effectiveness of screening, partner's attitude, loss of periods. All at $P < 0.05$</p> <p>No difference for other factors – need for HRT, risks of surgery, recovery time, desire for children.</p>	Funding source: Not stated
Hallowell 2000 ⁵⁴⁰	Interviews EL = 3	Information needs of women undergoing oophorectomy	23	Women; Undergone bilateral oophorectomy; pre-menopausal Country: UK	Themes related to patient information needs	<p>Information needs of women:</p> <p>Oophorectomy will lead to menopause</p> <p>What menopausal symptoms to expect</p> <p>The need to use HRT</p> <p>Risks and benefits of HRT</p> <p>Financial cost of long-term prescriptions</p> <p>Type of surgery being undertaken</p> <p>Convalescence</p> <p>Inherited genetic mutations</p>	Funding source: Not stated
Parker 2005 ⁶⁰⁴	Modelling EL = 3	Oophorectomy or no oophorectomy; without or with estrogen therapy	Unknown	Women undergoing oophorectomy at time of hysterectomy for benign conditions	Risk of mortality by age 80 by hip fracture, ovarian cancer, breast cancer, stroke, coronary heart disease, other	<p>Ovarian conservation and no ET vs oophorectomy and no ET vs ovarian conservation and ET vs oophorectomy and ET.</p> <p>Proportion of women aged 50 to 54 alive at age 80 (%):</p> <p>Ovarian conservation and no ET = 62.46</p> <p>Oophorectomy and no ET = 53.88</p> <p>Ovarian conservation and ET = 62.75</p> <p>Oophorectomy and ET = 62.15</p>	<p>Funding source: No stated</p> <p>Study summary: Ovarian conservation until at least age 65 benefits long-term survival for women at average risk of ovarian cancer when undergoing hysterectomy for benign disease.</p>
Wagner 2000 ⁵³⁹	Survey EL = 3	Opinions on prophylactic oophorectomy and/or mastectomy	138 individuals in 35 families	Women; <i>BRCA1</i> or <i>BRCA2</i> gene mutation Country: Austria	Willingness to undergo surgery; attitude to surgery; surveillance vs surgery; feelings associated with surgery; effect of surgery on QoL; Motivation in	<p>Women's views about oophorectomy (both affected and non-affected carriers) agree vs disagree:</p> <p>Willingness to undergo surgery: 30 vs 0</p> <p>Attitude to surgery: 15 vs</p> <p>Surveillance vs surgery: 25 vs 4</p> <p>Feelings associated with surgery:</p> <p>Anxiety = 15 vs 8</p>	Funding source: Not stated

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
					favour of surgery.	Helplessness = 9 vs 11 Invasion of privacy = 10 vs 13 Effect of surgery on QoL: General = 13 vs 6 Female identity = 12 vs 12 Sexuality = 11 vs 13 Motivation in favour of surgery: Future plans = 10 vs 11 Reduced cancer risk = 17 vs 7 Fear of dying of breast cancer = 16 vs 8	

Table 14.1 Surgical competencies in HMB – comparative studies

Bibliographic information	Study type and evidence level	No. of patients	Population characteristics	Intervention and comparison	Follow-up	Outcome measures	Effect size	Source of funding and additional comments
Arndt 1995 ⁵⁵⁰	Case series EL = 2+	2220 Total abdominal hysterectomies; total cholecystectomy = 4370; transurethral prostatectomy = 2851; Intervertebral disc excision = 1764.	MedisGroup Comparative Hospital Database: total cholecystectomy; transurethral prostatectomy; Total abdominal hysterectomies; Intervertebral disc excision. Country: USA	total cholecystectomy; transurethral prostatectomy; Total abdominal hysterectomies; Intervertebral disc excision.	N/A	Volume–outcome relationship on length of stay and cost	<p>Effect of surgeon volume of total charge based on multivariate regression: beta-coefficient = 0.005, T-statistic = 0.71 (NS). Cost was significantly influence by patient age and severity.</p> <p>Effect of surgeon volume on length og stay: beta-coefficient = 0.021, T-statistic = 2.98 ($P < 0.05$). Length of stay more influenced by age and severity</p> <p>All other procedures show stronger volume outcome relationships.</p> <p>Total cholecystectomy: beta-coef = -0.128 and t-statistci = 20.38; transurethral prostatectomy – beta-coef = -0.49 and t-statistic = 8.13; Intervertebral disc excision – beta-coef = -0.091 and t-statistic = 20.48.</p>	Funding source: Not stated

