

# Heavy Menstrual Bleeding

## Evidence Tables

### Evidence table - Health economic studies for all sections of guideline

Bibliographic Information	Study Details	Outcomes	Population Characteristics	Analysis Details	Results and Comments
Edwards 2006 417	<p>Study Type: Cost-utility analysis</p> <p>Model or Clinical Trial: Clinical trial</p> <p>Perspective of Analysis: Health care provider</p>	<p>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.</p> <p>Primary Clinical Outcomes: Quality of life measures were the primary outcome measure.</p>	157 women with uterine fibroids (myomas) recruited from six gynaecology departments in Scotland and two centres in England.	<p>Currency: GBP</p> <p>Year of Costing: 2004</p> <p>Discount rate(s) used for costs:</p> <p>Discount rate(s) used for benefits:</p>	<p>Results: No statistically significant differences in quality of life as measured by the SF-36, EQ-5D and GHQ-28 -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 £1685.36 compared with £2566.87).</p> <p>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.</p>

Bibliographic Information	Study Details	Outcomes	Population Characteristics	Analysis Details	Results and Comments
Sculpher 1998 551	Study Type: Cost-utility analysis  Model or Clinical Trial: Modelling  Perspective of Analysis: Health care system	Source of Utility Values: Utility weights derived using TTO techniques with 60 women with menorrhagia.  Primary Clinical Outcomes: Reduced menstrual blood loss.		Currency: GBP  Year of Costing: 1994  Discount rate(s) used for costs: 6%  Discount rate(s) used for benefits: 6%	Results: AH is more costly over a two year period, but results in more QALYs. The incremental cost 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 557	Study Type: Cost-utility analysis  Model or Clinical Trial: Clinical trial  Perspective of Analysis: Health care 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 Quality Adjusted Life Years.		Currency: GBP  Year of Costing: 1999  Discount rate(s) used for costs:  Discount rate(s) used for benefits:	Results: When LH was compared VH, mean costs were £401 higher for LA, and mean QALYs per patient were 0.0015 higher. The ICER for this is £267333. Taking into account uncertainty, LA 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

Bibliographic Information	Study Details	Outcomes	Population Characteristics	Analysis Details	Results and Comments
					<p>for LH compared to AH may be much more favourable to LH.</p> <p>The time frame of the study means that no discounting was undertaken.</p>
<p>Lumsden 2000 498</p>	<p>Study Type: Cost-utility analysis</p> <p>Model or Clinical Trial: Clinical trial</p> <p>Perspective of Analysis: Health care system</p>	<p>Source of Utility Values: Utility values assessed using EQ-5D visual analogue scale.</p> <p>Primary Clinical Outcomes: QALY; length of operation, total length of stay, admission to ITU, additional surgery required, readmissions and blood transfusions</p>		<p>Currency: GBP</p> <p>Year of Costing: 0</p> <p>Discount rate(s) used for costs:</p> <p>Discount rate(s) used for benefits:</p>	<p>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.</p> <p>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 one year. Appropriate measures were taken to address the problem of follow-up.</p>

Bibliographic Information	Study Details	Outcomes	Population Characteristics	Analysis Details	Results and Comments
Cameron 1996  558	Study Type: 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.
Garside 2004  559	Study Type: Cost-utility analysis  Model or Clinical Trial: Modelling  Perspective of Analysis: Health care system	Source of Utility Values: Utility values for hysterectomy and ablation taken from Sculpher (ref ID 23988). 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.

Bibliographic Information	Study Details	Outcomes	Population Characteristics	Analysis Details	Results and Comments
Raju 1994 504	<p>Study Type: Cost-effective analysis</p> <p>Model or Clinical Trial: Clinical trial</p> <p>Perspective of Analysis: Health care system</p>	<p>Source of Utility Values:</p> <p>Primary Clinical Outcomes: The main clinical outcome indicators were length of operation, hospital stay, recovery time and time to return to work.</p>		<p>Currency: GBP</p> <p>Year of Costing:</p> <p>Discount rate(s) used for costs: N/A</p> <p>Discount rate(s) used for benefits: N/A</p>	<p>Results: Mean cost for LH was £1260 compared with £1750 for AH. No ICERs were reported. The authors conclude that LH should be preferred to AH for the patient group studied.</p> <p>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 v AH.</p>
Cameron 1996 558	<p>Study Type: Cost analysis</p> <p>Model or Clinical Trial: Clinical trial</p> <p>Perspective of Analysis: Other</p>	<p>Source of Utility Values: N/A</p> <p>Primary Clinical Outcomes: Successful surgery.</p>		<p>Currency: GBP</p> <p>Year of Costing: 1994</p> <p>Discount rate(s) used for costs: 6%</p> <p>Discount rate(s) used for benefits: n/a</p>	<p>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.</p> <p>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.</p>

Bibliographic Information	Study Details	Outcomes	Population Characteristics	Analysis Details	Results and Comments
<p>Jack 2005 <small>405</small></p>	<p>Study Type: Cost-effective analysis</p> <p>Model or Clinical Trial: Clinical trial</p> <p>Perspective of Analysis: Health care system</p>	<p>Source of Utility Values: HRQoL outcomes were measured using the SF-12 measure.</p> <p>Primary Clinical Outcomes: HRQoL</p>	<p>Two hundred and ten women with a complaint of excessive menstrual loss.</p>	<p>Currency: GBP</p> <p>Year of Costing: 2002</p> <p>Discount rate(s) used for costs:</p> <p>Discount rate(s) used for benefits:</p>	<p>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.</p> <p>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 one year to date. Longer term results would be of benefit, though it seems likely that the results will not be affected.</p>

## Chapter 3 – Definition of HMB

### Menstrual bleeding patterns, prevalence of HMB, presence of uterine pathology, and risk-factors associated with HMB -

#### Comparative Studies

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Clevenger-Hoeft 1999 <sup>82</sup>	Study Type: Comparison; cohort; prospective  Evidence level: 2+	180 - 100 asymptomatic, 80 AUB	Population characteristics: Women; Aged 30>  Country: USA	Presence of pathology in people with and without AUB	No follow-up	Presence of pathology; Accuracy of test - specificity, sensitivity	<p>Presence of pathology by symptom status: Asymptomatic (n = 100; 39.5 years) - 10% polyps, 1% myomas, 13% intramural myomas</p> <p>AUB patients (n = 80; 41.1 years) - 32.5% polyps, 21.2% myomas, 57.5% intramural myomas</p> <p>P&lt;0.05 for all groups comparisons</p> <p>Accuracy of sonohysterography for identifying pathology in 48 women with histopathology available: sensitivity = 97%, specificity = 86%, PPV = 94%, NPV = 92%</p>	<p>Funding Source: Not stated</p> <p>Study summary: Study shows that women with AUB have higher prevalence of uterine pathology than those without.</p>



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Fraser 1990 <sup>41</sup>	Study Type: Epidemiology; diagnostic  Evidence level: 2+	316	Population characteristics: Women; menorrhagia; no clear pathology  Country: Australia	Hysteroscopy or laparoscopy to identify pathology	n/a	Presence of pathology by MBL	<p>Presence of pathology by level of MBL (&lt;60ml, 60 to 120 ml, &gt;120ml, All patients) : Total numbers: 47, 59, 33,182. 43 MBL was not measured.</p> <p>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.</p>	<p>Funding Source: Not stated</p> <p>Study summary: Increased levels of HMB were associated with increased levels of uterine pathology. Fibroids were associated with HMB. Endometriosis was on slightly associated with increases in MBL.</p>
Granleese 1990 <sup>70</sup>	Study Type: prospective case-control  Evidence level: 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 psycho-social factors and menorrhagia	1 survey	MBL - alkaline haematin; personality scores - Eysenck personality questionnaire; sexual behaviour questionnaire; personal history questionnaire	<p>MBL - menorrhagic group (n=22) = 90ml (SD 60), range 13-194ml. Controls (n = 22) = 34ml (SD 7), range 22.51.</p> <p>Menstruation symptomology scores: menorrhagic = 27.41 (9.05) vs. 13.05 (7.42) control (P&lt;0.001).</p> <p>Personality scores (Eysenck scale): psychotism - clinical = 1.64 (1.43) vs. control =</p>	<p>Funding Source: Not stated</p> <p>Study summary: Women complaining of menorrhagia should be objectively tested to ensure correct treatment, as no difference in psychological impact.</p>

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>3.64 (1.65), <math>P &lt; 0.001</math>; extraverted = 10 (6.02) vs. 13.23 (3.35), <math>p = 0.017</math>; neuroticism = 13.36 vs. 14.91, <math>p = 0.079</math>; lie scale = 11.54 (4.23) vs. 5 (3.32), <math>P &lt; 0.001</math>.</p> <p>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.</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Granleese 1990 70	Study Type: prospective case-control  Evidence level: 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 psycho-social factors and menorrhagia	1 survey	MBL - alkaline haematin; personality scores - Eysenck personality questionnaire; sexual behaviour questionnaire; personal history questionnaire	MBL - menorrhagia group (n=22) = 90ml (SD 60), range 13-194ml. Controls (n = 22) = 34ml (SD 7), range 22.51.  Menstruation symptomology scores: menorrhagia = 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. :

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Harlow 2004 <sup>141</sup>	Study Type: Systematic review  Evidence level: 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 <sup>68</sup>	Study Type: Cross-sectional survey  Evidence level: 2-	226: split between <60ml and >60ml 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 versus objective menorrhagia		psychosocial factors; QoL - sf-36; MBL - alkaline haematin	Using univariate analysis, difference between <60ml and >60ml 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.	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 & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							Using multivariate analysis - unemployment, anxiety, perceived inconvenience, abdominal pain and ferritin were significant factors in explaining variance.	
James 2004 <sup>148</sup>	Study Type: systematic review; diagnostic studies  Evidence level: 2-	107 articles identified	Population characteristics: MEDLINE. 1990 to 2003. Keyword search only.	Testing for Von Willebrand's 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 <sup>147</sup>	Study Type: Epidemiology  Evidence level: 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Philipp 2003 <sup>560</sup>	Study Type: Cohort; epidemiology  Evidence level: 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 v 2 (p = 0.105); ADP 3 v 1 (p = 0.5); Arachidonic acid 6 vs. 1 (p=0.13). ATP release: ADP 30 vs. 7 (p = 0.0009); Arachidonic acid 16 v 1 (p = 0.001); Collagen 18 vs. 5 (p = 0.04); Thrombin 1 v 0 (na).	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 <sup>53</sup>	Study Type: Systematic review  Evidence level: 2-	11 studies included in review	Population characteristics: Women; menorrhagia; screened for von Willebrand  Search undertaken on MEDLINE only using keyword search.	vWD as risk factor in menorrhagia	n/a	Prevalence of von Willebrand's	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 out-patient	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			Country:				<p>clinics, 1 on coagulation clinic, 1 on administrative database, 2 on population study, 1 not stated.</p> <p>Menorrhagia state based on history in 5 studies, PBAC in 2, Alkaline Haematin in 2, and not stated in 2.</p> <p>VWF:Ag test only one used across studies, RiCof was second most common.</p> <p>Cut-off for vWD varied between studies.</p> <p>Different study designs and inclusion criteria probably account for differences between studies.</p>	
Shapley 2000 <sup>66</sup>	Study Type: case-control; before-and-after study  Evidence level: 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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Shapley 2002 <sup>65</sup>	Study Type: Case-control  Evidence level: 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 versus 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 versus 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 <sup>64</sup>	Study Type: Cohort; case-control  Evidence level: 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 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 life - p = 0.01, 0.005.	Funding Source: Not stated  Study summary: Study suggests psychosocial impact of HMB is a reason why women seek help.



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							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	
Vercellini 1997 <sup>561</sup>	Study Type: Cohort; epidemiology  Evidence level: 2-	331 examined - 315 included. 163 with endometriosis and 152 with not.	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 in 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 (p = 0.007 Mann-Whitney u test).	Funding Source: Not stated  Study summary: Study suggests women with endometriosis have higher MBL than those without.
Woo 2002 <sup>52</sup>	Study Type: cohort; prospective case-control  Evidence level: 2+	76: 38 menorrhagia; 38 matched normal MBL.	Population characteristics: women  Country: Ireland	Association of Von Willebrand's disease to menorrhagia  menorrhagia patients vs. normal patients		MBL - alkaline haematin; vWD status	Comparison of factors between those with (n = 26) and without (n = 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.

<b>Bibliographic Information</b>	<b>Study Type &amp; Evidence Level</b>	<b>Number of Patients</b>	<b>Patient characteristics</b>	<b>Intervention &amp; Comparison</b>	<b>Follow-up</b>	<b>Outcome measures</b>	<b>Effect Size</b>	<b>Source of funding &amp; additional comments</b>
Zielhuis 1989 <sup>61</sup>	Study Type: Cross-sectional survey  Evidence level: 2-	592 - 399 useable responses: 193 exposed to perchloroethylene; 206 unexposed.	Population characteristics: women  Country: Netherlands	Exposure or not to perchloroethylene  Exposed versus 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.

## Chapter 3 – Definition of HMB

### Menstrual bleeding patterns, prevalence of HMB, presence of uterine pathology, and risk-factors associated with HMB -

#### Diagnostic studies

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Alexopoulos 1999 <sup>77</sup>	case-series; retrospective  Evidence Level: 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: Out-patient hysteroscopy is safe, acceptable and well-tolerated method.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Ash 1996 <sup>79</sup>	diagnostic; retrospective  Evidence Level: 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 <sup>75</sup>	diagnostic; comparative; prospective  Evidence Level: 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 Sensitivity = 58/62 = 0.94 Specificity = 17/21 = 0.81	Funding Source: not stated  Study Summary: Both TVS and SCHS are highly accurate methods at diagnosing pathology

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Critchley 2001 <sup>71</sup>	diagnostic; randomised - block; prospective; statistical analysis blinded  Evidence Level: 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.	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  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: High risk group: Hysteroscopy and biopsy = 83 (83%); Ultrasound and biopsy = 74 (74%)  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 high risk group - neuroticism = 18, extraversion = 27 openness = 26, agreeableness = 34, conscientiousness =	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'.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
			Country: UK		<p>34</p> <p>For moderate risk group - neuroticism = 21, extraversion = 28 openness = 27, agreeableness = 34, conscientiousness = 35</p> <p>For low risk group - neuroticism = 21, extraversion = 28 openness = 25, agreeableness = 33, conscientiousness = 34</p> <p>GHQ questionnaire scores: High-risk group - Somatic symptoms = 5.0, anxiety = 4.5, social dysfunction = 7.0, depression = 0.0, total = 17</p> <p>moderate-risk group - Somatic symptoms = 7.0, anxiety = 7.0, social dysfunction = 7.0, depression = 0.0, total = 21</p> <p>low-risk group - Somatic symptoms = 6.0, anxiety = 6.0, social dysfunction = 7.0, depression = 0.0, total = 20</p> <p>Difference between groups: Somatic symptoms, <math>p = 0.001</math>, anxiety <math>p = 0.001</math>, social dysfunction <math>p = 0.197</math>, depression <math>p = 0.044</math>, total <math>p = 0.001</math>.</p> <p>High-risk group: Visualisation - hysteroscopy (n = 100): 13 not possible, 87 possible, 3 not undertaken for other reasons, 84 completed, 79 successful visualisation. Ultrasound (n = 100): 0 not possible, 100 possible, 5 not undertaken for other reasons, 95 completed, 87 successful visualisation.</p> <p>Biopsy - hysteroscopy and Pipelle: 90 subjects, 89 samples taken, 50 had adequate sample. Hysteroscopy and Tao brush: 90 subjects, 89 undertaken, 83 had adequate sample. 'Blind' Pipelle: 75 subjects, 75 undertaken, 36 had adequate sample. 'Blind' Tao brush: 75 subjects, 75</p>	

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
					<p>undertaken, 61 had adequate sample.</p> <p>Success of visualisation and biopsy: hysteroscopy and Pipelle = 50%, hysteroscopy and Tao brush = 83%, ultrasound and Pipelle = 36%, ultrasound and Tao brush = 61%.</p> <p>Moderate-risk group:            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:            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:            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:            Visualisation - hysteroscopy (n = 31): 5 not possible, 26</p>	

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
					<p>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:  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:  High-risk group:  Possible cancer - hysteroscopy = 3, ultrasound = null.  Endometrial thickness &gt; 4mm - hysteroscopy = null, ultrasound = 34.  Endometrial/uterine polyp - hysteroscopy = 17, ultrasound = 4  Uterine fibroids - hysteroscopy = 7, ultrasound = 29.  Cervix suspicious - hysteroscopy = 1, ultrasound = null.  Cervical polyp - hysteroscopy = 9, ultrasound = null</p> <p>Moderate 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</p> <p>Low-risk group:  Endometrial/uterine polyp - hysteroscopy = 1, ultrasound = 2  Uterine fibroids - hysteroscopy = 1, ultrasound = 6.  Cervical polyp - hysteroscopy = 1, ultrasound = null</p> <p>Abnormalities identified by biopsy:  High-risk group:</p>	



Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
					<p>Endometrial cancer = 5. Hyperplasia = 2. Atrophic endometrium = 12. Inactive endometrium = 106. Cyclic endometrium = 26. Other = 27</p> <p>moderate-risk group: Endometrial cancer = 3. Hyperplasia = 3. Atrophic endometrium = 0. Inactive endometrium = 19. Cyclic endometrium = 213. Other = 59</p> <p>Low-risk group: Endometrial cancer = 0. Hyperplasia = 0. Atrophic endometrium = 0. Inactive endometrium = 2. Cyclic endometrium = 91. Other = 0</p> <p>Sensitivity (%), specificity (%), PPV (%), PNV (%) of investigations for endometrial cancer:            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).            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)            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)            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:            Ultrasound = 0, hysteroscopy = 12, blind biopsy = 9</p> <p>Investigation 'unpleasant':            Hysteroscopy = 27%, ultrasound = 11%, biopsy = 29%. (rates higher for low-risk group).</p>	

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Eldred 1994 <sup>145</sup>	Epidemiology; case-control  Evidence Level: 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 >80ml, 22 had MBL <80ml.  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 <sup>80</sup>	diagnostic; pre- and post treatment  Evidence Level: 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 >10cm.  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
Higham 1999 <sup>47</sup>	Diagnostic  Evidence Level: 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 616ml (median 79ml) in subject menorrhagia, and 2.5 to 288ml (median 36ml) 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.	Funding Source: Not stated  Study Summary: Despite some correlation between clinical measures and MBL, objective measurement of MBL is still required.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
					Association between height and MBL: $r = 0.2$ , $p < 0.01$ .	
Loffer 1989 <sup>86</sup>	Diagnostic; comparison  Evidence Level: II	187	women; AUB - 47 post-menopausal, 192 menorrhagia, 20 menometrorrhagia, 18 metrorrhagia  Country: USA	D&C; hysteroscopy	<p>Pathology identified: Menorrhagia = 68 normal, 13 polyps, 16 fibroids, 3 hyperplasia, 0 cancer, 2 endometriosis.</p> <p>Sensitivity, specificity, PPV, NPV of D&amp;C compared to histology: 65% (32/49), 100% (102/102), 100% (32/32), 17% (17/102)</p> <p>Sensitivity, specificity, PPV, NPV of hysteroscopy with tissue sample compared to histology: 98% (48/49), 100% (102/102), 100% (48/48), 1% (1/102)</p> <p>In 91 patients with negative hysteroscopy only 1 had pathology identified by biopsy.</p>	<p>Funding Source: Not stated</p> <p>Study Summary: Study shows value of hysteroscopy for identification of uterine pathology.</p> <p>Reviewer Comments: Retrospective analysis without standards techniques for biopsy.</p>

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
MacKenzie 1978 <sup>74</sup>	Diagnostic  Evidence Level: 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 polypus = 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.
Miller 2001 <sup>562</sup>	Epidemiological cohort  Evidence Level: 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's disease	African-Americans had higher vWF:ag (p = 0.001), FVIII (P = 0.008) and vWF:Act (p= 0.006) than Caucasian population. VWF:Rcof, 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 to Caucasian population. This suggest tests should take account of these differences

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Motashaw 1990 <sup>83</sup>	No comparison group  Evidence Level: 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 & Co
Nagele 1996 <sup>73</sup>	Diagnostic  Evidence Level: 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.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Stovall 1991 <sup>78</sup>	randomised; comparative; blind  Evidence Level: 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.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Valle 1981 <sup>76</sup>	Diagnostic  Evidence Level: II	553	women; AUB;  Age range from 20 to 75  Country: USA	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  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.</p> <p>Post-menopausal women (n = 134)</p> <p>Number of pathologies identified via hysteroscopy; hysteroscopic biopsy; curettage histology.</p> <p>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</p>	<p>Funding Source: Not stated</p> <p>Study Summary: Hysteroscopy provides a useful method for identifying intrauterine pathology not available using 'blind' D&amp;C</p>

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Vercellini 1997 <sup>72</sup>	Diagnostic  Evidence Level: 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 to hysteroscopy = 96%, 86%, 91%, 94%  Sensitivity, specificity, PPV, PNV of hysteroscopy compared to hysterectomy (n = 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 <sup>81</sup>	diagnostic study  Evidence Level: 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.



## Chapter 3 – Definition of HMB

### Menstrual bleeding patterns, prevalence of HMB, presence of uterine pathology, and risk-factors associated with HMB -

#### Non-comparative Studies

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Allen 1990 <sup>84</sup>	Study Type: retrospective cohort  Evidence Level: 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 <sup>151</sup>	Study Type: cohort  Evidence Level: 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): <20ml (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 (<60ml) vs. heavy (>60ml). 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 80ml not 60ml.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Ballinger 1985 <sup>63</sup>	Study Type: Cohort  Evidence Level: 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, $\chi^2 = 20.11$ , $p = 0.0002$	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 <sup>51</sup>	Study Type: Cohort  Evidence Level: 3	Normal MBL estimation	100	women; 15-43 years; anaemia excluded  USA	MBL - alkaline haematin	For group (n = 100) MBL = 6.55 to 178.69ml, mean = 50.55 (SD 25.73) (though results skewed). 50% within 23.21 to 68.43ml range.  No relationship between MBL and age.  Relationship between duration and MBL; 3 days = 24.3 and 6 days = 58.66ml. 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 <sup>44</sup>	Study Type: Epidemiological cohort  Evidence Level: 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

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Campbell 1986 <sup>18</sup>	Study Type: Cohort  Evidence Level: 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	<p>For all women: Duration of menstruation: &lt;3 days = 5.7%; 3-7 days = 89%; &gt; 7 days = 5.3%.</p> <p>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.</p> <p>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).</p> <p>Duration (median days) of cycle by episode from menarche: 1st = 34 days (&lt;20 days = 6.4%, &gt;40 days = 38.3%); 10-12th = 31 days (7.7%, 13.2%); 19-24th = 31 days (9%, 7.9%).</p>	<p>Funding Source: WHO</p> <p>Study Summary: Study focuses on adolescent women just after menarche. Study shows high variation in menstruation symptoms occurs during this time-frame.</p>
Cazzola 1994 <sup>21</sup>	Study Type: Prospective Cohort  Evidence Level: 3	Menstrual cycle characteristics	1798 women - 36641 cycles	women included in Catholic Marriage Advisory Council  UK	Menstruation cycle length	<p>Cycle length (all records, n = 36641): mean = 28.31 days, SD 5.1, range 7-286.</p> <p>Cycle length (non-monophasic, 15-44 years, n = 36018 cycles): 28.04 days, 3.5, 15-44</p> <p>Cycle length (non-monophasic, 15-44 years, n = 1789 women): 28.46, 2.57, 21.3-38.6</p>	<p>Funding Source: Not stated</p>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Chiazze 1968 <sup>28</sup>	Study Type: Epidemiological cohort  Evidence Level: 3	description of menstrual cycle	2316 women - 30655 cycles	women  USA & 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.
Claessens 1981 <sup>149</sup>	Study Type: Epidemiology  Evidence Level: 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 von Willebrand's, 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.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Cole 1971 <sup>32</sup>	Study Type: Cohort  Evidence Level: 3	Factors associated with MBL	348	Women; 17-45 years	MBL - spectrophotometry; haemoglobin level	<p>MBL loss distribution (n = 280); &lt;50ml = 206; =50 - 99ml = 60; &gt;100ml = 14. Heavy defined as 45ml as represents upper 30%. =&gt;80 ml = 26 of 280.</p> <p>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%.</p> <p>MBL by parity: 0 = 26.4ml, 1 or 2 = 34.3ml, 3+ = 40.4ml.</p> <p>MBL by age: 17-19 = 27.5ml, 20-24 = 32.3ml, 25-29 = 36.3ml, 30-34 = 32.7ml, 35-39 = 37.4ml, 40-44 = 38.3ml</p> <p>MBL by height: &lt;160cm = 29.6, 160 cm = 37.6ml, 154+ = 38.4ml.</p>	<p>Funding Source: Not stated</p> <p>Study Summary: MBL was associated with age, parity and birth-weight of children.</p>
Cote 2003 <sup>45</sup>	Study Type: cross-sectional  Evidence Level: 3	cost of menorrhagia; factors associated of menorrhagia	2805 women involved in NHIS household survey	<p>women; 18-64 yrs old; natural menstruation in last 12 months and 3 months; never taken oestrogen containing drugs, except OCP; no reproductive cancer; no recent hysterectomy.</p> <p>USA</p>	Self-reported MBL; perception of general health; age	<p>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%); &gt;49 = 22 (5.9%) vs. 225 (9.3%), p &lt;0.00</p> <p>Ethnic group: white = 258 (69.2%) vs. 1844 (75.8%); others = 115 (30.8%) vs. 588 (24.2%), p = 0.01.</p> <p>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</p> <p>Perception of health: excellent = 85</p>	<p>Funding Source: Not stated</p> <p>Study Summary: Study provides data on association between subjective menorrhagia and socio-demographic factors.</p>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						(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), $p < 0.00$ .	
Cramer 1990 <sup>34</sup>	Study Type: Epidemiology  Evidence Level: 3	Prevalence of leiomyoma	100	Uterus collected after hysterectomy  USA	Prevalence of leiomyoma	In 100 uterus 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 <sup>35</sup>	Study Type: Educational tutorial  Evidence Level: 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-	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						factor: Reduced as number of pregnancies increased, age of last pregnancy increased, weight decreases, smoking increases and oral contraception use increases	
Decloedt 1999 <sup>87</sup>	Study Type: diagnostic; epidemiology; retrospective  Evidence Level: 3	hysteroscopy	673 hysteroscopies in 665 patients	women; AUB - menorrhagia, post-menopausal bleeding, etc; average age 47 years  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.
Emanuel 1995 <sup>42</sup>	Study Type: Cohort; epidemiology  Evidence Level: 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.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Farquhar 1999 <sup>85</sup>	Study Type:  Evidence Level: 3	Risk factors associated with endometrial hyperplasia	1033	Women; pre-menopausal; heavy or irregular menstrual bleeding  New Zealand	Risk factors associated with hyperplasia	<p>Biopsy results:            914 = normal            22 = polyps            20 = simple hyperplasia            22 = complex hyperplasia            3 = atypia hyperplasia            5 = endometrial cancer            46 insufficient material</p> <p>Risk factor frequency:            Age &gt; 40 = 56%            Age &gt; 45 = 27.1%            Weight &gt; 90kg = 21.1%            Nulliparity = 16%            Infertility = 7%            Diabetes = 3.4%            Previous breast cancer = 0.4%            Menstrual bleeding &gt; 7 days = 32%            Menstrual bleeding &gt; 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 oestrogen = 18%</p> <p>Factors associated with abnormal pathology or hyperplasia.</p> <p>Risk factor OR (95% CI) for abnormal pathology:            Weight &gt; 90kg = 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 &gt; 45 = 3.1 (1.5 to 6.1)            Nulliparity = 2.8 (1.1 to 7.2)            Family history of endometrial cancer = ns</p>	<p>Funding Source: University of Auckland</p> <p>Study Summary: The following are risk factors for endometrial hyperplasia in pre-menopausal women with abnormal menstrual bleeding: body weight <math>\geq</math> 90 kg, age <math>\geq</math> 45 years, infertility, family history of colonic carcinoma, and nulliparity. Current guidelines may need to be reconsidered.</p>



Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						<p>Risk factor OR (95% CI) for complex, atypia or carcinoma:  Weight &gt; 90kg = 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 &gt; 45 = ns  Nulliparity = 3.7 (1.2 to 10.9)  Family history of endometrial cancer = 5.8 (1.1 to 28.6)</p> <p>Regularity or duration of menstruation were not significant risk factors.</p>	
Friberg 2006 <sup>563</sup>	<p>Study Type: Epidemiological population study</p> <p>Evidence Level: 3</p>	Prevalence of bleeding disorders	1410 questionnaires sent out, 1019 replies received	<p>Secondary school pupils.</p> <p>Average age = 16.7 years</p> <p>Sweden</p>	Reporting of menstrual bleeding problems	<p>375 of 1019 reported menstruation as heavy.</p> <p>127 of 1019 reported receiving treatment for HMB.</p>	<p>Funding Source: Not stated</p> <p>Study Summary: Bleeding symptoms were relatively prevalent in this population and similar to other population-based studies.</p>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Gao 1987 152	Study Type: epidemiological cohort  Evidence Level: 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	<p>MBL(ml): range 4.1 to 273.6ml, mean 54.2 (SD 37). 5th and 95th percentiles = 14.2 and 124.1. 2sd range = 11.3 to 169.</p> <p>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</p> <p>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.</p> <p>Results by MBL: MBL, % haemoglobin &lt;12 g/dl, % ferritin &lt;16 ng/ml, % with both.            &lt;20ml (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%            &gt;100 (n=46) 30.4%, 82.6%, 26.1%.</p>	<p>Funding Source: United Nations Fund for Population Activities</p> <p>Study Summary: Study shows higher average MBL than with European and US populations</p>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Gath 1987 <sup>67</sup>	Study Type: cross-sectional survey  Evidence Level: 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 (n = 86) was ns for all except neuroticism (p<0.05). Pad use >8 (n = 38) was ns for all measures.  Subjective assessment: very heavy periods (n = 16) - P<0.001 on present case (case vs. non-case); P < 0.05 on present state (total core). P < 0.05 on GHG (higher scores). Ns for other scores. Interference with life from heavy periods (n = 59): ns on all scores except neuroticism (P < 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 <sup>58</sup>	Study Type: Cross-sectional survey  Evidence Level: 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's syndrome, TB. Ms, hysterectomy, BOS.  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.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Greenberg 1983 <sup>69</sup>	Study Type: Cohort  Evidence Level: 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) (p<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.
Hallberg 1966 <sup>30</sup>	Study Type: Cross-sectional survey  Evidence Level: 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	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.  MBL (ml) by age of 'series B' - subjective assessment of 'normal', haemoglobin >12 g/100ml, plasma iron >80 ug/100ml, 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.  All subjects: Haemoglobin concentration decrease (p<0.01) at >80ml MBL. MHC decrease (p < 0.01) at >80ml. Iron concentration decrease (p < 0.01) at > 80ml.  Series B - 95th percentile = 76.4ml	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 & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Hammouda 1967 <sup>88</sup>	Study Type: Epidemiology; retrospective; case-series  Evidence Level: 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	Age structure Of 660 women: 370 were aged 40 to 45, 205 were aged 45 to 50, and 85 were over 50 years old.  Endometrial findings: Normal = 504 Endometrial hyperplasia = 124 (18.8%) Atrophic = 32  Pathology findings: Myomas = 103 Adenomyosis = 24 Endometriosis = 20 Polyps = 32 Cysts of ovary = 6 Ovarian thecoma = 1 Carcinoma = 9	Funding Source: Not stated  Study Summary: Study shows that label of DUB is often over-used, and pathological cause of DUB can be found with proper investigation.
Harlow <sup>59</sup>	Study Type: Cohort  Evidence Level: 3	Examination of menstrual cycles	248	women; Aged 12- 14  USA	cycle length -days	Median cycle length (days): African- American (n=111) = 29.8 (21-85); European-American (n = 119) = 30.4 (22-53), p = 0.49.  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.	Funding Source: National Institute of Child Health and Development  Study Summary: Weight and high exercise are associated with increases cycle length.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Harlow 1991 <sup>29</sup>	Study Type: Epidemiological Cohort  Evidence Level: 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)	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.  Transition in cycle length within each category in any one month: <17 days (n=14) - <25 years old = 0.5%, 26-34 years old = 0.25%, >35 years old = 0.25%. 17-25 days (n = 207)- < 25 years old = 0.2%, 26-34 years old = 0.65%, >35 years old = 0.15%. 26-34 days (n = 708) - <25 years old = 0.19%, 26-34 years old = 0.65%, 35+ years old = 0.16%. 35-43 days (n = 103)- <25 years old = 0.13%, 26-34 years old = 0.65%, >35 years old = 0.19%. 44-59 days (n = 33) - <25 years old = 0.11%, 26-24 years old - 0.66%, >35 years old = 0.23%. >59 days (n = 17) - <25 years old = 0.29%, 25-34 years old = 0.4%, > 35 years old = 0.31%.	Funding Source: Not stated  Study Summary: Study shows a degree of variation in cycle length between cycles in same women.
Harlow SD; Campbell BC; 1994 <sup>17</sup>	Study Type: Cohort  Evidence Level: 3	Factors associated with duration of menstrual bleeding	179 - 1078 cycles	women; aged 17-19; not married; not pregnant; using hormonal contraceptives; not have children  USA	length of MBL (days)	Range of duration of MBL = 1 to 19 days. Median = 5. 97% between 3 and 8 days.	Funding Source: Not stated  Study Summary: Exercise associated with longer cycle length.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Hartz 1979 <sup>62</sup>	Study Type: Cohort  Evidence Level: 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 +16.94lbs (p<0.001); <21 days were +5.91 (P<0.05).  Weight associated with amount of flow (subjective); heavy flow 8.8lbs heavier than normal (p<0.01).	Funding Source: TOPS, inc (weight charity) and Obesity and Metabolic Research Program.
Hefnawi 1979 <sup>50</sup>	Study Type: Physiological study  Evidence Level: 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 <sup>31</sup>	Study Type: Epidemiological ; Cohort  Evidence Level: 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 60MBL. Anaemia increased rapidly at 60ml and then again at 120ml. Ferritin decreased at 20ml. Low ferritin at 40ml.  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 120ml, not 80ml. Suggests that 80ml definition of menorrhagia needs to be revised upwards.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Janssen 1997 <sup>48</sup>	Study Type: cohort, prospective  Evidence Level: 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 = 32.7ml (range 0.3-230.5). Incidence of menorrhagia = 13.5%.  Multiple regression and logistic regression analysis of risk factors for MBL: age ( $r^2 = 0.28^2 = 7.8\%$ ) 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 <sup>25</sup>	Study Type:  Evidence Level: 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 <sup>54</sup>	Study Type: Cohort; epidemiology  Evidence Level: 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.



Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Kato 1999 <sup>23</sup>	Study Type: cohort  Evidence Level: 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. with cycle length
Kjerulff 1996 <sup>37</sup>	Study Type: Retrospective case series  Evidence Level: 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;	<p>Black women were diagnosed with fibroids at earlier age than white women (p &lt; 0.001)</p> <p>Average age was 41.6 for white women and 37.5 for black women (p &lt; 0.001)</p> <p>Black women had hysterectomy at younger age than white women (p &lt; 0.001)</p> <p>Average age for white women = 44.6 and for black women was 41.7 (p &lt; 0.001)</p> <p>Black women waited longer before having hysterectomy (3.9 years versus 2.8, p = 0.002)</p> <p>Uterine weight was greater in black women compared to weight (420.8g versus 319.1g, p &lt; 0.001)</p> <p>Black women had more fibroids than white women (p , 0.001)</p> <p>Black women more likely to have subserosal or submucosal fibroids than white women (P &lt; 0.05)</p> <p>No difference between groups in size of largest fibroid.</p>	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						<p>No difference between groups in terms of symptoms, except anaemia and severe pelvic pain that were more common in black women.</p> <p>No difference within groups in terms of BMI, years since last birth, or age of hysterectomy and uterine weight.</p> <p>In multiple regression analysis, race and menopausal were associated with uterine weight (<math>p&lt;0.001</math>), while BMI, year since last birth and age of hysterectomy were not.</p>	
Kritz-Silverstein 1999 <sup>49</sup>	<p>Study Type: Cross-sectional survey</p> <p>Evidence Level: 3</p>	Effect of obesity, smoking alcohol consumption and exercise on menstruation	2912	women; serving in US Navy  USA	Regression analysis of factors	<p>Logistic regression of risk-factors for heavy periods showed that smoking, OR = 1.17 (<math>p&lt;0.001</math>), and high alcohol consumption, OR 1.4 (<math>P&lt;0.05</math>), were significant factors. Age, race, pay grade, BMI, exercise were non-significant.</p> <p>No assessment of existing pathology or parity.</p>	Funding Source: US Army Medical Research and Material Command

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Looker 1997 <sup>150</sup>	Study Type: Epidemiology  Evidence Level: 3	Blood test - haemoglobin levels, serum iron levels; questionnaire - socio-economic- cultural variables	24894	Men & 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 <sup>36</sup>	Study Type: Epidemiology  Evidence Level: 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

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Mahmood 1991 <sup>57</sup>	Study Type: Prospective; cohort study; epidemiology  Evidence Level: 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 <sup>20</sup>	Study Type: epidemiological cohort  Evidence Level: 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);	Funding Source: Not stated  Study Summary: Study demonstrates the variation in 'normal' menstruation that occurs.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						<p>&gt;40 = 4.12 (1.07).</p> <p>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%; &gt;40 = 42.6% vs. 7.4%.</p> <p>Variation in cycle length (within - women) over 2 cycles: only 10% same. &lt;24 days = 1131 and 1136 - 173 same, 25-39 = 894 &gt;40 = 64. 25-39 = 15036, 15105 - &lt;24 = 894 (most from 25-29 group. 25-39 = 13395, &gt;40 = 747. &gt;40 = 1120, 1046. &lt;24 = 69, 25-39 - 816, &gt;40 = 235</p>	
Monari 1998 <sup>22</sup>	Study Type: Prospective, cohort study  Evidence Level: 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.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Munster 1992 <sup>27</sup>	Study Type: Epidemiological survey  Evidence Level: 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.	<p>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.</p> <p>Menstrual cycle length by age for those with regular menstruation (irregular - no pattern or regularity over 1 year): (&lt;25 days; 26-31; 32&gt;) 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%.</p> <p>Maximum cycle variation (median days)(&lt;3, 3-8, 9-14, &gt;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</p> <p>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.</p>	<p>Funding Source: Multiple non-commercial funding</p> <p>Study Summary: Study shows that menstruation becomes less variable with age, up until pre-menopausal phase.</p>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Odujinrin 1991 <sup>26</sup>	Study Type: cohort  Evidence Level: 3	Menstrual cycle	950	Women. Aged 10 to 18 yrs.  Nigeria	Regularity of period; menstruation cycle length and flow; other symptoms; factors associated with irregularity	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, 3-5 days in 699 (78.6%), and >5 days in 143 (16.1%). 144 (16.2%) thought flow was heavy.	Funding Source: Not stated  Study Summary: Study focuses on period immediately after menarche rather than across the menstrual life-time.
Philipp 2005 <sup>564</sup>	Study Type: Epidemiological study  Evidence Level: 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's 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 <sup>95</sup>	Study Type: Epidemiology  Evidence Level: 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 80kg 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

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Rodeghiero, 1987 <sup>55</sup>	Study Type: epidemiology; cohort  Evidence Level: 3	Test for von Willebrand's 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 on 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 <sup>60</sup>	Study Type: cohort  Evidence Level: 3	Description of menstrual cycle length	344 community survey	Women; 23-45 yrs  Sweden	MBL versus parity; MBL versus 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).  Birth weight 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 <sup>56</sup>	Study Type: case-series; retrospective  Evidence Level: 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.



Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Shapley 2004 46	Study Type: Cross-sectional survey + prospective cohort  Evidence Level: 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.	<p>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.</p> <p>Increase with age (<math>p = 0.002</math>)</p> <p>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%.</p> <p>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; 35-55 = 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>	<p>Funding Source: NHS executive West Midlands</p> <p>Study Summary: Study shows high prevalence and incidence of HMB in general population in UK.</p>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Snowden 1983 <sup>137</sup>	Study Type: cohort  Evidence Level: 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>
Soliman <sup>93</sup>	Study Type:  Evidence Level: 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

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Sulaiman 2004 <sup>39</sup>	Study Type: non-comparative retrospective case series  Evidence Level: 3	Association of fibroids and MBL	50	women; MRI identified fibroids; under-going UAE  UK	MBL - alkaline haematin; fibroid size and location - MRI	MBL by number of fibroids: 1 or 2 = 195 (+/- 40.1) ml vs. 3+ = 236 (+/- 56.6) ml (ns).  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)  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).	Funding Source: Not stated  Study Summary: MBL correlated neither with size nor location of fibroids.
Thomas 1990 <sup>24</sup>	Study Type: Cohort  Evidence Level: 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%.	Funding Source: Not stated  Study Summary: Study shows cycle length in adolescent population in Nigeria.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Treloar 1967 <sup>19</sup>	Study Type: cohort  Evidence Level: 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 <sup>144</sup>	Study Type: Cohort  Evidence Level: 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.	<p>Funding Source: University of Queensland grant</p>
Utman 2002 <sup>43</sup>	Study Type: Cohort  Evidence Level: 3	Pathology associated with menorrhagia	250	women; 12-19 years; excessive menstrual bleeding (>5 pads a day)  Pakistan		<p>Aetiology: DUB = 226 (90.4%); Coagulation disorder = 20 (8%); fibroids = 2 (0.8%); Non-specific endometritis = 2 (0.8%).</p>	<p>Funding Source: Not stated</p> <p>Study Summary: Study shows that pathology is low amongst adolescents with HMB.</p>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Vercellini 1993 <sup>40</sup>	Study Type: epidemiological cohort  Evidence Level: 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 <sup>114</sup>	Study Type: Cross-sectional survey  Evidence Level: 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 > 80ml.	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.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Wegienka <sup>38</sup>	Study Type: Survey  Evidence Level: 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 <5cm = 7 (4.2); fibroid > 5cm = 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 2-5cm = 1.5 (1.2-2); Largest fibroid > 5cm = 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 <sup>565</sup>	Study Type: comparative cohort study  Evidence Level: 3	Prevalence of von Willebrand's 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 Willebrands factor, Factor VIII, Ristocetin cofactor, platelet function	Prevalence of vWD: menorrhagia = 11%, controls = 3.2%  vWD in women with menorrhagia compared to those without, odd ratio = 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.



## Chapter 3 – Definition of HMB

### Impact on Quality-of-Life by HMB – Comparative studies

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Abbott 2003 <sup>103</sup>	Study Type: Cohort  Evidence level: 2+	139 - 55 caveterm, 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 & 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 versus 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	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.



							<p>7.54), <math>p &lt; 0.0001</math>  SF-12 MCS: 43.28 (SD 4.55) vs. 49.31 (SD 10.07), <math>p &lt; 0.0001</math></p> <p>Endometrial ablation 12-months results versus general population:  EQ-5D index: ablation = 0.83 (SD 0.25 vs. general population = 0.89 (SD 0.17), <math>P = 0.03</math>  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</p>	
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Clark 2002 <sup>98</sup>	Study Type:  Evidence level: 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 (SF36) 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 <sup>120</sup>	Study Type:  Evidence level: 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 General health = 68.02  Change in scores after treatment Physical function = 4.84	Funding Source: Scottish Office - Department Health  Study summary: Study shows that benefits from surgery in terms of QoL have greater than with medical treatment

							<p>Social function = 7.57  Role - physical = 15.32  Role - emotional = 8.96  Mental health = 4.78  Energy = 7.07  Pain = 8.84  General health = -0.25</p> <p>Surgical group (n = 93)  (0 = worst, 100 = best)  Physical function = 81.94  Social function = 69.06  Role - physical = 56.72  Role - emotional = 53.41  Mental health = 59.14  Energy = 41.51  Pain = 57.95  General health = 65.10</p> <p>Change in surgical scores after treatment:  Physical function = 10.16  Social function = 17.44  Role - physical = 32.26  Role - emotional = 31.54  Mental health = 15.01  Energy = 20.53  Pain = 21.62  General health = 10.49</p> <p>All P &lt;0.05 compared to changes from medical treatments</p>	
Cooper 1999 <sup>104</sup>	Study Type: randomised - balanced blocks; allocation concealment - sequential envelopes; blinding not	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.	Microwave Endometrial Ablation (MEA); Transcervical Resection of the Endometrium (TCRE); pre-treatment of goserlin 3.6mg	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</p>	Funding Source: Microsulis plc

	mentioned Evidence level: 1++		Average age: MEA = 41.1, TCRE = 41.0  Country: UK	Surgery versus baseline; surgery versus surgery		<p>(76%), <math>p = 0.76</math></p> <p>Treatment acceptable: MEA = 109 (94%), TCRE = 112 (90%), <math>p = 0.34</math></p> <p>QoL score (SF-36) and standard deviation for MEA and TCRE, and change from baseline to 12-months: Physical functioning: 84.6 (SD 19.2), 82.2 (SD 23.3), <math>p=0.40</math>, 0.7 (SD 18.9), 2.4 (SD 16.8), <math>p = 0.45</math>. Social functioning: 60.1 (23.0), 60.1 (22.9), <math>p = 0.99</math>, 20.6 (26.5), 16.2 (24.4), <math>p = 0.18</math> Role - physical: 56.5 (42.2), 62.9 (41.7), <math>p = 0.24</math>, 23.9 (49.4), 11.3 (41.7), <math>p = 0.03</math> Role - emotional: 61.8 (42.5), 62.6 (43.2), <math>p = 0.88</math>, 17.0, 13.7, <math>p = 0.59</math> Mental health: 63.6 (18.8), 63.8 (21.7), <math>p = 0.92</math>, 6.3, 6.0, <math>p = 0.89</math> Energy/fatigue: 44.3(22.6), 43.3 (24.3), <math>p = 0.75</math>, 12.8 (21.7), 12.1 (23.0), <math>p = 0.80</math> Pain: 55.4 (28.2), 63.7 (26.1), <math>p = 0.02</math>, 14.8 (31.0), 7.2 (31.1), <math>p = 0.06</math>. General Health: 69.7 (21.7), 73.0 (19.4), <math>p = 0.22</math>, 2.4 (20.3), -2.9 (20.0), <math>p = 0.04</math>.</p>	
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Coulter 1995 118	Study Type: cohort; prospective  Evidence level: 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%),	Funding Source: Department of Health, UK
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							dissatisfied - 6 (10.9%).	
Hawe 2003 105	Study Type: blinded; randomised - block; allocation concealment - sealed, sequential envelopes  Evidence level: 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	Cavaterm - thermal balloon ablation; endometrial laser ablation; Pre- treatment of goserelin 3.6mg (used to maintain blinding)  Surgery versus 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%) versus laser = 13 (39%)  MBL (PBAC) at beeline 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% versus 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 versus 12- months for physical component	Funding Source: Not stated - Wallsten Medical supplied Cavaterm equipment  Study summary: Cavaterm is equivalent to laser ablation.

			<p>= 2.3 vs. Laser = 2.6</p> <p>MBL (PBAC):</p> <p>Cavaterm = 354.5 versus laser = 424.3</p> <p>Country: UK</p>			<p>Laser: physical component = 45.1, 50.4, 50.1; medical component = 43.0, 48.8, 48.9. Significant differences from baseline on all measures.</p> <p>QoL (EQ-5D) at baseline, 6- and 12-months:</p> <p>Cavaterm = 0.78, 0.81, 0.81</p> <p>Laser = 0.65, 0.80, 0.82.</p> <p>Cavaterm changes not significant, Laser changes significant.</p> <p>QoL (EQ-5D - vas) at baseline, 6-, 12-months.</p> <p>Cavaterm = 77.3, 82.1, 84.9</p> <p>Laser = 69.4, 80.9, 74.8</p> <p>Cavaterm and Laser only significant change at one time period.</p>	
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Hurskainen 2001 <sup>68</sup>	Study Type: Cross-sectional survey  Evidence level: 2-	226: split between <60ml and >60ml 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 versus objective menorrhagia		psychosocial factors; QoL - sf- 36; MBL - alkaline haematin	Using univariate analysis, difference between <60ml and >60ml 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 <sup>106</sup>	Study Type: randomised; allocation concealed; controlled	236: 119 LNG- IUS (57 had IUS; 10 nothing; 50 had	Population characteristics: women; menorrhagia; no pathology	LNG-IUS; hysterectomy  treatment versus baseline; 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	Funding Source: Government grant  Study summary: Study shows that at 5-years



	Evidence level: 1++	hysterectomy by 5 years); 117 hysterectomy (109 had hysterectomy by 5 years). 5 LNG-IUS, 7 hysterectomy lost to follow- up.	Country: Finland	versus treatment			<p>(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).</p> <p>At 5-years: 50 LNG-IUS users had hysterectomy. Another 10 women were without LNG-IUS in situ. 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>	LNG-IUS offered effective alternative to hysterectomy.
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Hurskainen 2001 107	Study Type: randomised; allocation concealed  Evidence level: 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 (30.0 to 33.2), Hysterectomy = 31 (30.0 to 32.0) Depression - IUS = 5.2	Funding Source: Government funded. IUD provided free by Leiras.  Study summary: Study shows LNG-IUS was effective alternative to hysterectomy at 12 months.
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							<p>(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 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</p>	
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							10 women had had LNG-IUS removed. 5 hysterectomy group cancelled operation.	
Learman 2004 121	Study Type: randomised - block; non- blinded; concealment  Evidence level: 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 - medroxyprogester one; 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%	medical treatment; hysterectomy  treatments versus 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	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.

			<p>Pervious treatment: hysterectomy = COC 39%, Prostaglandin inhibitors 13%, GnRH-a 10%, D&amp;C 19%, myomectomy 6%, endometrial ablation 3%</p> <p>Medicine = COC 50%, Prostaglandin inhibitors 19%, GnRH-a 6%, D&amp;C 38%, myomectomy 0%, endometrial ablation 0%</p> <p>Country: USA</p>			<p>41%, stress incontinence 25%</p> <p>Change in symptom frequency fro baseline at 6-months (intention-to- treat) Pelvic pain: hysterectomy = -2.3, medicine = -0.7, <math>p &lt; 0.01</math> Urinary urgency: hysterectomy = -0.7, medicine = 0.0, <math>p = 0.03</math> Urinary incomplete emptying: hysterectomy = -0.6, medicine = +0.1, <math>p = 0.03</math> Breast pain: hysterectomy = -1.3, medicine = -0.5, <math>p = 0.02</math> No difference for other pelvic, urinary or menopausal symptoms.</p> <p>Change in symptom frequency fro baseline at 2-years (intention-to- treat) Urinary incomplete emptying: hysterectomy = -0.8, medicine = -0.3, <math>p = 0.04</math> Hot flushes: hysterectomy = -0.6, medicine = 0.5, <math>p &lt; 0.01</math> No difference for other pelvic, urinary or menopausal symptoms.</p> <p>Change in symptoms for groups as treated: Hysterectomy only groups produced</p>	
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							<p>significant reduction in symptoms, except for stress incontinence (<math>p = 0.34</math>) and urge incontinence (<math>p = 0.74</math>)</p> <p>Medicine then hysterectomy group produced same results, except hot flushes not significant (<math>p = 0.13</math>)</p> <p>Medicine only group produced significant reductions in symptoms for pelvic pain, pelvic pressure, and stress incontinence (<math>p &lt; 0.05</math>), all other changes were non-significant.</p>	
Shapley 2002 65	<p>Study Type: Case-control</p> <p>Evidence level: 2+</p>	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 versus 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 &lt;4 or &gt;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 64	Study Type: Cohort; case- control  Evidence level: 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 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 - = 0.02, 0.17; mood -p = 0.53, 0.97; sex life - p = 0.12, 0.03; social 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	Funding Source: Not stated  Study summary: Study suggests psychosocial impact of HMB is a reason why women seek help.
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## Chapter 3 – Definition of HMB

### Impact of QoL of HMB – Non-comparative studies

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Ballinger <sup>63</sup>	Study Type: Cohort  Evidence Level: 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, $\chi^2 = 20.11$ , $p = 0.0002$	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.



Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Byles 1997 <sup>110</sup>	Study Type: Qualitative; focus groups  Evidence Level: 3	Women's experience of menstrual disorders	200	Women; 30-50 years; complaining of heavy, frequent or painful periods.  Country: Australia		<p>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.</p> <p>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.</p> <p>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.</p>	<p>Funding Source: Not stated</p> <p>Study Summary: Interaction between health professional and patient important in the management of menstrual disorders.</p>
Chapple 1999 <sup>111</sup>	Study Type: Qualitative  Evidence Level: 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.	<p>Funding Source: Not stated</p> <p>Study Summary: Nurse's may be able to provide information and education to women about menorrhagia.</p>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Cote 2002 115	Study Type: Cross-sectional survey  Evidence Level: 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 \$1692 earnings.	Funding Source: Not stated  Study Summary: Study highlights the potential economic impact of HMB. .
Cote 2003 45	Study Type: cross-sectional  Evidence Level: 3	cost of menorrhagia; factors associated of menorrhagia	2805 women involved in NHIS household survey	women; 18-64 yrs old; natural menstruation in last 12 months and 3 months; never taken oestrogen 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 < 0.00.	Funding Source: Not stated  Study Summary: Study provides data on association between subjective menorrhagia and socio-demographic factors.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Coulter 1994 117	Study Type: Cohort  Evidence Level: 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 108	Study Type: Cohort; prospective  Evidence Level: 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%	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.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						<p>vs. 47% (<math>p&lt;0.001</math>), social unease = 23% vs. 43% (<math>p&lt;0.001</math>), anxiety = 6% vs. 40% (<math>p&lt;0.001</math>), loss of concentration = 12% vs. 31% (<math>p&lt;0.001</math>).</p> <p>Patients after vs. patients before surgery (p-values for after surgery figures versus general population figures:  Worry = 61% vs. 89% (<math>p&lt;0.01</math>),  Somatic features of depression = 37% vs. 85%, (<math>p&lt;0.001</math>), tension = 64% vs. 77% (<math>p&lt;0.001</math>); irritability = 22% vs. 62% (ns), situational anxiety = 48% vs. 55% (<math>p&lt;0.001</math>), lack of energy = 27% vs. 53% (<math>p&lt;0.001</math>), simple depression = 24% vs. 47% (ns), social unease = 28% vs. 43% (ns), anxiety = 22% vs. 40% (<math>p&lt;0.001</math>), loss of concentration = 22% vs. 31% (<math>p&lt;0.05</math>).</p>	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Marshall 1998 <sup>112</sup>	Study Type: Qualitative; semi-structured interviews  Evidence Level: 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>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Mikhail <sup>116</sup>	Study Type: Survey  Evidence Level: 3	Women's health experiences and concerns	200	Women; 40-60 years of age  Country: Egypt	QoL	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%.  Would seek medical helps - heavy menstrual bleeding = 100%. Same as blood in stool or urine.	Funding Source: Not stated  Study Summary: Study shows that HMB seen as serious symptom in this population.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
O'Flynn 2000 <sup>132</sup>	Study Type: qualitative; cross-sectional survey  Evidence Level: 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: 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

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Smith 2004 <sup>109</sup>	Study Type: cohort  Evidence Level: 3	UAE	80	<p>Women; undergone UAE</p> <p>Baseline: Age: 45.6 Mean BMI: 27.4 Mean uterine size (weeks): 14.7 Symptoms: menorrhagia: 84% Pain: 38.2% Mass symptoms: 48.1%</p> <p>Previous treatments: COC; Pupron; myomectomy; Endometrial ablation</p> <p>Uterine volume( cm<sup>3</sup>): 678.4</p> <p>Country: USA</p>	QoL	<p>QoL for UAE (n = 64) - baseline (SD), post-UAE (SD), change (SD), p-value: Symptom severity (0 to 100): 61.61 (20.95), 26.42 (23.38), 35.19 (23.58), p &lt; 0.0001 Concern (0 to 100): 38.83 (30.31), 82.27 (22.48), -43.44 (31.48), p &lt; 0.0001. Activities (0 to 100): 44.81 (29.48), 84.71 (24.29), -39.89 (30.46), P &lt; 0.0001 Energy/mood (0 to 100): 48.90 (31.68), 79.85 (25.67), -30.96 (29.66), p &lt; 0.0001. Control: 48.75 (31.10), 82.27 (25.85), -33.51 (30.52), p &lt; 0.0001. Self-conscious: 47.14 (31.57), 73.31 (28.91), -26.17 (29.24), p &lt; 0.001. Sexual function: 48.17 (32.87), 78.28 (26.80), -30.11 (33.15), p &lt; 0.0001. HRQL total: 44.92 (25.24), 80.58 (23.66), -35.66 (27.10), p&lt;0.0001.</p>	<p>Funding Source: Not stated</p> <p>Study Summary: Women who undergo UAE have a significant decrease in symptom severity and increase in HRQOL, associated with high levels of satisfaction with the procedure, even when subsequent therapies are pursued.</p>



Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Spies 1999 119	Study Type: Cohort  Evidence Level: 3	UAE	50 - 17 completed 12 month follow-up	women; fibroids; scheduled for UAE  Country: USA	QOL - fibroid specific questionnaire	<p>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.</p> <p>Pain (higher=worse, lower=better): baseline = 31.08, 3-months = 13.96, 6-months = 19.09.</p> <p>Scores for symptoms: HMB: baseline = 36.61, 3 months = 90.81 (p&lt;0.001), 6-months = 85.03 (P&lt;0.001).</p>	<p>Funding Source: Cardiovascular and interventional radiology research and education foundation.</p> <p>Study Summary: UAE improves QoL of patients with fibroids.</p>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Warner 2004 <sup>113</sup>	Study Type: Cohort  Evidence Level: 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 (&lt;50ml, 50-79ml, 80-119ml, &gt;120ml): 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 &lt; 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 50-79ml and 80-199ml groups.</p>	<p>Funding Source: Chief Scientist's Office grant</p> <p>Study Summary: Little difference between two groups around 80ml. 80ml definition is of limited clinical usefulness.</p>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Ruta 1995 101	Study Type: Survey development  Evidence Level: 3	SF-36 vs menorrhagia severity score				<p>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 &amp; fatigue = 0.46, pain = 0.51, general health = 0.38.</p> <p>15 item questionnaire for assessing severity of menstrual bleeding on quality-of-life.</p> <p>Internal-reliability (<math>p &lt; 0.001</math>); validity - significant correlation on all SF-36 scales.</p>	Study Summary: Questionnaire may be using in selecting treatment for menorrhagia.

## Chapter 3 – Definition of HMB

### Estimation of Menstrual Blood Loss & QoL – Comparative studies

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Hurskainen 2001 <sup>68</sup>	Study Type: Cross-sectional survey  Evidence level: 2-	226: split between <60ml and >60ml 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 versus objective menorrhagia		psychosocial factors; QoL - sf-36; MBL - alkaline haematin	Using univariate analysis, difference between <60ml and >60ml 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	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.

							analysis - unemployment, anxiety, perceived inconvenience, abdominal pain and ferritin were significant factors in explaining variance.	
Rees 1991 <sup>129</sup>	Study Type: cohort  Evidence level: 2-	17	Population characteristics: Women; subjective menorrhagia  Country: UK	Informed of normal MBL	3-years	Treatment use	All 17 women had MBL <80ml 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.

## Chapter 3 – Definition in HMB

### Estimation of Menstrual Blood Loss – Diagnostic studies

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Barr 1999 <sup>136</sup>	Diagnostic  Evidence Level: 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 <sup>122</sup>	diagnostic  Evidence Level: 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.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Chimbira 1980 <sup>138</sup>	Diagnostic  Evidence Level: II	92	Women; menorrhagia - subjective  Country: UK	assessment of MBL	Objective vs. subjective MBL assessment: 23 of 68 (34%) of cycles termed light were > 80ml; 28 of 59 periods (47%) termed heavy were < 80ml; 32 of 57 termed medium were > 80ml.  Quantity of sanitary towels/tampons used: <10 pads = 11ml; 31-40 pads = 141ml; >40 = 113ml; 41-50 = 58ml (but small numbers at higher levels).  Duration of menstruation: median = 2 to 9 days (45 to 83ml). 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 <sup>135</sup>	Diagnostic  Evidence Level: III	53	women; 30-52 years; DUB; referred for ablation  Country: UK	alkaline haematin test; PBAC	Median MBL = 73ml, 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.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Fraser 1984 <sup>139</sup>	Diagnostic  Evidence Level: III	69	women; menorrhagia - subjective  Country: Australia	factors influencing MBL	<p>Perception of menstrual loss (n = 60) patients able to differentiate 'lightest' from 'heaviest' periods during study (<math>p &lt; 0.001</math>). 45% correctly assessed order of MBL for all four periods.</p> <p>Daily MBL versus patient assessment: "spotting" = 2.5ml; light = 5.7ml; moderate = 16.1ml; very heavy = 22ml. Spotting to light, <math>P &lt; 0.001</math>; light to moderate, <math>P &lt; 0.001</math>; moderate to heavy, <math>p &lt; 0.02</math>.</p> <p>Age difference in MBL perception: <math>&lt;27</math> years - light = 5.1ml, moderate = 13.8ml and heavy = 11.6ml. <math>&gt;36</math> years - light = 10.1ml, moderate = 20.1ml and heavy = 20.1 ml. Difference between groups were: ns, <math>&lt;0.5</math>, <math>&lt;0.001</math>.</p> <p>Duration and MBL: lightest = 4.7 days, heaviest = 5.8 days</p>	<p>Funding Source: Not stated</p> <p>Study Summary: Studies provides some indication of correlation between patient assessment of MBL and objective measures, but that alkaline haematin remains only reliable method.</p>



Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Fraser 2001 <sup>566</sup>	Diagnostic test  Evidence Level: II	56 - 3 failed to complete 2 cycles	women; menstruating; no 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) = (total fluid (ml)) <sup>1.07243/2.9319</sup>  pads only: estimated blood loss (ml) = (total fluid (ml)) <sup>1.0955/2.878</sup>  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) = (total fluid (ml)) <sup>1.0955/2.878</sup> * 0.796	Funding Source: Not stated  Study Summary: Carefully measured total fluid could be inexpensive method of estimating MBL.
Gannon 1996 <sup>130</sup>	diagnostic  Evidence Level: II	372	women; menorrhagia; scheduled for ablation; fibroids >5cm excluded.  Mean average age = 40yrs (24 to 54)  Country: UK	spectrophotometric analysis	Mean average MBL (n=373) 63ml (2-808ml). MBL <80ml in 231 (62%), and >80ml 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 problem than before.	Funding Source: Yorkshire Regional Health Authority  Study Summary: Objective measurement of MBL can be 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.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Heath 1999 <sup>140</sup>	Diagnostic Evidence Level: 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 <sup>133</sup>	diagnostic Evidence Level: II	18 women: 55 cycles. 1 gynaecologist: 122 cycles at clinic.	Women - involved in separate drug trial. Mean average age = 39yrs.  Country: UK	alkaline haematin; pictorial blood loss assessment chart - PBAC	Patient PBAC versus 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 versus 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 <sup>47</sup>	Diagnostic Evidence Level: 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 616ml (median 79ml) in subject menorrhagia, and 2.5 to 288ml (median 36ml) 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.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Janssen 1995 <sup>126</sup>	diagnostic  Evidence Level: II	288 (489 menstrual cycles)	Women; menstruating; not pregnant.  Mean age = 33.4yrs; mean parity = 1.3 (40.3% nulliparous)  Country: Netherlands	alkaline haematin; pictorial blood loss chart	66 (56%) of women complaining of menorrhagia had ml >80ml. 52 (44%) of women complaining of menorrhagia had MBL <80ml. 23 (13.5%) of women who did not complain of menorrhagia had MBL >80ml. 147 (86.5%) who did not complain of menorrhagia had MBL <80ml.  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%; +PV =69.2% and -PV = 95.3%. +PV and -PV 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 versus 52% of women with MBL <80ml.	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 <sup>100</sup>	Diagnostic questionnaire  Evidence Level: 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. further validation.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Pendergrass 1984 <sup>127</sup>	diagnostic  Evidence Level: 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.
Reid <sup>134</sup>	Diagnostic  Evidence Level: 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 389.4ml, 63 had MBL > 80ml. 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%, + predictive value = 62%, - predicative value 60%.  Up to 10x difference in ml and PBAC scores.	Funding Source: Leiras Oy  Study Summary: PBAC has not been validated, and should not be used.
Shaw 1972 <sup>123</sup>	diagnostic  Evidence Level: 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 <sup>124</sup>	Diagnostic test  Evidence Level: II	21	women;  Country: Netherlands	calculation of MBL	Recovery rate from alkaline haematin test by added blood using existing equation (see paper): 10ml (n = 4) recovered 10.9ml (109%); 40ml (n = 4) recovered 41.4 (104%); 80 (n = 4) recovered 77.1 (96%); 140 (n = 3) recovered 132.3 (95%); 200 (n = 3) recovered 181 (91%). New equation (see paper) 10ml (n = 4) recovered 9.8 ml (98%); 40ml (n = 4) recovered 40.7 (102%); 80 (n = 4) recovered 78.3 (98%); 140 (n = 3) recovered 139.1 (99%); 200 (n = 3) recovered 196.2 (98%).	Funding Source: Not stated  Study Summary: Study shows alkaline haematin test is accurate and precise method.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Vasilenko 1988 <sup>125</sup>	Diagnostic  Evidence Level: III	10	women; non-pregnant  Country: USA	Spectrometer	Extraction efficiency of used pad versus 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 <sup>128</sup>	Diagnostic  Evidence Level: II	121: 62 subjective menorrhagia; 59 subjective controls. 13 failed to complete study.	women; presenting with menorrhagia  Country: UK	PBAC; alkaline haematin	PBAC compared to Alkaline Haematin: sensitivity = 86% and specificity = 88% (assume at 80ml 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 > 80ml. Including extraneous estimation - 45 of 61 had MBL > 80ml.  No correlation between extraneous blood loss and pad blood loss, $r = 0.58$ .	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 RW;Brickley MR;Evans L;Edwards MJ; 1998 <sup>102</sup>	Diagnostic  Evidence Level: 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.

## Chapter 3 – Definition of HMB

### Estimation of Menstrual Blood Loss & QoL – Non-comparative studies

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Chapple 2001 <sup>131</sup>	Study Type: Qualitative interviews  Evidence Level: 3	How to measure of MBL in general practice	73	GPs  Country: UK		<p>Main themes:</p> <p>Most GPs tried to estimate MBL using duration of menses or pad use, but not see as accurate.</p> <p>Objective measurement using alkaline haematin not practical due to workload.</p> <p>PBAC a more practical option.</p> <p>MBL not the important factor, that MBL is interfering with life is the important issue.</p>	<p>Funding Source: Not stated</p> <p>Study Summary: Study highlights disagreement within general practice about assessment of HMB, and need for guidance on this issue.</p>
Hefnawi 1979 <sup>50</sup>	Study Type: Physiological study  Evidence Level: 3	factors associated with MBL	812 - 774 participated	Women; aged 14 - 49; regular menstrual bleeding  Country: Egypt	MBL correlates	<p>Mean MBL = 25.6, median MBL = 20.2</p> <p>MBL and age: <math>r = +0.06</math> (ns). MBL and parity <math>r = +0.21</math>. MBL and systolic blood pressure <math>r = +0.18</math>. MBL and diastolic blood pressure, <math>r = +0.12</math>.</p>	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Jenkinson 1996 <sup>99</sup>	Study Type: Evidence Level: 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 to 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 <sup>143</sup>	Study Type: Postal survey  Evidence Level: 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) socio-economic 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.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Shapley 1995 <sup>142</sup>	Study Type: Cross-sectional community survey  Evidence Level: 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 <sup>137</sup>	Study Type: cohort  Evidence Level: 3	Assessment of menstruation cycles	5292	women; menstruating  Country: 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>



Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Warner 2004 <sup>113</sup>	Study Type: Cohort  Evidence Level: 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 (&lt;50ml, 50-79ml, 60 (80?)-119ml, &gt;120ml): 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 &lt; 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 50-79ml and 80-199ml groups.</p>	<p>Funding Source: Chief Scientist's Office grant</p> <p>Study Summary: Little difference between two groups around 80ml. 80ml definition is of limited clinical usefulness.</p>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Barer <sup>51</sup>	Study Type: Cohort  Evidence Level: 3	Normal MBL estimation	100	women; 15-43 years; anaemia excluded  USA	MBL - alkaline haematin	For group (n = 100) MBL = 6.55 to 178.69ml, mean = 50.55 (SD 25.73) (though results skewed). 50% within 23.21 to 68.43ml range.  No relationship between MBL and age.  Relationship between duration and MBL; 3 days = 24.3 and 6 days = 58.66ml. 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.

## Chapter 4 – Patient Education & Patient Choice

### Patient Choice – Comparative studies

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Longo 2006 <sup>254</sup>	Study Type: Randomised at practice level  Evidence level: 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 246	Study Type: Randomised; concealed  Evidence level: 1++	272 eligible, 187 recruited, 94 randomised to medical treatment, 93 to TCRE. By two 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 versus 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	Funding Source: Scottish Office Department of Health  Study summary: The results at two 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.
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							<p>(79%), <math>p = 0.002</math>  Cure or acceptable improvement = 53 (61%) vs. 69 (81%), <math>p = 0.017</math>  Treatment acceptable = 65 (77%) vs. 79 (93%), <math>p = 0.004</math></p> <p>Menstrual status:  No bleeding or light = 36 (42%) vs. 50 (58%), <math>p = 0.04</math>  Unchanged or heavier = 16 (18%) vs. 5 (6%), <math>p = 0.02</math></p> <p>Bleeding score = 6.8 (SD 9.9) vs. 5.4 (SD 8.1)</p>	
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## Chapter 4 – Patient Education & Patient Choice

### Patient Choice – non-comparative studies

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Augustus 2002 <sup>230</sup>	Study Type: Qualitative; interviews  Evidence Level: 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

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Bourdrez 2004 <sup>247</sup>	Study Type: Prospective; cohort  Evidence Level: 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.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Coulter 1994 <sup>249</sup>	Study Type: Survey  Evidence Level: 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		<p>Patient had preference: Age at completion of full time-education: &lt;16 OR = 1, 17-18 OR = 1.02, &gt;19 OR = 3.35 (1.95 to 5.76)</p> <p>Previous consultation for menstrual problems: none OR = 1.00, 1&gt; OR = 2.22 (1.38 to 3.60)</p> <p>Specialist gynaecological consultation within 1 year: none = 1.00, 1&gt; = 1.94 (1.06 to 3.53)</p> <p>Preference for surgery: symptoms mild or moderate = 1.00, sever OR = 2.59 (1.21 to 5.76)</p> <p>GPs aware of patient preference in 34.4%</p> <p>Factors associated with referral for surgery (p &lt; 0.05) were: GPs prediction of treatment, patient's preference, what GP thought patient wanted, previous surgery, age of patient, and sex of GP.</p>	<p>Funding Source: Not stated</p> <p>Study Summary: Study shows a mismatch between patient preferences and the management they receive.</p>
Entwistle 2001 <sup>251</sup>	Study Type: Qualitative; interviews  Evidence Level: 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



Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Entwistle, 2006 <sup>255</sup>	Study Type: Survey & interviews  Evidence Level: 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	<p>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%</p> <p>Too little information provided: Different kinds of hysterectomy = 26% Advantages of different types of hysterectomy = 36% Disadvantages of different types of hysterectomy = 44% Types of hysterectomy being undertaken = 26% Advantages of removing cervix = 60% Disadvantages of removing cervix = 65% Whether cervix is being removed = 41%</p> <p>Interviews: Most women reported having little input into decision about type of hysterectomy undertaken.</p>	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Fry 2001 <sup>256</sup>	Study Type: Survey  Evidence Level: 3	Factors influencing decision to have oophorectomy	58 - 30 having oophorectomy, 28 ovarian screening	women  Country: UK	Factors related to oophorectomy	Frequency of item being rated high or extremely important: Reducing risk of ovarian cancer, reducing cancer worry, Age, worries about effectiveness of screening, partner's attitude, loss of periods. All at $p < 0.05$  No difference for other factors - need for HRT, risks of surgery, recovery time, desire for children, etc.	Funding Source: Not stated
Groff 2000 <sup>234</sup>	Study Type: Qualitative; focus groups  Evidence Level: 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	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						female doctors as thought they were less likely to suggest hysterectomy.  There were differences between sub-groups about above theme.	
Leung 2005 <sup>257</sup>	Study Type: Survey  Evidence Level: 3	Patient preferences	324 questionnaires, 200 returned	Women; menorrhagia; Chinese  Country: Hong Kong	Patient preferences and knowledge	Of respondents: 70.5% knew of drug therapies, 7.5% of LNG-IUS, 4.5% of ablation, 28% of hysterectomy.  6% wanted amenorrhoea, 7.5% wanted oligomenorrhoea, 86.5% wanted eumenorrhoea.  87% wanted drug treatment as first line treatment, 3% LNG-IUS, 3% ablation, 7% no treatment.  45% wanted LNG-IUS if drug treatment failed, 16% ablation, 4.5% hysterectomy, 34.5% no treatment  Main reason for not choosing a treatment was not knowing about it.	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Lindberg 2001 <sup>252</sup>	Study Type: Qualitative; interviews  Evidence Level: 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:  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>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Marsh 2002 <sup>258</sup>	Study Type: Evidence Level: 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: No pain during procedure Likely not to need for repeat procedure Do not want to see procedure happening</p> <p>Reasons for not preferring day case: Fasting Pre-assessment clinic visit needed Waiting for procedure in hospital</p> <p>Reasons for preferring outpatient: Quick process Able to see what is happening Able to see inside womb</p> <p>Reasons for not preferring outpatient: Procedure could be uncomfortable Procedure may have to be repeated Sitting in examination chair for 10 to 15 minutes</p>	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Nevadunsky 2001 <sup>250</sup>	Study Type: Survey  Evidence Level: 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 <sup>236</sup>	Study Type: Decision support strategy  Evidence Level: 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 -	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						<p>personal (skills, motivation, self-confidence, previous experience), external support networks.</p> <p>Demographic characteristics: client, practitioner.</p> <p>Provide decision support: provide information - health situation, options, outcomes, other opinions and choices.</p> <p>Re-align expectations of outcomes</p> <p>Clarify personal values for outcomes</p> <p>Provide guidance and coaching - steps in decision-making, communicating with others, handling pressure, accessing support and resources.</p> <p>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</p> <p>Outcomes of decision: Persistence with others, improved quality of life, reduced distress, reduced regret, informed use of resources.</p>	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Sculpher <sup>248</sup>	Study Type: Cohort  Evidence Level: 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 & discomfort = 0.68 Hospital stay as short as possible = 0.59 Reduce periods = 0.42 Resume sex life as soon as possible = 0.59 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%	Funding Source: Not stated  Study Summary: Many women referred for surgery for menorrhagia have conflicting objectives from treatment.



Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Uskul 2003 <sup>231</sup>	Study Type: qualitative; interviews  Evidence Level: 3	Women's experience of hysterectomy	29	Women; scheduled for hysterectomy  Country: Canada	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

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Vuorma 2003 <sup>242</sup>	Study Type: Comparative; cohort  Evidence Level: 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	Items correlated with choosing hysterectomy over conservative treatment: Age, OR = 95% CI 1.00 to 1.16 Wish for further pregnancies, 95% CI OR = 0.09 to 0.60 Menstrual pain, OR = 95% CI 1.02 to 1.21 Irregular periods, OR = 95% CI 1.07 to 3.96 Education less than 12 years, OR = 95% CI 1.47 to 4.62 Unemployed, OR = 95% CI 1.10 to 11.7 Number of visits to gynaecologist for HMB, OR = 95% CI 1.21 to 2.47  Factors, such as inconvenience caused by HMB were not significant.	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Wade 2000 <sup>233</sup>	Study Type: Case-series; survey  Evidence Level: 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	Seven major themes were identified: Positive aspects - 61 of 102 outlined positive aspects of hysterectomy, including relief from symptoms, accurate information, supportive physician, involvement in decision-making.  HRT - fears and concerns about using HRT based on lack of information.  Insufficient information - 38 of 102 thought insufficient information had been given about hysterectomy and physical impact.  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.	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Webb 1986 <sup>232</sup>	Study Type: Qualitative interviews  Evidence Level: 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

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Williams 2000 <sup>237</sup>	Study Type: Cohort  Evidence Level: 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> <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>	Funding Source: not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Wu 2005 253	Study Type: Decision-tree  Evidence Level: 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

## Chapter 4 – Patient Education & Patient Choice

### Patient education – comparative studies

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Cheung 2003 <sup>245</sup>	Study Type: randomised  Evidence level: 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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Garrud 2001 <sup>243</sup>	Study Type: randomised  Evidence level: 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 <sup>239</sup>	Study Type: Randomised - block; concealed allocation; no blinding  Evidence level: 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	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 & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>treatment, 1 wanted no treatment.</p> <p>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.</p> <p>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.</p> <p>Trend for information group not to want treatments compared to control group.</p> <p>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.</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>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.</p> <p>Information (OR 95% CI 1.46 to 4.20) and interview (OR 95% CI 1.72 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>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<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: Quality of life outcomes: 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: 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 to control group.</p> <p>Patient satisfaction: 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</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>groups in satisfaction with treatment outcome.</p> <p>Long-term follow-up: Quality of life outcomes: 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: 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 to control group.</p> <p>Patient satisfaction: 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>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
O'Connor 2002 <sup>238</sup>	Study Type: Systematic review  Evidence level: 1+	11995 articles identified, 35 studies included.	Population characteristics: 1) searching electronic medical and social science databases; 2) scanning the tables of contents 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; 3) searching personal _les; and 4) contacting known developers and evaluators through a shared decision making list-serve and e-mail contacts in May 2002. We searched the following electronic databases: MEDLINE	Decision aids in healthcare	n/a	Decision regret; anxiety; persistence with choice; general health outcome; satisfaction with decision; disease specific symptom outcomes	Among the trials comparing decision aids to usual care, decision aids performed better in terms of: a) greater knowledge 18.75 [ 13.14, 24.35 ] b) more realistic expectations (RR 1.4, 95%CI: 1.1 to 1.9); c) lower decisional conflict related to feeling informed (WMD -9.1 of 100, 95%CI: -12 to -6); d) increased proportion of patient that controlled decision making (RR 1.49 95% CI:0.99, 2.25 ); e) reduced practitioner controlled decision-making (RR = 0.68 [ 0.53, 0.89 ]) and f) reduced proportion of people who remained undecided post intervention RR = 0.43 [ 0.27, 0.70 ].  When simpler were compared to more detailed decision aids, the relative improvement was significant in: a) knowledge (WMD 4 out of 100, 95% CI: 3 to 6); b) more realistic expectations (RR 1.5, 95% CI: 1.3 to 1.7); and c) greater agreement between values and choice. Decision	Funding Source: Canadian Institute of Health Research (formally MRC) CANADA  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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			(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).				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.	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Redman 1986  567	Study Type: prospective; cohort  Evidence level: 2-	43 - 19 in information group, 24 in control group	Population characteristics: Women; schedule for abdominal hysterectomy.  Country: UK	Information booklet about hysterectomy	n/a	Patient satisfaction with operation; patient satisfaction with communication; patient knowledge of hysterectomy	Patient satisfaction: no difference between groups  Satisfaction with communication: $p < 0.01$ in favour of information group.  Knowledge of hysterectomy: $p < 0.01$ in favour of information group.	Funding Source: Not stated
Ridgeway 1982  244	Study Type: randomised  Evidence level: 1-	60 - 20 to information, 20 to cognitive help, 20 to control. Plus 10 who had no information.	Population characteristics: Women; scheduled for abdominal hysterectomy  Country: UK	Cognitive assessment - reassurance and positive attitude; information booklet	4 post-operation interviews	Pre-operative symptoms; post- operative symptoms	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.  Post-operative results: Cognitive group had fewer symptoms, and fewer days of pain than information group, same total activities.	Funding Source: Not stated
Vuorma 2003  240	Study Type: randomised  Evidence level: 1-	569 - 206 in pre-treatment cohort (178 at 12 months), 184 (156 at 12 months) in randomised information, 179 (159 at 12 months) in	Population characteristics: Women; subjective menorrhagia.  Groups were comparable at baseline.	Information booklet; no information	12 months	Treatment preference; treatment received.	Treatment preference at baseline: Information group (n = 184): 49% wanted hysterectomy, 32 wanted conservative treatment, 19% had no clear preference.  Control group (n = 179):	Funding Source: Not stated  Study summary: More women had clear preference after being given information.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
		control group	Country: Finland				<p>45% wanted hysterectomy, 37% wanted conservative medical treatment, 18% had no clear preference.</p> <p>Treatment plan at 3-months</p> <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 &lt; 0.05)</p> <p>No difference between information and control groups for knowledge, satisfaction with clinic or anxiety.</p>	



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Vuorma 2004 <sup>241</sup>	Study Type: randomised; concealed; blinding not possible  Evidence level: 1-	1880 approached, 962 willing to participate, 569 eligible - 206 to pre-trial group, 184 to intervention group, 179 to control group	Population characteristics: Women; aged 35 to 54 years; referred due to menorrhagia or fibroids.  Average age = 44.4, 47% sterilised, 63% had heavy flow, 24% had irregular periods, 46% had pelvic pain.  Country: Finland	Decision aid booklet (about menorrhagia and treatments); no treatment	12-months	SF-36; VAS perceived health, anxiety and psychosomatic symptoms; menstrual symptoms, Sexuality; satisfaction with treatment.	Differences between groups on sf-36 scores, VAS perceived health, anxiety and psychosomatic symptoms; menstrual symptoms, Sexuality; satisfaction with treatment.  No statistical difference between intervention and control group, except for emotional role (p = 0.01), where intervention group improved more.  Both groups significantly improved from baseline for all outcomes, except sexuality scores.  No statistically significant differences between groups in terms of health service use or cost.	Funding Source:  Study summary: Study shows that patient information booklet had not impact on treatment outcome.

## Chapter 4 – Patient Education & Patient Choice

### Patient Education – non-comparative studies

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Augustus 2002 <sup>230</sup>	Study Type: Qualitative; interviews  Evidence Level: 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

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Groff 2000 <sup>234</sup>	Study Type: Qualitative; focus groups  Evidence Level: 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
O'Connor 2002 <sup>236</sup>	Study Type: Decision support strategy  Evidence Level: 4	Decision support system		Country: Canada	Decision support factors	<p>Assess needs of woman: Perceptions of decision - knowledge, expectations, values, decisional conflicts, stage of decision making, predisposition towards options.</p> <p>Perceptions of others - perceptions</p>	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						<p>of others, support, pressures, roles in decision making</p> <p>Resources to make decision - personal (skills, motivation, self-confidence, previous experience), external support networks.</p> <p>Demographic characteristics: client, practitioner.</p> <p>Provide decision support: provide information - health situation, options, outcomes, other opinions and choices.</p> <p>Re-align expectations of outcomes</p> <p>Clarify personal values for outcomes</p> <p>Provide guidance and coaching - steps in decision-making, communicating with others, handling pressure, accessing support and resources.</p> <p>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</p> <p>Outcomes of decision: Persistence with others, improved quality of life, reduced distress, reduced regret, informed use of resources.</p>	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Scriven 1997 <sup>229</sup>	Study Type: Survey  Evidence Level: 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 <sup>235</sup>	Study Type: Survey  Evidence Level: 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	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						<p>Disadvantages of treatments other than hysterectomy.</p> <p>Patients felt not enough information about risks and disadvantages of surgery.</p> <p>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</p> <p>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</p> <p>When asked questions about if doctor had been supportive during decision-making between 15% to 30% were neutral or dissatisfied.</p> <p>When asked various questions about if hysterectomy was the right decision about 10% of women were neutral or disagreed.</p>	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Uskul 2003 231	Study Type: qualitative; interviews  Evidence Level: 3	Women's experience of hysterectomy	29	Women; scheduled for hysterectomy  Country: Canada	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

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Vuorma 2003 <sup>242</sup>	Study Type: Comparative; cohort  Evidence Level: 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	Items correlated with choosing hysterectomy over conservative treatment: Age, OR = 95% CI 1.00 to 1.16 Wish for further pregnancies, 95% CI OR = 0.09 to 0.60 Menstrual pain, OR = 95% CI 1.02 to 1.21 Irregular periods, OR = 95% CI 1.07 to 3.96 Education less than 12 years, OR = 95% CI 1.47 to 4.62 Unemployed, OR = 95% CI 1.10 to 11.7 Number of visits to gynaecologist for HMB, OR = 95% CI 1.21 to 2.47  Factors, such as inconvenience caused by HMB were not significant.	Funding Source: Not stated



Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Wade 2000 <sup>233</sup>	Study Type: Case-series; survey  Evidence Level: 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	Seven major themes were identified: Positive aspects - 61 of 102 outlined positive aspects of hysterectomy, including relief from symptoms, accurate information, supportive physician, involvement in decision- making.  HRT - fears and concerns about using HRT based on lack of information.  Insufficient information - 38 of 102 thought insufficient information had been given about hysterectomy and physical impact.  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.	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Webb 1986 <sup>232</sup>	Study Type: Qualitative interviews  Evidence Level: 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

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Williams 2000 <sup>237</sup>	Study Type: Cohort  Evidence Level: 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> <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>	Funding Source: not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Wade 2000 <sup>233</sup>	Study Type: Case-series; survey  Evidence Level: 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	Seven major themes were identified: Positive aspects - 61 of 102 outlined positive aspects of hysterectomy, including relief from symptoms, accurate information, supportive physician, involvement in decision-making.  HRT - fears and concerns about using HRT based on lack of information.  Insufficient information - 38 of 102 thought insufficient information had been given about hysterectomy and physical impact.  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.	Funding Source: Not stated

## Chapter 5 – Investigations for HMB

### Tests for exclusion of underlying conditions – Comparative studies

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Baxter 2002 159	Study Type: randomised; single-blind; concealed  Evidence level: 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	Flexible hysteroscopy; rigid hysteroscopy	30 minutes	Pain levels	Pain level (10cm 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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			= 5 vs. 7 Part of trial = 0 vs. 2  Country: UK					
Clark 2002 <sup>158</sup>	Study Type: Systematic review  Evidence level: 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	Funding Source: University of Birmingham Interdisciplinary Research Fund & Birmingham Women's Hospital R&D fund  Study summary: hysteroscopy is good at identifying endometrial cancer, but less so for identifying endometrial disease.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>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</p> <p>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.</p> <p>Factors such as study setting, study population and patient selection impact on results.</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
De Kroon 2003 157	Study Type: Diagnostic; meta-analysis  Evidence level: Ib	109 studies identified, 24 included in review	Population characteristics: Search strategy: MEDLINE, EMBASE, DARE, Cochrane library, ISI - current contents  Studies examining saline contrast hysterosonography in AUB  Country: Netherlands	Saline contrast hysterosonography for AUB	No follow-up	Sensitivity, specificity, PPV, PNV	<p>Pooled results for studies were 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, negative post-test probability = 0.04</p> <p>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</p> <p>Pooled results for studies for identification fibroids - sensitivity = 0.87, specificity = 0.92, positive likelihood ratio = 11.0, negative likelihood ratio = 0.07</p> <p>Pooled results for studies for identification endometrial polyps - sensitivity = 0.86, specificity = 0.81, positive likelihood ratio = 5.23, negative likelihood ratio = 0.12</p>	<p>Funding Source: Not stated</p> <p>Study summary: SIS is an accurate method for evaluating uterine cavity in women with AUB.</p>



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>Success rate for SIS in 24 studies = 93%.</p> <p>5 complications reported in 2278 procedures.</p>	
Dueholm 2002 <sup>155</sup>	<p>Study Type: Systematic review</p> <p>Evidence level: Ib</p>	18 papers	<p>Population characteristics: MEDLINE search - 1982 to 2001, English language, diagnostic accuracy of Transvaginal ultrasound, hysterosonographic examination, Hysteroscopy, Magnetic resonance imaging.</p> <p>Country: Denmark</p>	Accuracy of Transvaginal ultrasound, hysterosonographic examination, Hysteroscopy, Magnetic resonance imaging.	No follow-up	Accuracy of test - sensitivity, specificity	<p>TVS (n = 11 studies) overall diagnostic accuracy - sensitivity = 87% (range 24% to 96%), specificity = 82% (range = 29% to 93%).</p> <p>For identification of polyps - sensitivity = 80% (range = 31% to 94%).</p> <p>For identification of submucous myomas - sensitivity = 94% (range 62% to 100%).</p> <p>HSE overall diagnostic accuracy - sensitivity = 94% (range 83% to 100%), specificity = 85% (range = 72% to 99%)</p> <p>For identification of polyps - sensitivity = 93% (range 67% to 100%), specificity = 96% (range 93% to 100%).</p> <p>Hysteroscopy - no combined results reported.</p> <p>MRI - no combined</p>	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>results shown.</p> <p>Highlights that many studies use endometrial sampling as gold-standard which is inappropriate.</p>	
Farquhar 2003 <sup>154</sup>	<p>Study Type: systematic review; diagnostic</p> <p>Evidence level: Ib</p>	19 papers	<p>Population characteristics: MEDLINE and EMBASE 1980 to 2001. Search terms and MESJH terms used.</p> <p>Standard inclusion/exclusion criteria used.</p> <p>Standard quality assessment used.</p> <p>Standard data extraction used</p> <p>Country: New Zealand</p>	Transvaginal ultrasound; sonohysterography; hysteroscopy; histopathology - operative hysteroscopy or hysterectomy	No follow-up	<p>Accuracy of diagnostic method - sensitivity, specificity, PPV, NPV, +LR, -LR; patient discomfort</p>	<p>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.</p> <p>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.</p> <p>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.</p>	<p>Funding Source: Not stated</p> <p>Study summary: Although high degree of variation in studies, all tests were moderately accurate at identifying pathology.</p>

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>Sonohysteroscopy 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.</p> <p>Sonohysteroscopy vs. histopathology or hysteroscopy for identification of submucous fibroids: 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):</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>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%</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>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 <sup>153</sup>	<p>Study Type: Systematic review</p> <p>Evidence level: 2++</p>	55 articles included	<p>Population characteristics: MEDLINE</p> <p>Two searches designed.</p> <p>Inclusion/exclusion criteria systematically applied.</p> <p>Systematic quality assessment</p>	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).</p> <p>Likelihood ratio at serum ferritin levels (ug/l)</p> <p>&gt; 100 = 0.08</p> <p>45 to 100 = 0.54</p> <p>35 to 44 = 1.83</p> <p>25 to 34 = 2.54</p> <p>24 to 15 = 8.83</p> <p>&lt; 15 = 51.85</p> <p>Red cell protoporphyrin (n = 288) Area under ROC curve = 0.77 (0.71 to 0.83)</p> <p>Likelihood ratio at red cell protoporphyrin levels (ug/l)</p> <p>&lt;50 = 0.12</p> <p>51 to 150 = 0.56</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 & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>151 to 250 = 2.01 251 to 350 = 6.05 &gt;351 = 8.31</p> <p>Mean cell volume (N = 436) Area under ROC curve = 0.76 (0.72 to 0.80)</p> <p>Likelihood ratio at mean cell volume levels (um<sup>3</sup>)</p> <p>&gt;90 = 0.29 85 to 89 = 0.76 80 to 84 = 0.91 75 to 79 = 1.00 70 to 74 = 3.33 &lt; 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>&gt;50 = 0.15 30 to 49 = 0.43 20 to 29 = 0.52 10 to 19 = 0.81 5 to 9 = 2.54 &lt; 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</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							level: < 15 = 0.61 15 to 16 = 0.84 17 to 20 = 1.78 > 21 = 2.72.	
James 2004 <sup>148</sup>	Study Type: systematic review; diagnostic studies  Evidence level: 2-	107 articles identified	Population characteristics: MEDLINE. 1990 to 2003. Keyword search only.  Country:	Testing for Von Willebrand's 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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Krassas 1994 <sup>147</sup>	Study Type: Epidemiology  Evidence level: 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.



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Philipp 2003 <sup>560</sup>	Study Type: Cohort; epidemiology  Evidence level: 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 v 2 (p = 0.105); ADP 3 v 1 (p = 0.5); Arachidonic acid 6 vs. 1 (p=0.13). ATP release: ADP 30 vs. 7 (p = 0.0009); Arachidonic acid 16 v 1 (p = 0.001); Collagen 18 vs. 5 (p = 0.04); Thrombin 1 v 0 (na).	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 <sup>53</sup>	Study Type: Systematic review  Evidence level: 2-	11 studies included in review	Population characteristics: Women; menorrhagia; screened for von willebrand  Search undertaken on MEDLINE only using keyword search.	vWD as risk factor in menorrhagia	n/a	Prevalence of von willebrand's	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 out-patient	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			Country:				<p>clinics, 1 on coagulation clinic, 1 on administrative database, 2 on population study, 1 not stated.</p> <p>Menorrhagia state based on history in 5 studies, PBAC in 2, Alkaline Haematin in 2, and not stated in 2.</p> <p>VWF:Ag test only one used across studies, RiCof was second most common.</p> <p>Cut-off for vWD varied between studies.</p> <p>Different study designs and inclusion criteria probably account for differences between studies.</p>	

## Chapter 5 – Investigations for HMB

### Tests for exclusion of underlying pathology – Diagnostic studies

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Anastasiadis 2000 <sup>160</sup>	retrospective; comparison  Evidence Level: 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 <sup>161</sup>	diagnostic; comparison  Evidence Level: 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 >5mm - neoplastic = 18, non-neoplastic = 75; <= 5mm - neoplastic = 1, non-plastic = 11. Sensitivity = 95%, specificity = 37%, PPV = 19%, NPV = 97%.	Funding Source: Not stated

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Ash 1996 <sup>79</sup>	diagnostic; retrospective  Evidence Level: 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 <sup>162</sup>	diagnostic; retrospective; case-series; part-blinded  Evidence Level: 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 endometriosi s = 8, polyps = 10, hyperplasia = 3, chronic endometriosi s = 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.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Bain 2002 <sup>224</sup>	Randomised; blinded; controlled; diagnostic  Evidence Level: 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 & 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 & biopsy; endometrial biopsy alone	Outcomes:  Semantial 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 = -.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 to biopsy alone.
Ben-Baruch 1994 <sup>218</sup>	diagnostic comparison  Evidence Level: II	269 - 172 Pipelle curette, 97 had D&C (45 from Pipelle group later had histology available).	women; non-pregnant; referred for investigation due to AUB  Country: Israel	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.  Difference between groups was significant ( $p < 0.0001$ )  Of 45 Pipelle's where D&C or hysterectomy were later performed, the diagnosis was the same in 43 (95.5%).	Funding Source: Not stated  Study Summary: Study shows Pipelle curettage is useful meted for diagnosis of endometrial pathology.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Ben-Yehuda 1998 <sup>163</sup>	diagnostic; comparative; retrospective  Evidence Level: III	373	women; AUB; undergone D&C & 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 to 33 for D&C.  True-positive = 54, false-positive = 115, false-negative = 50, true-negative = 154.	Funding Source: Not stated
Bernard 1997 <sup>164</sup>	prospective; comparison  Evidence Level: 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 Hypertrophy = 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.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Bettocchi 2001 <sup>568</sup>	diagnostic; comparative; retrospective  Evidence Level: 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 to 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 <sup>165</sup>	Diagnostic; retrospective; case-series  Evidence Level: 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 to histology for identification of intra-cavity masses had a sensitivity of 99%, specificity of 98%.  Accuracy of endometrial thickness compared to sonohysteroscopy for identification of pathology, at 5mm 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.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Bronz 1997 <sup>75</sup>	diagnostic; comparative; prospective  Evidence Level: II	139	women; referred due to AUB; 83 women pre-menopausal, 56 post-menopausal  Country: Switzerland	transvaginal sonography; saline infusion sonography; histology - reference	<p>Results for pre-menopausal women:</p> <p>Benign polyps identified in 33 women by histology, TVS identified 21, SCHS identified 32.</p> <p>Submucous fibroids identified in 22 women by histology, TVS identified 21, SCHS identified 21.</p> <p>Endometrial hyperplasia identified in 5 women by histology, TVS identified 5, SCHS identified 2.</p> <p>No endometrial carcinoma reported</p> <p>REVIEWER CALCULATED: For TVS Sensitivity = <math>48/62 = 0.77</math> Specificity = <math>19/21 = 0.90</math></p> <p>For SCHS Sensitivity = <math>58/62 = 0.94</math> Specificity = <math>17/21 = 0.81</math></p>	<p>Funding Source: not stated</p> <p>Study Summary: Both TVS and SCHS are highly accurate methods at diagnosing pathology</p>



Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Cepni 2005 <sup>156</sup>	diagnostic; prospective; cohort; comparison  Evidence Level: 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 to 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 to 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 to 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 to 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 to 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 to 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 <sup>166</sup>	prospective; cohort; diagnostic; non-blinded  Evidence Level: 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

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Critchley 2001 71	diagnostic; randomised - block; prospective; statistical analysis blinded  Evidence Level: 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	High Risk = post-menopausal Moderate-risk = pre-menopausal, <40, no risk factors – family history Low risk = pre-menopausal, <40  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: High risk group: Hysteroscopy and biopsy = 83 (83%); Ultrasound and biopsy = 74 (74%)  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 high risk group - neuroticism = 18, extraversion = 27 openness = 26, agreeableness = 34, conscientiousness = 34	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'.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
					<p>For moderate risk group - neuroticism = 21, extraversion = 28 openness = 27, agreeableness = 34, conscientiousness = 35</p> <p>For low risk group - neuroticism = 21, extraversion = 28 openness = 25, agreeableness = 33, conscientiousness = 34</p> <p>GHQ questionnaire scores: High-risk group - Somatic symptoms = 5.0, anxiety = 4.5, social dysfunction = 7.0, depression = 0.0, total = 17</p> <p>moderate-risk group - Somatic symptoms = 7.0, anxiety = 7.0, social dysfunction = 7.0, depression = 0.0, total = 21</p> <p>low-risk group - Somatic symptoms = 6.0, anxiety = 6.0, social dysfunction = 7.0, depression = 0.0, total = 20</p> <p>Difference between groups: Somatic symptoms, <math>p = 0.001</math>, anxiety <math>p = 0.001</math>, social dysfunction <math>p = 0.197</math>, depression <math>p = 0.044</math>, total <math>p = 0.001</math>.</p> <p>High-risk group: Visualisation - hysteroscopy (n = 100): 13 not possible, 87 possible, 3 not undertaken for other reasons, 84 completed, 79 successful visualisation. Ultrasound (n = 100): 0 not possible, 100 possible, 5 not undertaken for other reasons, 95 completed, 87 successful visualisation.</p> <p>Biopsy - hysteroscopy and Pipelle: 90 subjects, 89 samples taken, 50 had adequate sample. Hysteroscopy and Tao brush: 90 subjects, 89 undertaken, 83 had adequate sample. 'Blind' Pipelle: 75 subjects, 75 undertaken, 36 had adequate sample. 'Blind' Tao brush: 75 subjects, 75 undertaken, 61 had adequate sample.</p>	

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
					<p>Success of visualisation and biopsy: hysteroscopy and Pipelle = 50%, hysteroscopy and Tao brush = 83%, ultrasound and Pipelle = 36%, ultrasound and Tao brush = 61%.</p> <p>Moderate-risk group:            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:            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:            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:            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</p>	

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
					<p>reasons, 31 completed, 31 successful visualisation.</p> <p>Biopsy:  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:  High-risk group:  Possible cancer - hysteroscopy = 3, ultrasound = null. Endometrial thickness &gt; 4mm - hysteroscopy = null, ultrasound = 34.  Endometrial/uterine polyp - hysteroscopy = 17, ultrasound = 4  Uterine fibroids - hysteroscopy = 7, ultrasound = 29.  cervix suspicious - hysteroscopy = 1, ultrasound = null.  Cervical polyp - hysteroscopy = 9, ultrasound = null</p> <p>Moderate 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</p> <p>Low-risk group:  Endometrial/uterine polyp - hysteroscopy = 1, ultrasound = 2  Uterine fibroids - hysteroscopy = 1, ultrasound = 6.  Cervical polyp - hysteroscopy = 1, ultrasound = null</p> <p>Abnormalities identified by biopsy:  High-risk group:  Endometrial cancer = 5. Hyperplasia = 2. Atrophic endometrium = 12. Inactive endometrium = 106. Cyclic endometrium = 26. Other = 27</p>	

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
					<p>moderate-risk group: Endometrial cancer = 3. Hyperplasia = 3. Atrophic endometrium = 0. Inactive endometrium = 19. Cyclic endometrium = 213. Other = 59</p> <p>Low-risk group: Endometrial cancer = 0. Hyperplasia = 0. Atrophic endometrium = 0. Inactive endometrium = 2. Cyclic endometrium = 91. Other = 0</p> <p>Sensitivity (%), specificity (%), PPV (%), PNV (%) of investigations for endometrial cancer:            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).            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)            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)            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:            Ultrasound = 0, hysteroscopy = 12, blind biopsy = 9</p> <p>Investigation 'unpleasant':            Hysteroscopy = 27%, ultrasound = 11%, biopsy = 29%. (rates higher for low-risk group).</p>	