Table 14.2 Surgical competencies in HMB – non-comparative studies

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Abramovich 1995 ⁵⁴⁶	Audit EL =	Endometrial ablation	978	Women; undergone endometrial ablation Country: UK	Complication rates; satisfaction levels	<p>Operative complications:</p> <p>Fluid overload = 61 Uterine perforation = 11 Excessive bleeding = 35 Immediate surgery = 12 Death = 1</p> <p>Satisfaction at 12 months:</p> <p>Very satisfied = 283 (53%) Satisfied = 167 (31%) Dissatisfied = 65 (12%) Very dissatisfied = 22 (4%)</p> <p>Further treatment for failed EA by 24 months:</p> <p>Repeat ablation = 84 Hysterectomy = 73 Drug treatment = 107 HRT = 60</p> <p>No association between operator experience and outcomes.</p>	Funding source: Clinical Response and Audit Group :
Altgassen 2004 ⁵⁵¹	Case series EL = 3	Laparoscopic-assisted vaginal hysterectomy	929 patients – 33 surgeons	<p>Laparoscopic-assisted vaginal hysterectomy</p> <p>Split into 3 groups: O, A, B</p> <p>O = surgeons doing fewer than 30 procedures</p> <p>A = Procedures 1 to 30 for surgeons doing more than 30</p> <p>B = Procedures > 30 for surgeons doing more than 30 procedures.</p> <p>Country: Germany</p>	Volume–outcome assessment	<p>Change in duration, intraoperative complications and postoperative complications with experience:</p> <p>1 to 10 ($n = 273$) – 145.8 min, 7, 22 11 to 20 ($n = 131$) – 144.7, 5, 14 21–30 ($n = 97$) – 148.3, 3, 12 31–40 ($n = 80$) – 131.3, 0, 8 41–50 ($n = 75$) – 138.4, 0, 3 51–75 ($n = 129$) – 122.1, 2, 12 76–100 ($n = 98$) – 117.3, 0, 8 > 100 ($n = 46$) – 120.8, 0, 0</p> <p>Analysis showed reduction in complication rates after 30 procedures.</p> <p>Group O (< 30 procedures):</p> <p>Intra-operative complications = 5 (1.9%) Post-operative complications = 17 (6.5%)</p> <p>Group A (Procedures 1 to 30 in surgeons undertaking > 30):</p> <p>Intra-operative complications = 10 (4.2%) Post-operative complications = 31 (12.9%)</p> <p>Group B (Procedures > 30 in surgeons undertaking > 30):</p> <p>Intra-operative complications = 2 (0.5%) Post-operative complications = 30 (7.0%)</p> <p>Significant difference between A and B, and between A and O. Not difference between O and B.</p>	Funding source: Not stated .
Luft 1987 ⁵⁵²	Audit EL = 3	Volume–outcome relationship	20249			Actual vs expected mortality by volume performed: 1 to 24 hysterectomies per year OR = 1.874; 361 or more hysterectomies per year OR = 0.733	
Overton 1997 ⁵⁴⁵	Audit EL = 3	Endometrial ablation	18641 cases	Women; undergone endometrial ablation Country: UK	Complications rates; Operator experience	<p>Peri-operative complications:</p> <p>Loop and ball = 171 (4.20%) Loop alone = 229 (6.40%) Laser = 46 (2.70%)</p>	

Heavy menstrual bleeding

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
						<p>Ball alone = 13 (2.10%) Total = 474 (4.44%)</p> <p>Intra-operative emergency surgical procedures.</p> <p>Loop and ball = 50 (1.36%) Loop alone = 69 (2.39%) Laser = 6 (0.34%) Ball alone = 6 (1.11%) Total = 135 (1.26%)</p> <p>Immediate complication by operator experience:</p> <p>< 100 = 107 (8.1%) 101–200 = 26 (4.0%) 201–300 = 36 (5.6%) 301–400 = 9 (4.1%) 401–500 = 12 (5.0%) > 500 = 7 (4.8%)</p> <p>$P < 0.005$ for trend</p> <p>Uterine perforations by experience:</p> <p>< 100 = 53 (4.0%) 101–200 = 4 (0.6%) 201–300 = 11 (1.7%) 301–400 = 3 (1.4%) 401–500 = 2 (0.8%) > 500 = 1 (0.7%)</p> <p>$P < 0.00005$</p> <p>Operative haemorrhage by experience:</p> <p>< 100 = 52 (4.0%) 101–200 = 16 (2.5%) 201–300 = 26 (4.0%) 301–400 = 5 (2.3%) 401–500 = 10 (4.1%) > 500 = 4 (2.8%)</p> <p>$P > 0.040$ for trend</p>	
Overton 1995 ⁵⁴⁴	Audit/Survey EL = 3	Endometrial ablation	7426	endometrial ablation. Part of MISTLETOE survey Country: UK	Training standards of those performing endometrial ablation	<p>Training standards for TCRE:</p> <p>Of 5388 undertaken 1095 were by surgeons who had not attended a training course and who were not supervised. 1686 were undertaken by surgeon who had not attended a course. 2790 were undertaken with no prior supervision.</p> <p>Training standards for laser ablation:</p> <p>Of 983 undertaken 15 were by surgeons who had not attended a training course and who were not supervised. 16 were undertaken by surgeon who had not attended a course. 73 were undertaken with no prior supervision.</p>	Funding source: Not stated
Roos 1986 ⁵⁵³	Audit EL = 3	Volume–outcome relationship	6609	Country: Canada		adjusted OR comparing low to high volume by procedure: hysterectomy = 1.35 (95% CI 1 to 1.82)	

Bibliographic information	Study type and evidence level	Aim of study	No. of patients	Population characteristics	Outcomes	Results	Source of funding and additional comments
Spies 2001 ⁵⁴⁷	Training guideline EL = 4	Training standards required for UAE		Country: USA		Training fellowship: 100 arteriographic procedures, including at least 50 visceral catheterisations and 25 selective embolisation procedures. Qualification by experience: As above Radiation safety training also required.	Funding source: Not stated
Spies 2004 ⁵⁴⁹	Consensus statement EL = 4	Consensus statement on credentials needed to perform UAE	No patients	Country: USA	Experience; Audit standards	Two consensus statements reported: SIR report suggests volume of 25 operations required, McLucas suggests 12.5 in order to be competent.	Funding source: Not stated

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Heavy menstrual bleeding

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Heavy menstrual bleeding

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Heavy menstrual bleeding

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