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
De Crespigny 1997 <sup>167</sup>	diagnostic; comparative; prospective  Evidence Level: 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 Sonohystrosalpingography (SIS); transvaginal ultrasound (TVS); hysteroscopy - reference, not whole sample	55 of 60 examinations completed.  Disagreement between SIS and TVS: 12 polyps identified on SIS but not TVS; 7 had endometrial polyp on TVS but not on SIS.  11 hysteroscopies avoided due to SIS. 15 of 16 hysteroscopies agreed with SIS.	Funding Source: not stated
De Vries 2000 <sup>168</sup>	Diagnostic; prospective; cohort  Evidence Level: II	62	Women; premenopausal; AUB; scheduled for hysteroscopy  Country: Netherlands	Transvaginal Sonography; Saline Infusion Sonography; Hysteroscopy	Accuracy of TVS at identifying intrauterine pathology compared to hysteroscopy: sensitivity = 60% (12 of 20), specificity = 93% (39 of 42), +LR = 8, -LR = 0.43  Accuracy of SIS at identifying intrauterine pathology compared to hysteroscopy: sensitivity = 68% (14 of 16), specificity (39 of 41) = 95%, +LR = 10, -LR = 0.13	Funding Source: Not stated  Study Summary: SIS was more accurate test than TVS for identifying uterine pathology.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Dijkhuizen 2000 <sup>225</sup>	systematic review; meta-analysis  Evidence Level: 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: 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&amp;C or both were, respectively, used as reference method. The specificities were 99.7%, 99.6% and 99.9%, respectively. Study quality criteria - blinding, prospective - had no impact on study outcomes.</p> <p>Identification of atypical hyperplasia: 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&amp;C or both were, respectively, used as reference method. The specificities were 100%, 99.1% and 100%, respectively.</p> <p>Studies show statistically significant (<math>p = 0.01</math>) differences between Pipelle method and others in terms of sensitivity and specificity for identification of hyperplasia.</p>	<p>Funding Source: Not stated</p> <p>Study Summary: Pipelle biopsy is superior to other methods in identification of endometrial cancer and hyperplasia.</p>
Dijkhuizen 1996 <sup>169</sup>	diagnostic; blinded  Evidence Level: 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>	<p>Funding Source: Not stated</p> <p>Study Summary: Limited use in women with irregular menstrual bleeding</p>



Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Dijkhuizen 2000 <sup>170</sup>	diagnostic; prospective; cohort  Evidence Level: II	50 - received both transvaginal ultrasound & 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 to histopathology for identification of pathology: sensitivity = 61%, specificity = 96%, +LR = 16, -LR = 0.41  Saline infusion sonography: Accuracy of SIS compared to 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 <sup>171</sup>	diagnostic; prospective; cohort; comparative  Evidence Level: 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 to pathology for identification of polyps or submucous myomas: sensitivity = 92%, specificity = 62%, PPV = 80%, NPV = 82%  Diagnostic accuracy of transvaginal ultrasound compared to pathology for identification of any abnormality (including hyperplasia at >12mm cut-off): sensitivity = 93%, specificity = 54%, PPV = 79%, NPV = 82%  Diagnostic accuracy of saline contrast sonohysteroscopy compared to pathology for identification of polyps or submucous myomas: sensitivity = 99%, specificity = 72%, PPV = 85%, NPV = 98%  Diagnostic accuracy of saline contrast sonohysteroscopy compared to pathology for identification of any abnormality (including hyperplasia at >12mm 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

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Dueholm 2001 <sup>172</sup>	Diagnostic; prospective; comparative  Evidence Level: 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 <=4mm and 0.077 where <=7mm.  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 <sup>145</sup>	Epidemiology; case-control  Evidence Level: 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 >80ml, 22 had MBL <80ml.  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 <sup>173</sup>	Diagnostic; comparative; prospective  Evidence Level: 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.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Emanuel 1995 <sup>174</sup>	diagnostic comparison; prospective  Evidence Level: II	279 - 19 not evaluable	women; referred by GP due to AUB  Country: Netherlands	Transvaginal ultrasonography; hysteroscopy - reference	<p>Patient population (n = 260): menorrhagia = 109; metrorrhagia = 104; postmenopausal bleeding = 47</p> <p>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.</p> <p>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.</p>	<p>Funding Source: Not stated</p> <p>Study Summary: Transvaginal sonography effective at excluding pathology in AUB</p>
Fedele 1992 <sup>80</sup>	diagnostic; pre- and post treatment  Evidence Level: II	43	women; recurrent menorrhagia; enlarged uterus; no evidence of leiomyomas on examination; scheduled for hysterectomy; .  Country: Italy	transvaginal ultrasound; histopathology post-hysterectomy - reference	<p>Ultrasonography results: 22 of 43 had adenomyosis, 4 had leiomyomas &gt;10cm.</p> <p>Pathologist: 20 had adenomyosis, confirming 16 US findings, 6 were excluded, 4 new cases.</p> <p>US sensitivity = 80%, specificity = 74%, PPV 73%, PNV = 81%.</p>	<p>Funding Source: Not stated</p>

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Fedele 1991 175	diagnostic; comparative  Evidence Level: 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 between type of pathology.
Ferry 1993 221	diagnostic; comparative  Evidence Level: 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 569	Diagnostic; comparison  Evidence Level: 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

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Fukuda 1993 <sup>177</sup>	diagnostic; comparative  Evidence Level: 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	<p>TVS identified - 22 submucous myomas, 10 intramural myomas, 4 endometrial polyps. TVHS identified - 20 submucous myomas, 12 intramural myomas, 4 endometrial polyps.</p> <p>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.</p> <p>Misdiagnosis rates were: 36% for TVS, an 2.8% for TVHS.</p> <p>Sensitivity: TVS = 73.7%, TVHS = 100%</p> <p>Specificity: TVS = 52.9%, TVHS = 93.8%</p> <p>PPV: TVS = 63.6%, TVHS = 95%</p> <p>PNV: TVS = 64.3%, TVHS = 100%</p>	<p>Funding Source: Not stated</p> <p>Study Summary: TVHS better than TVS for diagnosis of fibroids.</p>

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Garuti 2001 <sup>178</sup>	diagnostic; comparison; retrospective  Evidence Level: 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 to 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

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Gimpelson 1988 220	diagnostic; comparative; retrospective  Evidence Level: III	276	women; referred for investigation due to AUB, postmenopausal bleeding, suspected myoma; infertility  Country: USA	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 hyperplasia = 1, Other = 6  9 cases (3%) biopsy provided reduced results.  In 8 cases D&C missed diagnosis.	Funding Source: Not stated  Study Summary: Study shows direct biopsy better than D&C at identifying pathology.
Goldchmit 1993 570	Diagnostic; comparison  Evidence Level: II	176 - 41 postmenopausal, 135 pre-menopausal	women; scheduled for D&C  Country: Israel	Pipelle biopsy; D&C; sonography	Sensitivity, specificity, PPV, NPV for Pipelle biopsy compared to histology for identifying pathology: 82%, 99%, 93%, 98%  Sensitivity, specificity, PPV, NPV for Pipelle biopsy & endometrial thickness > 5mm compared to histology for identifying pathology: 92%, 96%, 92%, 96%  Pipelle versus 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 179	Diagnostic; screening  Evidence Level: III	433	women; referred for assessment due to AUB - menorrhagia, metrorrhagia, etc.; peri-menopausal; >39 years of age; using contraceptives or pregnant excluded  Country: USA	Endovaginal ultrasound	Results of Ultrasound: 280 (65%) had thin, distinct, symmetric endometrial echo <5mm = diagnosed with DUB.  153 (35%) had saline sonohysterography - 44 due to inadequate ultrasound, 109 due to endometrium > 5mm.  Sonohysterography results:  61 (40%) endometrium < 3mm, 58 (38%) polyps, 22 (7%) submucous myomas, 10 (7%) thick symmetric endometrium >3mm; 2 (1%) inadequate scan.	Funding Source: Not stated  Study Summary: Imaging allows for identification of pathology that is potentially missed by biopsy alone.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Guven 2004 <sup>180</sup>	diagnostic; randomised; non-blinded  Evidence Level: Ib	197 - 139 pre-menopausal, 67 postmenopausal	Women; presenting with history of AUB  Country: Turkey	Transvaginal ultrasonography; hydrosoneography; surgical histopathology - reference	Diagnostic accuracy of transvaginal sonography: sensitivity = 56%, specificity = 68%, PPV = 75%, NPV = 48%  Diagnostic accuracy of hydrosoneography: sensitivity = 81%, specificity = 73%, PPV = 83%, NPV = 70%  No data on acceptability or success of methods	Funding Source: Not stated  Study Summary: Hydrosoneography is more accurate than TVS in detection of uterine pathology.
Harmanli 2005 <sup>181</sup>	Evidence Level: 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 versus 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% PNV = 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 <sup>571</sup>	Diagnostic; comparative; prospective  Evidence Level: 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



Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Indman 1995 <sup>182</sup>	diagnostic; comparative  Evidence Level: II	238	women; referred for evaluation of AUB; aged 25 to 75  Country: USA	transvaginal ultrasound; hysteroscopy; curettage	<p>Hysteroscopy versus 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.</p> <p>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.</p> <p>Ultrasound sensitivity = 94%, specificity = 89%, PPV = 87%, NPV = 89%.</p>	<p>Funding Source: not stated</p> <p>Study Summary: Transvaginal ultrasound provides excellent diagnostic outcome.</p>

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Kavak 1996 <sup>183</sup>	diagnostic; comparative; cohort  Evidence Level: 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 0mm to 18mm, mean = 6.99 (+/- 3.4mm).  No disease group, mean = 7.04 (+/- 2.9mm) Benign disease group, mean = 7.45 (+/- 3.4mm) Carcinoma group, mean = 15 (+/- 1.4mm) (P<0.01 for carcinoma group vs. others).  Sensitivity for endometrial disease = 88.5% based on 5mm 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 to histology sensitivity = 22/23 specificity = 38/38 PPV = 22/22 PNV = 38/39  excluding insufficient material	Funding Source: Not stated

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Kelekci 2005 <sup>184</sup>	Randomised; double blind; no mention of concealment  Evidence Level: 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 <sup>185</sup>	Diagnostic; comparative; prospective  Evidence Level: 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.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Khanna 2001 <sup>186</sup>	diagnostic; cohort; comparative  Evidence Level: III	70	women; AUB; excluded if pregnant; unmarried with pelvic infection, endocrine problems or coagulation disorder.  Women aged 20> years; 9 of 70 had menorrhagia  Country: India	Transvaginal ultrasound, saline infusion sonography; hysteroscopy - reference	Transvaginal ultrasound compared to histopathology for identification pathology at 5mm 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 to histopathology for identification of pathology: true-positive = 19, false-positive = 6, true-negative = 43, false-negative = 2 (15 with atrophy) - REVIEWER CALCULATED  Sensitivity = 90.4%, specificity = 87.5%  Hysteroscopy compared to histopathology for identification of pathology: sensitivity = 97.2%, specificity = 90.6%, PPV = 92.1%, NPV = 96.6%	Funding Source: Not stated
Koonings 1990 <sup>187</sup>	Diagnostic; comparison; RCT  Evidence Level: 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.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Koss 1984 <sup>222</sup>	Epidemiologic al study  Evidence Level: 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 Isacca devices	<p>Success of device: Mi-Mark successful in 1117 (86.39%) of cases. Isaac successful in 1194 (92.34%) of cases (P &lt; 0.001)</p> <p>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.</p> <p>Prevalence of carcinoma: 16 occult carcinomas, 2 missed carcinomas from 2586 women. 6.96 per 1000</p> <p>Prevalence of Hyperplasia: 17 hyperplasia, 4 polyps with hyperplasia fro 2586. 8.12 per 1000.</p> <p>Incidence of carcinoma = 1.71 per 1000.</p> <p>Incidence of hyperplasia = 1.71 per 1000.</p> <p>Risk-factors: White versus non-white OR = 1.65:1 (NS). Parity OR = 1.07:1 (NS). Onset of menopause: &lt;49 = 5.1 per 1000, &gt;56 = 32.3 per 1000. (p &lt; 0.04). Obesity OR = 1.26:1 (NS). Oestrogen OR = 1.31:1 (NS).</p>	<p>Funding Source: National Cancer Institute</p> <p>Study Summary: Study shows the risk factors for endometrial cancer.</p>

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Krampl 1997 <sup>188</sup>	Diagnostic  Evidence Level: 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 +/- 5.83.  Pipelle vs. hysterectomy (n=75), average age = 52.75 +/- 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 <sup>189</sup>	diagnostic; prospective; comparative; blind assessment  Evidence Level: Ib	100	Women referred for AUB; excluded if had biopsy within 12 months, multiple, large fibroids causing discomfort  Country: Norway	transvaginal ultrasonography; sonohysteroscopy; 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: Sonohysteroscopy has considerably better results than transvaginal ultrasound.

<b>Bibliographic Information</b>	<b>Study type &amp; Evidence level</b>	<b>Number of patients &amp; prevalence</b>	<b>Population Characteristics</b>	<b>Type of test and Reference standard</b>	<b>Sensitivity &amp; Specificity &amp; PPV &amp; NPV</b>	<b>Study Summary</b>
Laughead 1997 <sup>190</sup>	diagnostic  Evidence Level: II	124 - 114 underwent saline solution infusion sonohysterography. 10 with thin endometrium (< 4mm) 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 13.7cm); 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
Law 1993 <sup>191</sup>	Diagnostic  Evidence Level: 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 <sup>192</sup>	Diagnostic; comparison; randomised; blind  Evidence Level: 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.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Litta 1996 <sup>193</sup>	diagnostic  Evidence Level: 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 versus 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 <sup>86</sup>	Diagnostic; comparison  Evidence Level: 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 to histology: 65% (32/49), 100% (102/102), 100% (32/32), 17% (17/102)  Sensitivity, specificity, PPV, NPV of hysteroscopy with tissue sample compared to 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.



Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
MacKenzie 1978 <sup>74</sup>	Diagnostic  Evidence Level: 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 polypus = 21 (2.0%) Endometrial carcinoma = 15 (1.4%) Inadequate sample = 85 (8.3%) No curetings = 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 <sup>194</sup>	Diagnostic; comparative; non-blinded  Evidence Level: 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.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Mathew 2000 <sup>195</sup>	Diagnostic; prospective; cohort  Evidence Level: II	110	Women; presenting with AUB  70 with menorrhagia, 29 with metrorrhagia, 11 were post-menopausal bleeding  Country: Oman	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
Mihm 2002 <sup>196</sup>	diagnostic; comparison; cohort; blinded  Evidence Level: 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 & biopsy compared to 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 & biopsy is an accurate method for identification of pathology.
Miller 2001 <sup>562</sup>	Epidemiologic cohort  Evidence Level: 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's disease	African-Americans had higher vWF:ag (p = 0.001), FVIII (P = 0.008) and vWF:Act (p= 0.006) than Caucasian population. VWF:Rcof, 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 to Caucasian population. This suggest tests should take account of these differences

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Nagele 1996 <sup>73</sup>	Diagnostic  Evidence Level: 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 <sup>197</sup>	diagnostic; randomised (alternate)  Evidence Level: 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 CO2  Requiring cervical dilation for hysteroscopy: saline = 17.9% vs. 35.4% for CO2  Visualisation: OR of poor or very poor = 1.94 (95% CI 0.61 to 6.74)  Hysteroscopy unsuccessful in 2 saline and 4 CO2 patients.  Pain during procedure was: 4 for saline group and 11 for CO2 group (OR = 0.33, 95% CI 0.08 to 1.20)	Funding Source: Not stated  Study Summary: Saline is equivalent to CO2 in terms of use for distension for hysteroscopy.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Nanda 2002 <sup>198</sup>	diagnostic; prospective; comparative  Evidence Level: 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 <sup>199</sup>	Diagnostic; comparative; prospective  Evidence Level: 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 & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Paschopoulos 2001 <sup>200</sup>	diagnostic; retrospective; case-series  Evidence Level: 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 <sup>201</sup>	Prospective; cohort  Evidence Level: 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

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Pasqualotto 2000 <sup>202</sup>	Retrospective; diagnostic  Evidence Level: III	375	Women; referred with AUB.  Patient characteristics: average age = 49.4 (+/- 13.5); BMI = 28.5 (+/- 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
Pasrija 2004 <sup>203</sup>	diagnostic; cohort  Evidence Level: 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 to histopathology: sensitivity = 84.8%, specificity = 79%, PPV = 82.4%, NPV = 82%.  Saline infusion sonohysteroscopy compared to histopathology: sensitivity = 94.1%, specificity = 88.5%, PPV = 91.4%, NPV = 92%	Funding Source: Not stated

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Philipp 2005 <sup>572</sup>	diagnostic comparison  Evidence Level: II	81	women; subjective menorrhagia (>7 days bleeding); pathology or IUD excluded. Non-pregnant. NSAIDs or anti-platelet treatments 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	Haemostatic testing; platelet function analyser (PFA-100); bleeding time (BT)	Sensitivity, specificity, PPV and NPV of PFA-100 compared to haematology for identifying vWD = 80%, 89%, 33%, 98%  Sensitivity, specificity, PPV and NPV of BT compared to haematology for identifying vWD = 60%, 68%, 12%, 96%  Based on vWF = vWF/Rco 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

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Pungetti 1990 <sup>204</sup>	Evidence Level: 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 <sup>205</sup>	diagnostic; comparison; prospective; blinded  Evidence Level: 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.



Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Ryu 2004 <sup>206</sup>	comparative; diagnostic; retrospective  Evidence Level: 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 & biopsy, hysterectomy (reference)	Accuracy of transvaginal ultrasound compared to pathology for identification uterine pathology: sensitivity = 0.79, specificity = 0.46, PPV = 0.83, NPV = 0.39  Accuracy of hysterosonography compared to 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 <sup>207</sup>	Diagnostic; randomised; trial; non-blinded  Evidence Level: 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: age = 53.2 parity = 1.70 Gravidity = 1.97  Country: USA	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

<b>Bibliographic Information</b>	<b>Study type &amp; Evidence level</b>	<b>Number of patients &amp; prevalence</b>	<b>Population Characteristics</b>	<b>Type of test and Reference standard</b>	<b>Sensitivity &amp; Specificity &amp; PPV &amp; NPV</b>	<b>Study Summary</b>
Salim 2005 <sup>208</sup>	Diagnostic; double-blind  Evidence Level: 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 <sup>209</sup>	diagnostic; comparative  Evidence Level: 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

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Schwarzler 1998 <sup>210</sup>	Diagnostic; comparison; prospective; partial-blinded  Evidence Level: 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	<p>Sensitivity, specificity, PPV, NPV of TVS for identification of any pathology compared to operative hysteroscopy: 67%, 89%, 88%, 71%. Polyps: 56%, 97%, 86%, 87%. Fibroids: 82%, 98%, 82%, 96%</p> <p>Sensitivity, specificity, PPV, NPV of sonohysterography for identification of any pathology compared to operative hysteroscopy: 87%, 91%, 92%, 86%. Polyps: 84%, 97%, 91%, 85%. Fibroids: 94%, 98%, 89%, 99%</p> <p>Sensitivity, specificity, PPV, NPV of diagnostic hysteroscopy for identification of any pathology compared to operative hysteroscopy: 90%, 91%, 92%, 89%. Polyps: 92%, 100%, 100%, 97%. Fibroids: 88%, 100%, 100%, 98%.</p> <p>Discomfort with TVS - 58% had no discomfort, 40% had slight discomfort and 2% found treatment unpleasant.</p> <p>Discomfort with sonohysterography - 34% had no discomfort, 53% had slight discomfort, 13% found the test unpleasant. This resulted in 1% of sonohysteroscopies being halted.</p> <p>No data on hysteroscopy.</p>	<p>Funding Source: Austrian FWF Foundation</p> <p>Study Summary: Study shows that sonohysterography is an alternative to hysteroscopy, and better than transvaginal ultrasound.</p>
Smith 1991 <sup>211</sup>	diagnostic; comparative  Evidence Level: III	45	women; postmenopausal bleeding  Country: USA	Transvaginal ultrasound; Histopathology	<p>Ultrasound compared to histopathology: normal-normal = 22, normal-abnormal = 0, abnormal-normal = 14, abnormal-abnormal = 9</p>	<p>Funding Source: Not stated</p> <p>Study Summary: Ultrasound may be a useful initial diagnostic method for assessing endometrial pathology</p>

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Stovall 1991 78	randomised; comparative; blind  Evidence Level: 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.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Tahir 1999 <sup>223</sup>	diagnostic; randomised  Evidence Level: 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 & curettage; outpatient - vaginal ultrasound, outpatient hysteroscopy - reference, Pipelle endometrial biopsy.	<p>Patient population: menorrhagia - inpatient = 75 &amp; 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: 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 <math>\chi^2</math>, <math>p = 0.0076</math>), but detected 2 hyperplasia and 1 carcinoma not found on hysteroscopy.</p> <p>Patient pain (VAS) = inpatient median score = 1.5, outpatient = 3.5 (<math>p &lt; 0.0001</math>)</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>

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Taylor 2001 <sup>212</sup>	diagnostic; health service research; cohort  Evidence Level: III	264	women; pre- menopausal; AUB  Country: UK	Ultrasound - abdominal or vaginal; hysteroscopy - reference; bleeding pattern	Comparison of ultrasound with hysteroscopy for identification of pathology: true-positive = 15, false-positive = 16, true negative = 140, false-negative = 25  Sensitivity = 37.5%, specificity = 89.7%	Funding Source: Not stated  Study Summary: Ultrasound had no additional impact on patient management, in those with normal findings.
Teal 1998 <sup>219</sup>	Diagnostic  Evidence Level: 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	Of 114 patients: 112 procedures attempted 95 successful entry to endometrial cavity (83%) 9 no sample obtained (8%) 17 Unsuccessful entry to endometrial cavity (15%) 62 Adequate material for histology (54.4%) 24 material inadequate for histology (21%) Of which 2 were later found to have cancer (1.8%)  Subsequent D&C/H&C 40 (35%)	Funding Source: Not stated  Study Summary: Successful Pipelle curette is a useful diagnostic tool, but when unsuccessful or ambiguous then a more definitive method must be used.
Torrejon 1997 <sup>213</sup>	Comparative; case-series; retrospective  Evidence Level: III	1398 selected patients	Women; referred for AUB who underwent hysteroscopy then later D&C.  Country: Spain	hysteroscopy; D&C - reference	In pre-menopausal women the accuracy of hysteroscopy compared to D&C for identification of pathology was: sensitivity = 71.8%, specificity = 96.4%, PPV = 79.3%, NPV = 94.7%	Funding Source: Not stated  Study Summary: In AUB population, hysteroscopic is a should be a basic diagnostic tool.

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Towbin, 1996 <sup>214</sup>	diagnostic  Evidence Level: II	149	women; referred for excessive menstrual bleeding;  Country: USA	transvaginal ultrasonography; office hysteroscopy; inpatient hysteroscopy/hysterectomy - reference	140 of 149 underwent endometrial biopsy; 124 of 149 underwent ultrasonography; 149 of 149 underwent hysteroscopy.  Hysteroscopy identified: 42 as normal; 53 myoma; 36 endometrial polyps; 6 hyperplasia; 17 adenomyosis; 2 atrophic endometrium.  Ultrasonography identified: 59 as normal; 52 with leiomyoma; 11 with thickened uterine wall; 2 polypoid lesions.  Hysteroscopy: sensitivity = 79%, specificity = 93%  Ultrasonography: sensitivity = 54%, specificity = 90%	Funding Source: not stated  Study Summary: Study shows office hysteroscopy is a suitable method for investigating excessive menstrual bleeding
Valle 1981 <sup>76</sup>	Diagnostic  Evidence Level: 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.  Endometrial polyps = 37, 29, 5 Submucous leiomyoma = 12, 2, 0 Atrophic endometrium = 17, 15, 12 Adenomatous hyperplasia = 6, 5, 1 Adenocarcinoma = 3, 3, 1	Funding Source: Not stated  Study Summary: Hysteroscopy provides a useful method for identifying intrauterine pathology not available using 'blind' D&C

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Vercellini 1997 <sup>72</sup>	Diagnostic  Evidence Level: 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 to hysteroscopy = 96%, 86%, 91%, 94%  Sensitivity, specificity, PPV, PNV of hysteroscopy compared to hysterectomy (n = 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 <sup>81</sup>	diagnostic study  Evidence Level: 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.



Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Widrich 1996 215	Diagnostic; prospective; blinded  Evidence Level: Ib	130 - 113 both diagnostic procedures - 64 pathology results	women; referred for investigation  Country: USA	Saline infusion sonography; hysteroscopy; pathology - reference	<p>SIS compared to hysteroscopy (n = 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.</p> <p>SIS versus pathology (n = 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.</p> <p>Hysteroscopy versus pathology (n = 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.</p>	<p>Funding Source: Not stated</p> <p>Study Summary: SIS was well tolerated method. Both hysteroscopy and SIS had advantages and disadvantages in terms of diagnosis power.</p>
Widrich 1996 215	Diagnostic; prospective; blinded  Evidence Level: Ib	130 - 113 both diagnostic procedures - 64 pathology results	women; referred for investigation  Country: USA	Saline infusion sonography; hysteroscopy; pathology - reference	<p>SIS compared to hysteroscopy (n = 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.</p> <p>SIS versus pathology (n = 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.</p> <p>Hysteroscopy versus pathology (n = 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.</p>	<p>Funding Source: Not stated</p> <p>Study Summary: SIS was well tolerated method. Both hysteroscopy and SIS had advantages and disadvantages in terms of diagnosis power.</p>

Bibliographic Information	Study type & Evidence level	Number of patients & prevalence	Population Characteristics	Type of test and Reference standard	Sensitivity & Specificity & PPV & NPV	Study Summary
Wood, 1993 216	diagnostic  Evidence Level: 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

## Chapter 5 – Investigations for HMB

### Tests for exclusion of underlying conditions – Non-comparative studies

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
2001 <sup>217</sup>	Study Type: Recommendations of ACOG  Evidence Level: 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 <sup>151</sup>	Study Type: cohort  Evidence Level: 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): <20ml (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 (<60ml) vs. Heavy (>60ml). 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 80ml not 60ml.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Claessens 1981 <sup>149</sup>	Study Type: Epidemiology  Evidence Level: 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 von Willebrand's, 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. .
Decloedt 1999 <sup>87</sup>	Study Type: diagnostic; epidemiology; retrospective  Evidence Level: 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.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Gao 1987 152	Study Type: epidemiological cohort  Evidence Level: 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	<p>MBL (ml): range 4.1 to 273.6ml, mean 54.2 (SD 37). 5th and 95th percentiles = 14.2 and 124.1. 2sd range = 11.3 to 169.</p> <p>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</p> <p>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.</p> <p>Results by MBL: MBL, % haemoglobin &lt;12 g/dl, % ferritin &lt;16 ng/ml, % with both.            &lt;20ml (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%            &gt;100 (n=46) 30.4%, 82.6%, 26.1%.</p>	<p>Funding Source: United Nations Fund for Population Activities</p> <p>Study Summary: Study shows higher average MBL than with European and US populations</p>
Hallberg 1966 30	Study Type: Cross-sectional survey  Evidence Level: 3	Menstrual patterns	748 approached - data available on 476. Women either refused or were excluded.	women; age stratified 15-50; menstruating  Country: 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 &gt;12 g/100ml, plasma iron &gt;80 ug/100ml, MCHC &gt; 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>Funding Source: Swedish Medical Council</p> <p>Study Summary: MBL &gt;80 ml is seen as abnormal based on average MBL and change in blood counts.</p>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						<p>All subjects: Haemoglobin concentration decrease (<math>p &lt; 0.01</math>) at <math>&gt; 80\text{ml}</math> MBL. MHC decrease (<math>p &lt; 0.01</math>) at <math>&gt; 80\text{ml}</math>. Iron concentration decrease (<math>p &lt; 0.01</math>) at <math>&gt; 80\text{ml}</math>.</p> <p>Series B - 95th percentile = 76.4ml</p>	
Haynes 1979 <sup>146</sup>	Study Type: cohort  Evidence Level: 3	pattern of MBL	50 women	Women; MBL $> 80\text{ml}$  Country: UK	Description of MBL	<p>Daily MBL (<math>n = 11</math>) - 70% by 2nd day and 92% by 3rd.</p> <p>Duration of menses and MBL: no association between duration and total MBL.</p>	<p>Funding Source: Not stated</p> <p>Study Summary: No association between length of menses or distribution of MBL and having menorrhagia. No gross ovarian pituitary pathology in majority of patients.</p>
Janssen 1998 <sup>31</sup>	Study Type: Epidemiological ; Cohort  Evidence Level: 3	measurement of MBL	313	Women; aged 18-50; no amenorrhea.  Country: Netherlands	MBL - alkaline haematin; haemoglobin; anaemia; ferritin; subjective assessment of heavy bleeding	<p>Haemoglobin significantly decreased (<math>p &lt; 0.05</math>) at 60MBL. Anaemia increased rapidly at 60ml and then again at 120ml. Ferritin decreased at 20ml. Low ferritin at 40ml.</p> <p>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%, <math>&gt; 240 = 93.8</math></p>	<p>Funding Source: Not stated</p> <p>Study Summary: Risk of developing anaemia increases substantially at 120ml, not 80ml. Suggests that 80ml definition of menorrhagia needs to be revised upwards.</p>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Kadir 1998 <sup>54</sup>	Study Type: Cohort; epidemiology  Evidence Level: 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 <sup>150</sup>	Study Type: Epidemiology  Evidence Level: 3	Blood test - haemoglobin levels, serum iron levels; questionnaire - socio-economic-cultural variables	24894	Men & 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	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.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						not.	
Rodeghiero 1987 <sup>55</sup>	Study Type: epidemiology; cohort  Evidence Level: 3	Test for von Willebrand's 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.



## Chapter 6 – Hormonal Treatments for HMB

### Combined Oral Contraceptive for treatment of HMB – Comparative studies

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Coulter 1995 <sup>275</sup>	Study Type: Systematic review; meta-analysis  Evidence level: 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).	Funding Source: Not stated  Study summary: Studies of this preparation report greater reductions in blood loss but slightly more side effects than Mefenamic acid.

							<p>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>	
Fraser 1991 276	<p>Study Type: randomised</p> <p>Evidence level: 1+</p>	<p>45 in total. 7 dropped out. 38 assessed: 19 in Mefenamic (across 3 groups); 7 naproxen; 6 OCP; 6 Danazol</p>	<p>Population characteristics: Women; menorrhagia - ovulatory DUB; no pathology; no hormonal therapy within 3 months</p> <p>Country: Australia</p>	<p>Mefenamic acid (500mg x 3); naproxen; low dose monophasic oral contraceptive - ethinyl oestradiol 30ug &amp; levonorhestrel 150ug for 21 days; Danazol (200mg) daily</p> <p>Treatment versus baseline</p>	<p>8 consecutive cycles: 2 no treatment; 2 treatment; 2 no treatment; 2 treatment</p>	<p>MBL - alkaline haematin</p>	<p>Mefenamic acid - group 1 - control = 131.1ml (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&lt;0.001)(-39%);</p> <p>Naproxen - control = 131.1 ml versus treatment = 115.6 (SD 113) ml (P=0.079)(-12%);</p> <p>Oral contraceptive - 101 v 57.8, p&lt;0.001, -43%;</p> <p>Danazol - 90.3 v 45.5 (av), P&lt;0.001, -49%.</p> <p>Differences between Mefenamic v naproxen p=0.129; versus oral contraceptive P = 0.154; versus 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>

Iyer 2000 274	Study Type: Systematic review  Evidence level: 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
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## Chapter 6 – Hormonal Treatments for HMB

### Oral progestogens for treatment of HMB – Comparative Studies

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Bonduelle 1991 <sup>278</sup>	Study Type: randomised; open  Evidence level: 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 200mg daily fro 3 months; norethisterone 5mg X 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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Cameron 1987 <sup>264</sup>	Study Type: randomised  Evidence level: 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 >50ml  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 (200mg); Mefenamic acid (500mg x 3); norethisterone (5mg x 2); progesterone coil  treatment versus 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 = 203ml, treatment = 51ml; a - 75% change. Progesterone coil: pre-treatment = 64ml (p < 0.05), treatment = 45ml; 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Coulter 1995 <sup>275</sup>	Study Type: Systematic review; meta-analysis  Evidence level: 1+		Population characteristics: Searches undertaken on MEDLINE  Country:	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>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>	<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 & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Dunphy 1998 <sup>279</sup>	Study Type: randomised; double-blind  Evidence level: 1-	23: 11 medroxyproges- terone; 12 Danazol randomised; 9 medroxy, 9 Danazol analysed.	Population characteristics: women; menorrhagia (>80ml); >18 yrs; not pregnant; no contra-indications  Country: Canada	Danazol 200mg daily; medroxyprogesteron e acetate 10mg 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 = 7kg (SD 0.7)(p = 0.0078). Medroxy = 2.2kg (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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Fraser 1991 <sup>276</sup>	Study Type: randomised  Evidence level: 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 (500mg x 3); naproxen; low dose monophasic oral contraceptive - ethinyl oestradiol 30ug & levonorhestrel 150ug for 21 days; Danazol (200mg) daily  Treatment versus baseline	8 consecutive cycles: 2 no treatment; 2 treatment; 2 no treatment; 2 treatment	MBL - alkaline haematin	Mefenamic acid - group 1 - control = 131.1ml (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 versus treatment = 115.6 (SD 113) ml (P=0.079)(-12%);  Oral contraceptive - 101 v 57.8, p<0.001, -43%;  Danazol - 90.3 v 45.5 (av), P<0.001, -49%.  Differences between Mefenamic v naproxen p=0.129; versus oral contraceptive P = 0.154; versus Danazol p = 0.079.  Side-effects not reported.	Funding Source: Commercial funding  Study summary: All treatments reduce MBL.



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Higham 1993 <sup>260</sup>	Study Type: randomised; single blind  Evidence level: 1+	57: 19 Danazol 200mg; 19 Danazol reducing dose; 19 norethisterone	Population characteristics: women; regular cycle; menorrhagia (>80ml); no pathology; no concomitant treatment.  Danazol 200mg: 40.5 yrs, 65.6kg, cycle 28.2 days. Danazol reducing: 36.4 yrs, 63.1kg, 27.6 days. Norethisterone: 40.1yrs, 67.9kg, 28 days.  Country: UK	Danazol 200mg daily; Danazol 200mg cycle 1, 100mg cycle 2, 50mg cycle 3; Norethisterone 5mg x 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 200mg (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 200mg vs. norethisterone p = 0.017.  Side-effects: Danazol reducing dose = 15, Danazol 200mg = 17, norethisterone = 11.  10 withdrawals: 5 Danazol reducing - lack of efficacy; side-effects; 3 Danazol 200mg - side- effects; 2 norethisterone - side- effects..	Funding Source: Sanofi Winthrop Ltd  Study summary: Danazol more effective than norethisterone.
Irvine 1998 <sup>267</sup>	Study Type: randomised, allocation concealed  Evidence level: 1+	44: 22 LNG- IUS, 22 norethisterone. 8 did not complete - 6 norethisterone, 2 IUS.	Population characteristics: women; 18-45 yrs; no pathology; no hormonal 3 months or injected contraceptives in	LNG-IUS; norethisterone (5mg from day 5-26 of cycle)  treatment versus baseline; treatment versus 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 20ml at 3rd cycle (P<0.001) (-83%).	Funding Source: Not sated  Study summary: LNG- IUS is an alternative to hysterectomy and ablation.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			12 months.  LNG-IUS group: av. 38.5 yr, 158.5cm height, 69.9kg weight. Norethisterone: 39 yrs, 159.5cm, 71.4 kg.  Country: UK				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	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Lethaby 2004 <sup>277</sup>	Study Type: Systematic review  Evidence level: 1++	7 RCTs	Population characteristics: For the update of this review in 2003 we searched the Cochrane Menstrual Disorders & 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			Seven (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].	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			Country:					

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Preston 1995 <sup>281</sup>	Study Type: Randomised; double-blind; placebo- controlled; concealed; cross-over  Evidence level: 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 yrs, 71.2 kg. Net: 39.3 yrs, 63.5kg (P < 0.048)  Setting: university O&G department  Country: UK	Tranexamic acid (1g x 4) for 4 days or norethisterone (5mg x 2) for 8 days or Placebo  Treatment v treatment; treatment v placebo	4 consecutive cycles: 2 baseline/placebo; 2 treatment	Menstrual blood loss - alkaline haematin; QoL; side-effects	Tranexamic acid (n=25): Change from 175ml to 97ml (95% CI 62 to 108)(P<0.0001); 45% reduction (+23 to -93; p<0.0001). Norethisterone (n = 21): Change from 173ml to 208 ml (-64 to +2)(p=0.26); 20% increase (+114 to -62; 9<0.0001). Between groups difference was 113ml (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. :

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Fraser IS; 1990 <sup>282</sup>	Study Type: cohort; comparative  Evidence level: 2-	16: 10 with menorrhagia	Population characteristics: women; confirmed menorrhagia  Country: Australia	Norethisterone 5mg X 3; Medroxyprogesterone acetate (MPA) 10mg X 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 = 104ml and 6.4 days duration; 2nd baseline = 107.5ml and 6.6 days; 1st treatment = 72ml, 5.4 day; 2nd = 67ml, 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

## Chapter 6 – Hormonal Treatments for HMB

### LNG-IUS for treatment of HMB – Comparative studies

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Barrington 2003 262	Study Type: randomised  Evidence level: 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 >12cm  Country: UK	LNG-IUS; thermal balloon ablation  treatment versus baseline	6 months	MBL - PBAC	MBL (mean): IUS pre-treatment = 107ml vs. 31ml post-insertion (-71%); Ablation pre-treatment = 122ml vs. 61ml post-surgery (-50%). No difference between groups (p=0.689).  MBL (median): IUS pre-treatment = 75ml vs. 19ml post-insertion; Ablation pre-treatment = 101ml vs. 27ml post-surgery.	Funding Source: not stated  Study summary: Study shows LNG-IUS and thermal ablation are equivalent.
Busfield 2006 263	Study Type: randomised; non-blinded; concealed  Evidence level: 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)	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 (SD86.5) vs. 94.7 (SD 112.0); p = 0.002	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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			<p>&gt; 3cm in diameter), laboratory abnormalities, hysteroscopic abnormalities (endometrial polyps), irregular bleeding, chronic pelvic pain, severe dysmenorrhoea, medical contraindications to procedures, untreated abnormal cervical cytology.</p> <p>Baseline characteristics (LNG-IUS versus TBA):</p> <p>Age &lt; 40 = 7 vs. 13</p> <p>Age 40 to 44 = 21 vs. 16</p> <p>Age 45 to 49 = 14 vs. 12</p> <p>BMI = 28.8 vs. 29.7</p> <p>Nulliparous = 1 vs. 0</p> <p>PBAC score = 490 (SD 419) vs. 502 (SD 422)</p> <p>Country: New Zealand</p>				<p>24 months = 20.6 (SD 28.8) vs. 75.4 (SD 75.4); <math>p = 0.002</math></p> <p>Amenorrhoea:</p> <p>LNG-IUS vs. TBA; <math>p</math>-value.</p> <p>3 months = 2 vs. 5; <math>p = 0.236</math></p> <p>6 months = 3 vs. 1; <math>p = 0.613</math></p> <p>12 months = 6 vs. 2; <math>p = 0.254</math></p> <p>24 months = 9 vs. 1; <math>p = 0.025</math></p> <p>QoL (SF-36):</p> <p>LNG-IUS vs. TBA:</p> <p>Baseline = 63.7 (SD 22.7) vs. 63.7 (SD 14.4)</p> <p>3 months = 77.7 (SD 17.0) vs. 78.2 (SD 13.7)</p> <p>12 months = 79.3 (SD 16.5) vs. 76.9 (SD 16.8)</p> <p>24 months = 77.5 (SD 20.1) vs. 74.9 (SD 18.8)</p> <p>Complications:</p> <p>No major complications reported in either group.</p>	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.



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Cameron 1987 <sup>264</sup>	Study Type: randomised  Evidence level: 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 >50ml  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 (200mg); Mefenamic acid (500mg x 3); norethisterone (5mg x 2); progesterone coil  treatment versus 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 = 203ml, treatment = 51ml; a - 75% change. Progesterone coil: pre-treatment = 64ml (p < 0.05), treatment = 45ml; 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Coulter A 1995 <sup>275</sup>	Study Type: Systematic review; meta-analysis  Evidence level: 1+		Population characteristics: Searches undertaken on MEDLINE	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>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>	<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 & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Crosignani 1997 <sup>265</sup>	Study Type: randomised; open; prospective  Evidence level: 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	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 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	Funding Source: National Research Council (Rome)  Study summary: LNG- IUS produces slightly less satisfactory results than resection at 12- months.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							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 <sup>266</sup>	Study Type: randomised; prospective  Evidence level: 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	FSM levels increased from 8.4 iu/m at baseline to 13.8 iu/m at 12 months versus 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.
Hurskainen 2004 <sup>106</sup>	Study Type: randomised; allocation concealed; controlled  Evidence level: 1++	236: 119 LNG-IUS (57 had IUS; 10 nothing; 50 had hysterectomy by 5 years); 117	Population characteristics: women; menorrhagia; no pathology  Country: Finland	LNG-IUS; hysterectomy  treatment versus baseline; treatment versus 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).	Funding Source: Government grant  Study summary: Study shows that at 5-years LNG-IUS offered effective alternative to hysterectomy.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
		hysterectomy (109 had hysterectomy by 5 years). 5 LNG-IUS, 7 hysterectomy lost to follow-up.					<p>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 (<math>p = 0.8, 0.9, 0.9</math>).</p> <p>At 5-years: 50 LNG-IUS users had hysterectomy. Another 10 women were without LNG-IUS in situ. 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>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Hurskainen 2001 <sup>107</sup>	Study Type: randomised; allocation concealed  Evidence level: 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)	Funding Source: Government funded. IUD provided free by Leiras.  Study summary: Study shows LNG-IUS was effective alternative to hysterectomy at 12 months.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>Anxiety - IUS = 32.9 (30.8 to 33.2), Hysterectomy = 31.1 (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</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>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>	



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Irvine 1998 <sup>267</sup>	Study Type: randomised, allocation concealed  Evidence level: 1+	44: 22 LNG-IUS, 22 norethisterone. 8 did not complete - 6 norethisterone, 2 IUS.	Population characteristics: women; 18-45 yrs; no pathology; no hormonal 3 months or injected contraceptives in 12 months.  LNG-IUS group: av. 38.5 yr, 158.5cm height, 69.9kg weight. Norethisterone: 39 yrs, 159.5cm, 71.4 kg.  Country: UK	LNG-IUS; norethisterone (5mg from day 5-26 of cycle)  treatment versus baseline; treatment versus 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 20ml 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 & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Istre 2001 <sup>268</sup>	Study Type: Randomised  Evidence level: 1+	60: 30 LNG-IUS; 30 resection - 6 discontinued treatment by 12 months.	Population characteristics: women; menorrhagia (PBAC > 75); pre-menopausal; 30-49 yrs; regular uterine cavity <10cm; no pregnant or wanting to become so, breast feeding; large fibroid >40cm; 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Lahteenmaki 1998 <sup>269</sup>	Study Type: randomised, open, allocation concealed  Evidence level: 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 = 87mm (77, 92) vs. 79mm (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 <sup>260</sup>	Study Type: Systematic review; meta-analysis  Evidence level: 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 versus placebo: No studies  LNG-IUS versus 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)	Funding Source: No funding

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			Controlled Trials (CENTRAL) (The Cochrane Library Issue 2, 2005) MEDLINE (1966 to July 2005) EMBASE (1980 to July 2005) Current Contents (1995 to July 2005) 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) Current Controlled Trials, comprising the ISRCTN Register (a database of randomised controlled trials with an International Standard Randomised Controlled Trial Number) (July 2005 )				OR 1.22 [0.28, 5.24]  Side effects - menstrual pelvic pain (n = 51) OR 4.53 [1.15, 17.83]  Side effects - intermenstrual bleeding and menstrual irregularity (n = 31) OR 4.34 [1.01, 18.66]  Side effects - breast tenderness (n = 82) OR 5.66 [2.02, 15.87]  Side effects - nausea (n = 51) OR 0.50 [0.09, 2.69]  Side effects - diarrhoea (n = 51) OR 0.28 [0.05, 1.76]  Side effects - upper respiratory infection (n = 51) OR 1.05 [0.27, 4.12]  Side effects - ovarian cysts (n = 51) OR 2.32 [0.56, 9.65]  Side effects - headache (n = 51) OR 1.07 [0.35, 3.24]  Withdrawal from treatment because of adverse events (n = 44 ) OR 0.37 [0.07, 1.82]	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			MetaRegister of Controlled Trials (an international database combining registers of ongoing randomised controlled trials in all areas of healthcare) (searched July 2005) The NHS Centre for Reviews and Dissemination databases				<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: Success of treatment (PBAC score &lt;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</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>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 versus 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>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Rauramo 2004 <sup>270</sup>	Study Type: randomised; open; equivalence  Evidence level: 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: 41.4yrs, 73.4kg. TCRE: 42.1 yrs, 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 endometriosis, 2 PID, 1 expulsion. 1 endometritis, 1 bleeding & pain from resection, plus 1 stroke	Funding Source: Schering Ag  Study summary: Both treatments effectively reduced MBL.
Reid 2005 <sup>271</sup>	Study Type: randomised; non-blinded; concealed  Evidence level: 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 > 5cm <sup>3</sup> , hypertension, abnormal thyroid or liver test function, asthma, IUCD in situ,	LNG-IUS (levonorgestrel 52mg); Mefenamic acid (500mg tid)	6 cycles	MBL (alkaline haematin); total fluid loss; PBAC score; adverse events	MBL (alkaline haematin[ml]: median (range)): LNG-IUS Baseline = 122 (81 to 375) Cycle 3 = 12 (0 to 240) Cycle 6 = 5 (0 to 45) (P<0.005 for change between measurements)  Mefenamic acid Baseline = 121 (85 to 389) Cycle 3 = 94 (29 to 219) (p<0.001 in favour of LNG-IUS) Cycle 6 = 100 (46 to	Funding Source: Schering Oy  Study summary: Both treatments reduce MBL, but LNG-IUS does this to a greater degree.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			<p>treated for menorrhagia or used hormonal treatments within 4 months.</p> <p>Baseline characteristics not described.</p> <p>Country: UK.</p>				<p>168) (<math>p &lt; 0.001</math> in favour of LNG-IUS) (<math>P &lt; 0.005</math> for change between measurements)</p> <p>Total fluid loss (ml; median (range)) LNG-IUS Baseline = 183 (103 to 527) Cycle 3 = 53 (0 to 459) Cycle 6 = 27 (0 to 156) (<math>P &lt; 0.005</math> for change between measurements)</p> <p>Mefenamic acid Baseline = 211 (91 to 491) Cycle 3 = 151 (57 to 280) (<math>p &lt; 0.001</math> in favour of LNG-IUS) Cycle 6 = 157 (76 to 319) (<math>p &lt; 0.001</math> in favour of LNG-IUS) (<math>P &lt; 0.005</math> for change between measurements)</p> <p>PBAC score (median (range)): LNG-IUS Baseline = 240 (91 to 545) Cycle 3 = 49 (0 to 286) Cycle 6 = 25 (0 to 402) (<math>P &lt; 0.005</math> for change between measurements)</p> <p>Mefenamic acid Baseline = 233 (77 to 469) Cycle 3 = 161 (77 to</p>	



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>262) (<math>p &lt; 0.001</math> in favour of LNG-IUS)  Cycle 6 = 159 (50 to 307) (<math>p &lt; 0.001</math> in favour of LNG-IUS)  (<math>P &lt; 0.005</math> for change between measurements)</p> <p>Adverse events:  LNG-IUS  Headache = 10  Abdominal pain = 8  Ovarian cyst = 6  Breast pain = 6  Nausea = 2  Diarrhoea = 1  Upper respiratory infection = 5</p> <p>Mefenamic acid  Headache = 10  Abdominal pain = 2  Ovarian cyst = 3  Breast pain = 2  Nausea = 4  Diarrhoea = 4  Upper respiratory infection = 5</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Soysal 2002 <sup>272</sup>	Study Type: randomised; blind  Evidence level: 1+	72: 36 ablation vs. 36 IUD. 1 ablation and 5 IUD not included in analysis due to treatment failure.	Population characteristics: Women; >40 yrs; completed family; menorrhagia; no pathology; no cancer.  LNG-IUS: 44.1 yrs. TBA: 43.8 yrs.  Country: Turkey	Thermal balloon ablation after GnRH- a; LNG IUD (20ug daily)  Treatment versus baseline; treatment versus 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Stewart 2001 <sup>261</sup>	Study Type: Systematic review  Evidence level: 1+		Population characteristics:  Country:	RCT; case-series		MBL	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.	Study summary: LNG-IUS is effective at reducing MBL associated with menorrhagia.

## Chapter 6 – Hormonal Treatments for HMB

### LNG-IUS for treatment of HMB – Non-comparative studies

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Hurskainen 2004 <sup>481</sup>	Study Type: randomised  Evidence Level: 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 (&gt;80ml 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>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>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						Women with menorrhagia had better outcomes with hysterectomy than LNG-OUS for: anxiety ( $p = 0.003$ ), general health ( $p = 0.04$ ), energy ( $p = 0.05$ ), and pain relief ( $p = 0.04$ ).	

## Chapter 6 – Hormonal Treatments for HMB

### Other pharmaceutical treatment for HMB – Comparative studies

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Beaumont 2004 <sup>283</sup>	Study Type: Systematic review  Evidence level: 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 = -35.6ml (95% CI -102, +31).	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Bonduelle 1991 <sup>278</sup>	Study Type: randomised; open  Evidence level: 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 200mg daily for 3 months; norethisterone 5mg X 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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Cameron 1987 <sup>264</sup>	Study Type: randomised  Evidence level: 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 >50ml  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 (200mg); Mefenamic acid (500mg x 3); norethisterone (5mg x 2); progesterone coil  treatment versus 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 = 203ml, treatment = 51ml; a - 75% change. Progesterone coil: pre-treatment = 64ml (p < 0.05), treatment = 45ml; 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.



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Chimbira 1980 <sup>285</sup>	Study Type: randomised  Evidence level: 1-	8 in placebo controlled study; 32 in Danazol dose study. Drop- outs not reported.	Population characteristics: MBL >60ml; no pathology  Country: UK	Danazol 100mg; Danazol 200mg; placebo  treatment versus placebo; treatment versus treatment; treatment versus baseline	6 cycles: 2 baseline; 2 placebo; 2 treatment. 12 weeks for dose study	MBL - alkaline haematin; side- effects	Placebo trial (n=8): baseline = 137ml and 100ml; placebo = 114ml and 121ml; Danazol = 50ml and 13ml.  200mg Danazol (n=16): baseline = 182ml and 184ml; Danazol = 142ml; 38ml; 26ml.  100mg Danazol (n=16): figures not given for baseline; Danazol: 52ml; 42ml; 52ml(<0.01).  Side-effects: 200mg = 24 side effects, plus 2.3kg average weight gain; 100mg = 18 side- effects, plus 2.1kg 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Chimbira 1979 <sup>326</sup>	Study Type: Case-series  Evidence level: 2-	22 recruited. 4 excluded. 18 included	Population characteristics: women; MBL>80ml  Aged 25 to 50 years.  Country: UK	Danazol (400mg for 12 weeks)  treatment versus baseline	7 months	MBL - alkaline haematin; peripheral blood measurements - platelets, plasminogen, Quick's test, Euglobulin, Fibronogen, Factor VII, Factor VIII, Factor X	MBL: pre-treatment mean = 231ml (SE 39) vs. 135ml (SE 33) in 1st treatment month and 21ml (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 treatment.	Funding Source: Sterling- Winthrop research division acknowledged.  Study summary: Study shows Danazol reduces MBL but has high levels of side-effects

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Coulter 1995 <sup>275</sup>	Study Type: Systematic review; meta-analysis  Evidence level: 1+		Population characteristics: Searches undertaken on MEDLINE  Country:	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>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>	<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 & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Dockeray 1989 <sup>286</sup>	Study Type: randomised; open  Evidence level: 1-	41 in total; 20 in Mefenamic acid group; 20 in Danazol group. 1 withdrawal, but group not stated	Population characteristics: Menorrhagia >80ml; 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 (500mg x 3) for 5 days; Danazol (100mg x 2) for 60 days  Treatment versus baseline; treatment versus 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 versus Danazol = 20% versus 60% (p<0.001).  6 (30%) Mefenamic patients reported side- effects versus 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Dunphy 1998 <sup>279</sup>	Study Type: randomised; double-blind  Evidence level: 1-	23: 11 medroxyproges- terone; 12 Danazol randomised; 9 medroxy, 9 Danazol analysed.	Population characteristics: women; menorrhagia (>80ml); >18 yrs; not pregnant; no contra-indications  Country: Canada	Danazol 200mg daily; medroxyprogesteron e acetate 10mg 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 = 7kg (SD 0.7)(p = 0.0078). Medroxy = 2.2kg (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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Lamb 1987 <sup>287</sup>	Study Type: randomised; double-blind  Evidence level: 1+	76 entered. At 1 month 19 Danazol, 17 placebo. At 3 months 15 Danazol, 9 placebo	Population characteristics: women; >25 yrs; menorrhagia; no pathology; between 45- 110kg; no cardiac, hepatic or renal impairment; no sensitivity to hormonal treatment; not pregnant.  Country: UK	Danazol (200mg 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Turnbull 1990 <sup>284</sup>	Study Type: non-randomised trial.  Evidence level: 2++	37 recruited; 20 had MBL > 80ml; 19 agreed to study	Population characteristics: women; MBL > 80ml; 34-46 years  Country: UK	gestrinone 2.5mg twice weekly; placebo  treatment vs. placebo	8 months: 2 placebo; 3 active treatment; 3 follow-up	MBL - alkaline haematin	Baseline MBL: median 173ml ( range 81-831ml).  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.

## Chapter 6 – Hormonal Treatments for HMB

### GnRH-a for the treatment of HMB – Comparative studies

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Carr 1993 <sup>294</sup>	Study Type: randomised; double-blind; ITT?; cross- over  Evidence level: 1+	16 randomised	Population characteristics: Women; menstruating; pre-menopausal; uterine fibroids > 12 weeks  Country: USA	GnRH-a; GnRH-a with medroxyprogesteron e 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



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Friedman 1988 <sup>295</sup>	Study Type: randomised; blinded?; concealed?  Evidence level: 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 <sup>296</sup>	Study Type: randomised  Evidence level: 1-	51 randomised; 26 (7 failed to complete) to Oestrogen; 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 oestrogen-progestin or progestin 'add-back'  treatment versus 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 oestrogen group improved, and 14 of 17 in progestin group improved.  Add-back results:  Hgb (g/dL) - oestrogen-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 (%) - oestrogen-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	Funding Source: TAP pharmaceutical and grant from Brigham and Women's Hospital  Study summary: Limited results suggest GnRH reduces menorrhagia.  Oestrogen-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 oestrogen-progestin add-back regimen was superior or equal to the progestin add-back regimen in all efficacy and safety parameters

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							Bone mineral density : oestrogen-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)	assessed.
Friedman 1991 <sup>292</sup>	Study Type: randomised; double-blind  Evidence level: 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; dyspareunia; menometrorrhagia	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; depression = 7 vs. 2; emotional liability = 5 vs. 1; decreased libido = 2 vs. 0.	Funding Source: TAP pharmaceutical  Study summary: Treatment reduces MBL compared to placebo but with high levels of adverse effects.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Nakayama 1999 <sup>297</sup>	Study Type: randomised; blinded?; concealed?; ITT?  Evidence level: 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 oestriol 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 <sup>298</sup>	Study Type: Randomised; double-blind  Evidence level: 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	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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>baseline)</p> <p>Bone mineral density (g/cm<sup>3</sup>): Baseline: 1056 vs. 1044 6-months: 1002 vs. 1035 P &lt; 0.01 for placebo group vs. baseline and vs. treatment.</p> <p>Bone mineral levels: Serum alkaline phosphatase, osteocalcin levels, urinary calcium/creatinine, hydroxyproline/creatinine ratios significantly increased in placebo group compared to baseline and treatment group (p &lt; 0.01)</p> <p>Lipid profile: Total cholesterol level, HDL-c level, Triglyceride level all increased from baseline and compared to treatment group (p &lt; 0.01).</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Palomba 2002 <sup>299</sup>	Study Type: randomised; single blind; conceal?; ITT?  Evidence level: 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): Age: 48.8 vs. 47.5 BMD - lumbar spine: 1.078 vs. 1.080  Country: Italy	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 to baseline and treatment group in placebo group ( $p < 0.05$ ). No difference in treatment group between baseline and follow-up.	Funding Source: Not stated
Palomba 2004 <sup>300</sup>	Study Type:  Evidence level: 1-	100 randomised; 50 to GnRH-a plus raloxifene, 45 completed;	Population characteristics: Women; pre- menopausal; Symptomatic	GnRH-a plus raloxifene; GnRH-a plus placebo	6 cycles	QoL - Kupperman index, Wechsler memory scale, mini-mental state examination,	GnRH-a plus raloxifene (n = 45) vs. GnRH-a plus placebo (n = 46) vs. normal population (n = 50):	Funding Source: Not stated  Study summary: Study shows that GnRH-a

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
		50 to GnRH-a plus placebo, 46 completed. 50 health pre-menopausal women acted population baseline	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): Age: 48.8 vs. 47.5 BMD - lumbar spine: 1.078 vs. 1.080  Country: Italy			Hamilton rating scale for depression, self-rating anxiety scale, SF-36, Women's Health Questionnaire.	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) self-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	cause reduction in cognitive functioning in women with symptomatic fibroids, but improves QoL to near normal levels. .

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							(8.6) 6th cycle = 42.5 (8.7) 48.1 (9.9) vs. 26.8 (9.4)	
Schlaff 1989 <sup>301</sup>	Study Type: randomised; double-blind; placebo; concealed?; ITT?  Evidence level: 1-	12 randomised; 5 received GnRH; 6 received placebo	Population characteristics: Women; symptomatic uterine fibroids; aged 29 to 47; fibroids > 3.5cm; 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 <sup>293</sup>	Study Type: randomised; prospective  Evidence level: 1-	67: 34 Buserelin MP; 33 Leuprolide.	Population characteristics: women; pre- menopausal; uterine fibroids; endometriosis.  Buserelin: 37 yrs, 158cm, 52kg.  Leuprolide: 33yrs, 158cm, 55kg.  Country: Japan	depo buserelin MP 1.8mg; depo leuprolide 1.88  treatment vs. treatment	20 weeks	MBL - menstruation, petechia, amenorrhoea; side-effects	Buserelin: 8-weeks = 52.9% amenorrhea; 20 weeks = 88.9% amenorrhea. Leupline: 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 Leupline.  11 of Buserelin and 15 of leupline group were lost to follow-up by 24 weeks.	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
West 1992 <sup>573</sup>	Study Type:  Evidence level: 2-	20 in total, 10 to goserelin and MPA combined from strat, 10 to goserlien only then MPA after 3-months	Population characteristics: Women; symptomatic uterine fibroids  Country: UK	goserelin and MPA combined from strat, goserlien only then MPA after 3-months	6 months	Fibroid volume; fibroid symptoms; vasomotor side-effects	goserelin and MPA combined from strat vs. goserlien 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 oestradiol in both groups.	Funding Source: Not stated



## Chapter 7 – Non-Hormonal Treatments for HMB

### Antifibrinolytics for treatment of HMB – Comparative studies

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Andersch 1988 <sup>308</sup>	Study Type: randomised; open; cross- over  Evidence level: 1+	15	Population characteristics: MBL >80ml; 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 1.5g x 3 for 3 days then 1g x 2 for 2 further days. Flurbiprofen (100mg x 2) for 5 days; Placebo  treatment v treatment; treatment v 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 +/- 52ml. Tranexamic acid: mean MBL = 155 +/- 33ml (53% reduction [perhaps misprint, should be 47%], P<0.01). Flurbiprofen: mean MBL 223 +/- 44ml (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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Bonnar 1996 <sup>307</sup>	Study Type: Randomised; intention to treat  Evidence level: 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 (500mgx4); Mefenamic acid (500mg x 3); Tranexamic acid (1g x 4); no treatment  treatments versus 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 89ml (24 to 214ml; 54% reduction; P<0.001). Mean MBL 164 (n=78) in control and 75m (n = 72) (89ml difference) in treatment. Tranexamic acid vs. Etamsylate: = -97ml (95% CI: 140 to 154; p<0.001); v Mefenamic acid = - 56ml ((95% CI 90 to 2ml; P<0.05)) (Perhaps misprint: may be 46ml 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	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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>Etamsylate, but no statistical difference. Mean MBL in pre-treatment = 170ml (n=81) v 175ml (n=63) (+3%)(figures do not match reported figures) during treatment. Difference between treatments: +97ml (95% CI: 140 to 154; p&lt;0.001) against Tranexamic acid; +51ml (95% CI: -96 to -6; p&lt;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 43ml (82 to 179)(20%) reduction in MBL (P&lt;0.001). Mean MBL in pre-treatment = 186ml (n = 69) and 148ml (n=64) during treatment (difference of 38ml). Mefenamic acid reduce MBL by 56ml (Perhaps misprint, should be 46ml) less than Tranexamic acid (95%</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>CI 90 to 2ml; <math>P &lt; 0.05</math>) and 51ml (95% CI: -96 to -6; <math>p &lt; 0.05</math>) 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>	
Callender 1970 <sup>306</sup>	<p>Study Type: Randomised; double-blind; cross-over</p> <p>Evidence level: 1+</p>	20. 16 completed.	<p>Population characteristics: Complain of menorrhagia or referred for anaemia; no significant clinical or histological abnormality.</p> <p>Total: 32yrs</p> <p>No setting specified, but study from Radcliffe Infirmary</p> <p>Country: UK</p>	<p>Tranexamic acid (1g x 4) for 4 days or placebo or no treatment</p> <p>treatment v placebo v no treatment</p>	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	<p>Tranexamic acid v no treatment (<math>t = 3.44</math>, <math>p &lt; 0.02</math>); Tranexamic acid v placebo (<math>t = 2.37</math>, <math>p &lt; 0.05</math>). No difference between placebo and no treatment.</p> <p>MBL (ml) during placebo phase = 185; during no treatment phase = 197; during Tranexamic acid phase = 122</p> <p>Side effects were: nausea, headache for Tranexamic acid - not fully reported.</p>	<p>Funding Source: Kabi Pharmaceuticals supplied treatments and paid for study.</p> <p>Study summary: Tranexamic acid is safe and effective for treating menorrhagia.</p>

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Coulter 1995 <sup>275</sup>	Study Type: Systematic review; meta-analysis  Evidence level: 1+		Population characteristics: Searches undertaken on MEDLINE  Country:	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>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>	<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 & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Edlund 1995 <sup>305</sup>	Study Type: Randomised; double-blind; double dummy; placebo- controlled  Evidence level: 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 > 80ml. Normal sized uterus. Excluded due to: concomitant disease; concomitant medication; previous thromboembolic, haemorrhage, or fibrinolytic disorders; creatinine >120 umol/l; cancer.  O&G departments in 3 medical centres  Country: Sweden	Tranexamic acid (1200 mg x 2) or (600mg x4) for 5 days or placebo  Treatment v 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%); 600mg x 4 (n = 28) - pre-treatment = 235.4 (83-728) to treatment = 162.6 (36-640) (p<0.001) (-31%); 1200mg x 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. .

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Lethaby 2004 <sup>302</sup>	Study Type: Systematic review; meta-analysis  Evidence level: 1++		Population characteristics:  Country:			MBL	<p>Antifibrinolytics vs. Etamsylate: 1 study - MBL = -97ml (-134.36 to -59.64) in favour of TXA.</p> <p>Side-effects reported. Withdrawals due to adverse events: RR 0.78 [95% CI 0.19, 3.15].</p> <p>Meta-analysis of 2 RCTs of Tranexamic versus placebo (n=48) -110.17 [95% CI --146.54 , -73.81); z=5.94 (p=0.001).</p> <p>Antifibrinolytic vs. NSAIDs: 1 study (n=49) - MBL = -46 (-76.02 to -15.98). Antifibrinolytic vs. Etamsylate: 1 study (n=50) - MBL = -97ml (-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>	Funding Source: No funding

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Nilsson 1967 <sup>304</sup>	Study Type: Randomised; double-blind; placebo- controlled  Evidence level: 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 x 6; increased to 0.5 to 1mg x6 for 4 days; or placebo  treatment dose a v treatment dose b v placebo	5 consecutive periods: 2 baseline; 3 treatment	Menstrual blood loss alkaline haematin; duration of period; side-effects	MBL for 0g = 149.1; 12g dosage = 96.1 (- 38% +/- 4.47); for 24g = 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%)  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.  No discontinuation from study	Funding Source: Not stated  Study summary: Tranexamic acid was safe and effective for menorrhagia.



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Preston 1995 <sup>281</sup>	Study Type: Randomised; double-blind; placebo- controlled; concealed; cross-over  Evidence level: 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 yrs, 71.2 kg. Net: 39.3 yrs, 63.5kg (P < 0.048)  Setting: university O&G department  Country: UK	Tranexamic acid (1g x 4) for 4 days or norethisterone (5mg x 2) for 8 days or Placebo  Treatment v treatment; treatment v placebo	4 consecutive cycles: 2 baseline/placebo; 2 treatment	Menstrual blood loss - alkaline haematin; QoL; side-effects	Tranexamic acid (n=25): Change from 175ml to 97ml (95% CI 62 to 108)(P<0.0001); 45% reduction (+23 to -93; p<0.0001). Norethisterone (n = 21): Change from 173ml to 208 ml (-64 to +2)(p=0.26); 20% increase (+114 to -62; 9<0.0001). Between groups difference was 113ml (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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Vermeylen 1968 <sup>309</sup>	Study Type: Randomised; double-blind  Evidence level: 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 (0.5g x 6) or placebo  treatment v placebo	6 consecutive menstrual periods	Menstrual blood loss (haemoglobin content) - alkaline haematin; duration of period; side-effects	MBL reduced by between 12-60% in active group compared to placebo, mean 35% (t-test p<0.001). Figures not given only shown in graph.  Side effects: nervousness, anorexia; dizziness; insomnia, vomitus, adnominal cramps, tinnitus, diarrhoea, skin eruption, headache, menstrual pain.	Funding Source: Not stated  Study summary: "Oral administration of Tranexamic acid (3g daily)...significantly decreases menstrual haemoglobin loss in women with so-called essential menorrhagia."

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Wellington 2003 <sup>303</sup>	Study Type: Systematic review  Evidence level: 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 2-4.5g 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:  164 vs. 75 - Bonnar  197 vs. 122 - Callender  168 vs. 69 - Gleeson  295 vs. 155 - Milsom  175 vs. 97 - Preston</p> <p>Only one study reported on QoL, showing improvement, but was non-comparative, non-blind design.</p> <p>Studies reported a variety of side-effects. 12% of patients reported adverse events, such as nausea, vomiting, diarrhoea, and dyspepsia.</p> <p>No reports of DVT in any study. Review shows that quality of studies was varied.</p>	<p>Funding Source: Not stated</p> <p>Study summary: "...oral Tranexamic acid is an effective and well tolerated treatment for idiopathic menorrhagia."</p>

## Chapter 7 – Non-Hormonal Treatments for HMB

### NSAIDs for the treatment of HMB – Comparative studies

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Andersch 1988 <sup>308</sup>	Study Type: randomised; open; cross- over  Evidence level: 1+	15	Population characteristics: MBL >80ml; 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 1.5g x 3 for 3 days then 1g x 2 for 2 further days. Flurbiprofen (100mg x 2) for 5 days; Placebo  treatment v treatment; treatment v 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 +/- 52ml. Tranexamic acid: mean MBL = 155 +/- 33ml (53% reduction [perhaps misprint, should be 47%], P<0.01). Flurbiprofen: mean MBL 223 +/- 44ml (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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Bonnar 1996 <sup>307</sup>	Study Type: Randomised; intention to treat  Evidence level: 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 (500mgx4); Mefenamic acid (500mg x 3); Tranexamic acid (1g x 4); no treatment  treatments versus 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 89ml (24 to 214ml; 54% reduction; P<0.001). Mean MBL 164 (n=78) in control and 75m (n = 72) (89ml difference) in treatment. Tranexamic acid v Etamsylate: = -97ml (95% CI: 140 to 154; p<0.001); v Mefenamic acid = - 56ml ((95% CI 90 to 2ml; P<0.05))(Perhaps misprint: may be 46ml 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 - 8ml increase with	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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>Etamsylate, but no statistical difference Mean MBL in pre-treatment = 170ml (n=81) v 175ml (n=63) (+3%)(figures do not match reported figures) during treatment. Difference between treatments: +97ml (95% CI: 140 to 154; p&lt;0.001) against Tranexamic acid; +51ml (95% CI: -96 to -6; p&lt;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 43ml (82 to 179)(20%) reduction in MBL (P&lt;0.001). Mean MBL in pre-treatment = 186ml (n = 69) and 148ml (n=64) during treatment (difference of 38ml). Mefenamic acid reduce MBL by 56ml (Perhaps misprint, should be 46ml) less than Tranexamic acid (95%</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>CI 90 to 2ml; <math>P &lt; 0.05</math>) and 51ml (95% CI: -96 to -6; <math>p &lt; 0.05</math>) 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 <sup>311</sup>	<p>Study Type: randomised; blinding not specified</p> <p>Evidence level: 1-</p>	32 in total: 17 Mefenamic group; 15 norethisterone group	<p>Population characteristics: MBL &gt;80ml; regular cycle; organic cause excluded.</p> <p>Average age: 40 years</p> <p>Setting: O&amp;G department</p> <p>Country: UK</p>	<p>Mefenamic acid 500mg x 3 for 5 days; norethisterone 5mg x 2 for 7 days</p> <p>treatment versus baseline</p>	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 = 123ml (86-237) and during treatment = 81ml (22-193) (<math>P &lt; 0.001</math>); a - 34% change. Norethisterone: MBL at baseline = 109ml (81-236) and during treatment = 92ml (43-189) (<math>P &lt; 0.002</math>); a - 15.5% change.</p> <p>Side-effects: headache (4 Mef. vs. 5 Nor), 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>

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Cameron 1987 <sup>264</sup>	Study Type: randomised  Evidence level: 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 >50ml  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 (200mg); Mefenamic acid (500mg x 3); norethisterone (5mg x 2); progesterone coil  treatment versus 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 = 203ml, treatment = 51ml; a - 75% change. Progesterone coil: pre-treatment = 64ml (p < 0.05), treatment = 45ml; 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.



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Chamberlain 1991 <sup>312</sup>	Study Type: Minimisation; double-blind; double-dummy.  Evidence level: 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 80ml>. 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 500mg x 4; Mefenamic 500mg x 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 acknowledges.  Study summary: Both treatments effective and perhaps should be used in combination.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Coulter 1995 <sup>275</sup>	Study Type: Systematic review; meta-analysis  Evidence level: 1+		Population characteristics: Searches undertaken on MEDLINE  Country:	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>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>	<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 & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Creatsas 1998 313	Study Type: randomised  Evidence level: 1-	48 in total: 23 in tenoxicam group; 25 in L-EE group	Population characteristics: adolescents; menorrhagia; not pregnant  Setting: University O&G department  Country: Greece	tenoxicam (20mg); L-EE (1 tablet)  Treatment versus no treatment period; treatment versus treatment	For one episode	Haematological parameters	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 versus L-EE for HCT = 35.9% v 32.6% $p = 0.02$ and Hb = 11.5% v 10.4% $p = 0.05$ .  3 (13%) patient in Tranexamic group reported mild GI disorders ( $p = 0.0028$ compared to L-EE)	Funding Source: Not stated  Study summary: Tenoxicam is considered an effective medication for the management of DUB during adolescence
Dock ray 1989 286	Study Type: randomised; open  Evidence level: 1-	41 in total; 20 in Mefenamic acid group; 20 in Danazol group. 1 withdrawal, but group not stated	Population characteristics: Menorrhagia >80ml; 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 (500mg x 3) for 5 days; Danazol (100mg x 2) for 60 days  Treatment versus baseline; treatment versus 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 versus Danazol = 20% versus 60% ( $p < 0.001$ ).  6 (30%) Mefanamic patients reported side-effects versus 15 (75%) with Danazol ( $p < 0.005$ ).  9 (45%) women in Mefenamic acid group and 10 (50%) in	Funding Source: Commercial funding  Study summary: Study showed Danazol reduced MBL more than Mefenamic acid, but was associated with more side-effects.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							Danazol group refused offer to continue with treatment	
Fraser 1991 276	Study Type: randomised  Evidence level: 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 (500mg x 3); naproxen; low dose monophasic oral contraceptive - ethinyl oestradiol 30ug & levonorhestrel 150ug for 21 days; Danazol (200mg) daily  Treatment versus baseline	8 consecutive cycles: 2 no treatment; 2 no treatment; 2 no treatment	MBL - alkaline haematin	Mefenamic acid - group 1 - control = 131.1ml (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 versus treatment = 115.6 (SD 113) ml (P=0.079)(-12%);  Oral contraceptive - 101 v 57.8, p<0.001, -43%;  Danazol - 90.3 v 45.5 (av), P<0.001, -49%.  Differences between Mefenamic v naproxen p=0.129; versus oral contraceptive P = 0.154; versus Danazol p = 0.079.  Side-effects not reported.	Funding Source: Commercial funding  Study summary: All treatments reduce MBL.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Fraser 1981 314	Study Type: randomised; cross-over; blinding and concealment not outlined.  Evidence level: 1-	85 entered. 69 completed.	Population characteristics: Women; report menorrhagia from any cause (including IUD induced)  Setting: patient recruited via advert, treated in University O&G department  Country: Australia	Mefenamic acid; placebo  treatment versus placebo	4 consecutive cycles - 2 with placebo; 2 with active treatment	MBL - alkaline haematin; pain; nausea; headache; diarrhoea; depression; breast symptoms; sanitary towel use; haematology	Placebo period MBL = 66.9ml (SE 4.7); Mefenamic acid = 48.1 (SE 4.4). -28.1% difference (P<0.001).  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<0.001).  Side-effects not reported.  Results for 16 (19%) women were not reportedly.	Funding Source: Commercial (Parke- Davis) and government grants (Australian national health and medical research council)  Study summary: ...Mefenamic acid should be of considerable value in Australia...

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Grover 1990 <sup>315</sup>	Study Type: randomised; double-blind  Evidence level: 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: 35.8yrs. Control: 35yrs.  Setting: O&G department  Country: India	Mefenamic acid (500mgx3); placebo  Treatment versus 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 <sup>316</sup>	Study Type: randomised; double-blind; cross-over; double dummy  Evidence level: 1++	41 entered. 5 MBL <80ml. 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: 40.5yrs. Group 2: 38.1yrs.  Setting: O&G department  Country: UK	Naproxen 550mg x 1 then 275 x 4 for 4 days; Mefenamic acid 500mg x 3  Treatment versus 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 129.3ml (n = 19) in two groups. Naproxen: MBL reduced by 52ml (44%) and 62ml (48%) in each group (p<0.001); Mefenamic: MBL reduced by 54ml (45.5%) and 61ml (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 cyclo-oxygenase inhibitors are useful for women with menorrhagia and a normal uterus...

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Jakubowicz 1978 317	Study Type: alternate allocation; placebo-controlled; double-blind; cross-over  Evidence level: 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 1000mg 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 310	Study Type: Systematic review  Evidence level: 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]	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
van Eijkeren 1992 <sup>318</sup>	Study Type: randomised; double-blind; placebo- controlled  Evidence level: 1++	19 entered. 8 did not complete. 11 assessed: 5 in placebo group; 6 in Mefenamic acid group	Population characteristics: Women; MBL >80ml; Age <=45; regular cycle; no IUD; no NSAIDs; no contraindications  Setting: not specified  Country: Netherlands	Mefenamic acid (500mg x 3); placebo  Treatment versus placebo; treatment versus 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.  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 & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Vargyas 1987 319	Study Type: randomised; double-blind; placebo controlled  Evidence level: 1+	32 in cross-over design	Population characteristics: women; MBL >60ml; 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 yrs.  Includes 7 women with IUD, 6 sterilised.  Setting: O&G department  Country: USA	Meclofenamate sodium 100mg x3 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.  Meclomen 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Ylikorkala 1986 <sup>320</sup>	Study Type: randomised; placebo- controlled; cross-over  Evidence level: 1-	25 in total: 11 with fibroids; 14 without fibroids	Population characteristics: Menorrhagia; fibroids or not  Country: Finland	Naproxen 500mg x 2 for 5 days; placebo  treatment versus 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.

## Chapter 7 – Non-Hormonal Treatments for HMB

### Etamsylate for treatment of HMB – Comparative studies

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Bonnar 1996 <sup>307</sup>	Study Type: Randomised; intention to treat  Evidence level: 1-	81 in total: 29 to ethamsylate; 25 Mefenamic acid; 27 tranexamic acid. 2 ethamsylate, 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 (500mgx4); Mefenamic acid (500mg x 3); tranexamic acid (1g x 4); no treatment  treatments versus 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 89ml (24 to 214ml; 54% reduction; P<0.001). Mean MBL 164 (n=78) in control and 75m (n = 72) (89ml difference) in treatment. Tranexamic acid v ethamsylate: = -97ml (95% CI: 140 to 154; p<0.001); v Mefenamic acid = - 56ml ((95% CI 90 to 2ml; P<0.05))(Perhaps misprint: may be 46ml 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 ethamsylate (40%), 3 Mefenamic acid (13%),	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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>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 - 8ml increase with ethamsylate, but no statistical difference Mean MBL in pre-treatment = 170ml (n=81) v 175ml (n=63) (+3%)(figures do not match reported figures) during treatment. Difference between treatments: +97ml (95% CI: 140 to 154; p&lt;0.001) against tranexamic acid; +51ml (95% CI: -96 to -6; p&lt;0.05) against Mefenamic acid.</p> <p>33% of patients wanted to continue with ethamsylate after trial.</p> <p>11 ethamsylate (40%), 3 Mefenamic acid (13%), 4 tranexamic acid (15%) withdraw from study. Poor efficacy was main reason.</p> <p>Mefenamic acid: a 43ml (82 to 179)(20%)</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>reduction in MBL (<math>P &lt; 0.001</math>). Mean MBL in pre-treatment = 186ml (<math>n = 69</math>) and 148ml (<math>n = 64</math>) during treatment (difference of 38ml). Mefenamic acid reduce MBL by 56ml (Perhaps misprint, should be 46ml) less than tranexamic acid (95% CI 90 to 2ml; <math>P &lt; 0.05</math>) and 51ml (95% CI: -96 to -6; <math>p &lt; 0.05</math>) more than against ethamsylate.</p> <p>74% of women wanted to continue with Mefenamic acid after the trial. 77% with tranexamic, and 33% with etamsylate.</p> <p>11 ethamsylate (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>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Harrison 1976 <sup>321</sup>	Study Type: Randomised; placebo- controlled; crossover; double blind  Evidence level: 1+	31 entered. Only 9 primary menorrhagia patients. 9 patients were excluded from analysis.	Population characteristics: Inclusion/exclusio n - 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	Ethamsylate; 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 ethamsylate and placebo = 59.4ml (p=<0.01); Mean MBL reduction with ethamsylate = 49.7 +/- 2.3 SE. 94% CI = 44.2 to 55.2, -46% MBL.  Side-effects: 34% (17 of 50) in placebo periods and 34% (18 of 53) in ethamsylate. None reported as serious.	Funding Source: Not reported  Study summary: "The results of the study suggest that ethamsylate is a safe and effective agent in the treatment of primary menorrhagia..."

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Lethaby 2004 <sup>302</sup>	Study Type: Systematic review; meta-analysis  Evidence level: 1++		Population characteristics:  Country:			MBL	<p>Antifibrinolytics vs. ethamsylate: 1 study - MBL = -97ml (-134.36 to -59.64) in favour of TXA.</p> <p>Side-effects reported. Withdrawals due to adverse events: RR 0.78 [95% CI 0.19, 3.15].</p> <p>Meta-analysis of 2 RCTs of tranexamic versus placebo (n=48) -110.17 [95% CI --146.54 , -73.81); z=5.94 (p=0.001).</p> <p>Antifibrinolytic vs. NSAIDs: 1 study (n=49) - MBL = -46 (-76.02 to -15.98). Antifibrinolytic vs. ethamsylate: 1 study (n=50) - MBL = -97ml (-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 Ethamsylate (1 study) RR = 0.78 [0.19, 3.15].</p>	Funding Source: No funding

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Lethaby 2004 <sup>310</sup>	Study Type: Systematic review  Evidence level: 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]	



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Chamberlain 1991 <sup>312</sup>	Study Type: Minimisation; double-blind; double-dummy.  Evidence level: 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 80ml>. 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 500mg x 4; Mefenamic 500mg x 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Coulter 1995 <sup>275</sup>	Study Type: Systematic review; meta-analysis  Evidence level: 1+		Population characteristics: Searches undertaken on MEDLINE  Country:	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>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>	<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>





## Chapter 8 – Indications for Surgery (Non-Hysterectomy)

### Indications for surgery (non-hysterectomy) – Comparative studies

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Vuorma 2003 <sup>574</sup>	Study Type: Comparative; cohorts  Evidence level: 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

## Chapter 8 – Indications for Surgery (Non-Hysterectomy)

### Indications for surgery (non-hysterectomy) – Non-comparative

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Bongers 2002 <sup>329</sup>	Study Type: Prognostic; case-series  Evidence Level: 3	Prognostic factors for treatment failure - age, duration of menstruation, dysmenorrhoea, position of uterus, uterine depth, endometrial thickness > 4mm	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 > 4mm = 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.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Bourdrez 2004 <sup>247</sup>	Study Type: Prospective; cohort  Evidence Level: 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.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Hurskainen 2004 481	Study Type: randomised  Evidence Level: 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 (&gt;80ml 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>



Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Sculpher <sup>248</sup>	Study Type: Cohort  Evidence Level: 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 & discomfort = 0.68 Hospital stay as short as possible = 0.59 Reduce periods = 0.42 Resume sex life as soon as possible = 0.59 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%	Funding Source: Not stated  Study Summary: Many women referred for surgery for menorrhagia have conflicting objectives from treatment.

## Chapter 9 – Surgery as first line treatment for HMB

### Surgery as first line treatment for HMB – Comparative studies

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Barrington 2003 <sup>262</sup>	Study Type: randomised  Evidence level: 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 >12cm  Country: UK	LNG-IUS; thermal balloon ablation  treatment versus baseline	6 months	MBL - PBAC	MBL (mean): IUS pre-treatment = 107ml vs. 31ml post-insertion (-71%); Ablation pre-treatment = 122ml vs. 61ml post-surgery (-50%). No difference between groups (p=0.689).  MBL (median): IUS pre-treatment = 75ml vs. 19ml post-insertion; Ablation pre-treatment = 101ml vs. 27ml post-surgery.	Funding Source: not stated  Study summary: Study shows LNG-IUS and thermal ablation are equivalent.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Cooper 1999 <sup>246</sup>	Study Type: Randomised; concealed  Evidence level: 1++	272 eligible, 187 recruited, 94 randomised to medical treatment, 93 to TCRE. By two 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 versus 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.	Funding Source: Scottish Office Department of Health  Study summary: The results at two 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 & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>patient satisfaction: Totally or generally satisfied with treatment = 48 (57%) vs. 68 (79%), <math>p = 0.002</math> Cure or acceptable improvement = 53 (61%) vs. 69 (81%), <math>p = 0.017</math> Treatment acceptable = 65 (77%) vs. 79 (93%), <math>p = 0.004</math></p> <p>Menstrual status: No bleeding or light = 36 (42%) vs. 50 (58%), <math>p = 0.04</math> Unchanged or heavier = 16 (18%) vs. 5 (6%), <math>p = 0.02</math></p> <p>Bleeding score = 6.8 (SD 9.9) vs. 5.4 (SD 8.1)</p>	
Crosignani 1997 <sup>265</sup>	Study Type: randomised; open; prospective  Evidence level: 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	<p>MBL outcome: LNG-IUS (n = 30) baseline = 184.8 ml (SD 62.2), 12-months = 38.8 (SD 37.1) (<math>P &lt; 0.001</math>). Endometrial resection (n = 30) baseline = 203.2 (SD 77.4), 12-months = 23.5 (SD 32.6) (<math>P &lt; 0.001</math>).</p> <p>Difference between LNG-IUS and resection <math>p = 0.015</math>.</p> <p>Patient satisfaction: LNG-IUS: 29 (85%) satisfied. Endometrial resection: 33 (94%)</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>

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			<p>IUD group - age 43.8, parity = 1.8, BMI = 25.3</p> <p>Endometrial resection group - age = 45.4, parity = 1.6, BMI = 24.0</p> <p>Country: Italy</p>				<p>satisfied.</p> <p>Mean SF-36 scores at 12-months (LNG-IUS vs. Resection):</p> <p>Physical functioning = 78.0 vs. 79.2.</p> <p>Role limitation = 72.5 vs. 74.2</p> <p>Bodily pain = 58.9 vs. 70.3</p> <p>General health = 64.1 vs. 70.3</p> <p>Vitality = 56.3 vs. 54.8</p> <p>Social functioning = 69.8 vs. 69.7</p> <p>Role limitation = 61.3 vs. 72.4</p> <p>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>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Halmesmaki 2004 <sup>266</sup>	Study Type: randomised; prospective  Evidence level: 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	FSM levels increased from 8.4 iu/m at baseline to 13.8 iu/m at 12 months versus 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Istre 2001 <sup>268</sup>	Study Type: Randomised  Evidence level: 1+	60: 30 LNG-IUS; 30 resection - 6 discontinued treatment by 12 months.	Population characteristics: women; menorrhagia (PBAC > 75); pre-menopausal; 30-49 yrs; regular uterine cavity <10cm; no pregnant or wanting to become so, breast feeding; large fibroid >40cm; 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 <sup>331</sup>	Study Type:  Evidence level: 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	Hysterectomy; expanded medical treatment  treatment vs. treatment; treatment vs. baseline	24 months	SF-36; Body image & 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:	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 & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			<p>treatments within 6 months; COC or IUD within 3 months; pelvic pathology for which surgery was indicated.</p> <p>Average age: hysterectomy = 42, medicine = 40 Health insurance = 65%, 81% &lt; high school education = 39%, 38% &lt;\$25000 income = 42%, 53% Uterine fibroids = 65%, 63%</p> <p>Pervious treatment: hysterectomy = COC 39%, Prostaglandin inhibitors 13%, GnRH-a 10%, D&amp;C 19%, myomectomy 6%, endometrial ablation 3%</p> <p>Medicine = COC 50%, Prostaglandin inhibitors 19%, GnRH-a 6%, D&amp;C 38%, myomectomy 0%, endometrial</p>				<p>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)</p> <p>Change in QoL scores from baseline to 6-months using intention to treat (hysterectomy, medicine, p-value for difference between groups):</p> <p>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 Psychological well-being score: hysterectomy = 8, Medicine = 0.2, p = 0.07 Overall health score: hysterectomy = 12,</p>	



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			ablation 0% Country: USA				<p>Medicine = 2, <math>p = 0.006</math>  Satisfaction with health:  hysterectomy = 31,  Medicine = 14, <math>p = 0.01</math></p> <p>Symptom resolution:  hysterectomy = 75,  medicine = 29, <math>p &lt; 0.001</math>  Satisfaction with symptom level:  hysterectomy = 44,  medicine = 7, <math>p &lt; 0.001</math></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, <math>p = 0.25</math>  SF-36 PCS score:  hysterectomy = 7,  Medicine = 9, <math>p = 0.19</math>  Body image score:  hysterectomy = 11,  Medicine = 12, <math>p = 0.97</math>  Satisfaction with sex:  hysterectomy = 17,  Medicine = 18, <math>p = 0.89</math>  Psychological well-being score: hysterectomy = 7,</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>Medicine =3, <math>p = 0.24</math>  Overall health score:  hysterectomy = 11,  Medicine = 9, <math>p = 0.64</math>  Satisfaction with health:  hysterectomy = 27,  Medicine = 25, <math>p = 0.68</math></p> <p>Symptom resolution:  hysterectomy = 70,  medicine = 256, <math>p = 0.09</math>  Satisfaction with symptom level:  hysterectomy = 46,  medicine = 40, <math>p = 0.36</math></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  SF-36 PCS score:  hysterectomy = 7,  Medicine = 11  Body image score:  hysterectomy = 12,  Medicine = 8  Satisfaction with sex:  hysterectomy = 17,  Medicine = 13  Psychological well-being score: hysterectomy = 7,  Medicine = 0.6  Overall health score:</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>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>	
Learman 2004 <sup>121</sup>	<p>Study Type: randomised - block; non-blinded; concealment</p> <p>Evidence level: 1+</p>	63 in total, 31 (2 lost to follow-up) to hysterectomy and 32 (2 lost to follow-up) to medical treatment	<p>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.</p> <p>Average age: hysterectomy = 42, medicine = 40</p>	<p>medical treatment; hysterectomy</p> <p>treatments versus baseline</p>	2 years	<p>Menstrual bleeding; Pelvic discomfort; urinary symptoms; menopausal symptoms</p>	<p>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%</p> <p>Continued vaginal bleeding at 6-months was 87% for medicine and 11% for hysterectomy (<math>p &lt; 0.001</math>).</p> <p>Continued vaginal bleeding at 24-months was 37% for medicine and 7% for hysterectomy (<math>p &lt; 0.001</math>).</p> <p>Continued bleeding in hysterectomy group due</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 & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			<p>Health insurance = 65%, 81%            &lt; high school education = 39%, 38%            &lt;\$25000 income = 42%, 53%            Uterine fibroids = 65%, 63%</p> <p>Pervious treatment:            hysterectomy = 39%,            COC 39%,            Prostaglandin inhibitors 13%,            GnRH-a 10%,            D&amp;C 19%,            myomectomy 6%,            endometrial ablation 3%</p> <p>Medicine = COC 50%,            Prostaglandin inhibitors 19%,            GnRH-a 6%, D&amp;C 38%,            myomectomy 0%,            endometrial ablation 0%</p> <p>Country: USA</p>				<p>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>Change in symptom frequency fro baseline at 6-months (intention-to-treat)            Pelvic pain:            hysterectomy = -2.3, medicine = -0.7, <math>p &lt; 0.01</math>            Urinary urgency:            hysterectomy = -0.7, medicine = 0.0, <math>p = 0.03</math>            Urinary incomplete emptying: hysterectomy = -0.6, medicine = +0.1, <math>p = 0.03</math>            Breast pain:            hysterectomy = -1.3, medicine = -0.5, <math>p = 0.02</math>            No difference for other pelvic, urinary or menopausal symptoms.</p> <p>Change in symptom frequency fro baseline at 2-years (intention-to-treat)            Urinary incomplete</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>emptying: hysterectomy = -0.8, medicine = -0.3, <math>p = 0.04</math></p> <p>Hot flushes: hysterectomy = -0.6, medicine = 0.5, <math>p &lt; 0.01</math></p> <p>No difference for other pelvic, urinary or menopausal symptoms.</p> <p>Change in symptoms for groups as treated: Hysterectomy only groups produced significant reduction in symptoms, except for stress incontinence (<math>p = 0.34</math>) and urge incontinence (<math>p = 0.74</math>)</p> <p>Medicine then hysterectomy group produced same results, except hot flushes not significant (<math>p = 0.13</math>)</p> <p>Medicine only group produced significant reductions in symptoms for pelvic pain, pelvic pressure, and stress incontinence (<math>p &lt; 0.05</math>), all other changes were non-significant.</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Marjoribanks 2004 <sup>330</sup>	Study Type: Systematic review  Evidence level: 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 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:	Surgical versus 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. 5-years (n = 140) Surgery 61/71 vs. medical 52/69; OR = 1.99 (0.84 to 4.73) in favour of surgery.  Amenorrhoea rates: 4-months (n = 186) Surgery 34/93 vs. medical 3/93; OR = 17.29 (5.08 to 58.87) in favour of surgery 2-year ( n = 173) Surgery 33/87 vs. medical 26/86; OR = 1.41 (0.75 to 2.65) in favour of surgery 5-years (n = 140) Surgery 41/71 vs. medical 47/73; OR = 0.76 (0.39 to 1.48) in favour of surgery  Bleeding score:	Funding Source: No funding  Study summary: Surgery, especially hysterectomy, reduces menstrual bleeding at one year more than medical treatments but 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>4-months (n = 183) WMD = 1.12.70 (115.04 to -10.36) in favour of surgery 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: 4-months (n = 183) - OR = 8.28 (4.29 to 15.97) in favour of surgery 2-year (n = 173) OR = 2.83 [ 1.46, 5.50 ] in favour of surgery 5-years (n = 140)- OR = 1.69 (0.77 to 3.70) in favour of surgery</p> <p>Extra surgery received: 2-year (n = 236) OR = 0.12 [0.06, 0.22] in favour of surgery 5-years (n = 140)- OR = 0.11 (0.06 to 0.22) in favour of surgery</p> <p>Physical function Four months + 10.16</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							(SD 16.51) + 4.84 (SD 16.72) p = < 0.05 Two years + 5.00 (SD 18.97) + 3.73 (SD 17.19) p = 0.65 Five years + 7.75 (SD 16.39) + 1.06 (SD 23.81) p = 0.10  Social function Four months + 17.44 (SD 16.51) + 7.57 (SD 26.26) p = < 0.05 Two years + 10.59 (SD 26.52) + 3.94 (SD 25.26) p = 0.10 Five years + 10.24 (SD 24.49) + 2.96 (SD 27.22) p = 0.10  Physical role Four months + 32.26 (SD 38.23) + 15.32 (SD 46.78) p = < 0.01 Two years + 18.60 (SD 44.58) + 12.95 (SD 44.58) p = 0.42 Five years + 31.62 (SD 33.15) + 15.14 (SD 39.77) p = 0.06  Emotional role Four months + 31.54	



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							(SD 45.94) + 8.96 (SD 49.93) p = <0.01 Two years + 22.48 (SD 50.47) + 11.25 (SD 45.17) p = 0.13 Five years + 33.81 (SD 34.11) + 14.35 (SD 40.61) p = 0.02  Mental health Four months + 15.01 (SD 19.00) + 4.78 (SD 16.69) p = <0.01 Two years + 9.98 (SD 19.14) + 7.17 (SD 19.20) p = 0.35 Five years + 13.26 (SD 16.94) + 3.62 (SD 18.21) p = 0.01  Energy/fatigue Four months + 20.53 (SD 20.76) + 7.07 (SD 20.23) p = <0.01 Two years + 14.58 (SD 21.96) + 10.06 (SD 19.57) p = 0.17 Five years + 17.31 (SD 22.35) + 10.62 (SD 18.79) p = 0.07  Pain	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>Four months + 21.62 (SD 31.33) + 8.84 (SD 26.39) p = &lt;0.01 Two years + 12.34 (SD 27.20) + 11.38 (SD 28.51) p = 0.82 Five years + 14.81 (SD 25.35) + 11.98 (SD 23.66) p = 0.6</p> <p>General health Four months + 10.49 (SD 20.85) - 0.25 (SD 15.99) p = &lt;0.01 Two years + 1.69 (SD 18.83) - 0.67 (SD 13.90) p = 0.36 Five 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>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<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</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>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>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Rauramo 2004 <sup>270</sup>	Study Type: randomised; open; equivalence  Evidence level: 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: 41.4yrs, 73.4kg. TCRE: 42.1 yrs, 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 & pain from resection, plus 1 stroke	Funding Source: Schering Ag  Study summary: Both treatments effectively reduced MBL.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Soysal 2002 <sup>272</sup>	Study Type: randomised; blind  Evidence level: 1+	72: 36 ablation vs. 36 IUD. 1 ablation and 5 IUD not included in analysis due to treatment failure.	Population characteristics: Women; >40 yrs; completed family; menorrhagia; no pathology; no cancer.  LNG-IUS: 44.1 yrs. TBA: 43.8 yrs.  Country: Turkey	Thermal balloon ablation after GnRH- a; LNG IUD (20ug daily)  Treatment versus baseline; treatment versus 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.

## Chapter 10 – Non-hysterectomy Surgery for HMB

### Dilation & Curettage for treatment of HMB – Comparative studies

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Haynes 1977 <sup>334</sup>	Study Type:  Evidence level: 2-	22	Population characteristics: women; MBL > 80ml  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.	

## Chapter 10 – Non-hysterectomy Surgery for HMB

### Endometrial ablation for treating HMB – Comparative studies

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
1999 Apr 336	Study Type: randomised; concealment; intention-to-treat  Evidence level: 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.



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Abbott 2003 <sup>342</sup>	Study Type: Randomised - 2:1 ratio, computer generated; concealment - opaque envelopes; double-blind  Evidence level: 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 - bi-polar 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	Funding Source: Not stated  Study summary: Both techniques are effective and safe, but Novasure produced better quality of life outcomes.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>indexes: EQ-5D vas scale (<math>p = 0.006</math>), EQ-5D index (<math>p = 0.001</math>), SF-12 PCS (<math>P &lt; 0.001</math>) or SF-12 MCS (<math>p = 0.016</math>).</p> <p>No difference between techniques, except for SF-12 MCS (<math>p = 0.04</math>)</p>	
Abbott 2003 <sup>103</sup>	<p>Study Type: Cohort</p> <p>Evidence level: 2+</p>	139 - 55 caveterm, 34 ELA, 13 ELITT, 37 NovaSure	<p>Population characteristics: Women; menorrhagia; PBAC &gt; 150; No intrauterine pathology; normal biopsy; Uterine length &lt;12 cm; pre-menopausal gonadotrophon level; Normal smear test; no plans for future childbearing.</p> <p>Country: UK &amp; Australia</p>	ELA, Cavaterm, ELITT, NovaSure	12 months	QoL: EQ-5D, SF-12	<p>Endometrial ablation versus general population at baseline: EQ-5D index: ablation = 0.72 (SD 0.28) vs. general population = 0.89 (SD 0.17), <math>P &lt; 0.0001</math></p> <p>EQ-5D vas: 75.79 (SD 17.21) vs. 85.19 (SD 15.51), <math>p &lt; 0.0001</math></p> <p>SF-12 PCS: 46.31 (SD 8.80) vs. 52.8, <math>p &lt; 0.0001</math></p> <p>SF-12 MCS: 43.28 (SD 4.55) vs. 51.9, <math>p &lt; 0.0001</math></p> <p>Endometrial ablation baseline versus 12-month: EQ-5D index: ablation = 0.72 (SD 0.28) vs. general population = 0.83 (SD 0.25), <math>P = 0.005</math></p> <p>EQ-5D vas: 75.79 (SD 17.21) vs. 82.49 (SD 15.28), <math>p &lt; 0.0001</math></p> <p>SF-12 PCS: 46.31 (SD 8.80) vs. 51.24 (SD</p>	<p>Funding Source: Unclear? Grants for research on ELITT and NovaSure</p> <p>Study summary: Quality of life in women who have undergone ablation is improved to normal level, equivalent to the general population.</p>

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>7.54), <math>p &lt; 0.0001</math>  SF-12 MCS: 43.28 (SD 4.55) vs. 49.31 (SD 10.07), <math>p &lt; 0.0001</math></p> <p>Endometrial ablation 12-months results versus general population:  EQ-5D index: ablation = 0.83 (SD 0.25) vs. general population = 0.89 (SD 0.17), <math>P = 0.03</math>  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</p>	
Alborzi 2002 <sup>406</sup>	<p>Study Type: randomised; blinding and concealment not mentioned</p> <p>Evidence level: 1-</p>	90 - 45 pre-treatment group, 45 control group	<p>Population characteristics: Women; menorrhagia - subjective; excluded if - active pelvic inflammatory disease, hyperplasia, malignancy; extensive uterine cavities; large fibroids; wish for future fertility</p> <p>Country: Iran</p>	Pre-treatment - Danazol 600mg daily for 4 to 6 weeks or Decapeptyl one ampule monthly for two months; control group	3 months	<p>Menstrual bleeding patterns; Duration of procedure; adverse events.</p>	<p>Operative time: Pre-treatment = 25 min (SD 4), control = 40 mins (SD 5)</p> <p>Distending medium used during procedure: Pre-treatment = 3.5 litres, Control = 4.5 litres</p> <p>Menstrual bleeding pattern (normal or no bleeding): Pre-treatment = 42 (93%), control = 42 (93%)</p>	<p>Funding Source: Not stated</p> <p>Study summary: Ablation is an effective treatment, but pre-treatment has no effect on patient outcome, though does reduce operating time.</p>

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Barrington 2003 <sup>262</sup>	Study Type: randomised  Evidence level: 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 >12cm  Country: UK	LNG-IUS; thermal balloon ablation  treatment versus baseline	6 months	MBL - PBAC	MBL (mean): IUS pre-treatment = 107ml vs. 31ml post-insertion (-71%); Ablation pre-treatment = 122ml vs. 61ml post-surgery (-50%). No difference between groups (p=0.689).  MBL (median): IUS pre-treatment = 75ml vs. 19ml post-insertion; Ablation pre-treatment = 101ml vs. 27ml post-surgery.	Funding Source: not stated  Study summary: Study shows LNG-IUS and thermal ablation are equivalent.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Bhattacharya 1997 <sup>343</sup>	Study Type: randomised - computer- generated; concealment - sealed envelopes  Evidence level: 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 mins (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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Bhattacharya 1996 Sep <sup>365</sup>	Study Type: Groups based on RCT  Evidence level: 2+	204 - 99 (21 non-responders) in hysterectomy, 105 (23 non-responders) in ablation	Population characteristics: Women; part of previous RCT for ablation versus hysterectomy for HMB  Country: UK	Hysterectomy; Endometrial ablation - ELA or TCRE	2 years	Bladder function; ovarian function	<p>Cystometry findings: Total bladder dysfunction - hysterectomy = 14 (31%), Ablation = 17 (35%)</p> <p>Bladder symptoms: Stress incontinence - hysterectomy = 32 (44%), ablation = 35 (44%) Urge incontinence - hysterectomy = 15 (21%), ablation = 15 (19%)</p> <p>Ovarian function: FSH level &gt; 40 - hysterectomy = 3 (6%), ablation = 5 (10%) Patients on HRT - hysterectomy = 8 (16%), ablation = 5 (10%) Hot flushes - hysterectomy = 25 (35%), ablation = 35 (44%)</p> <p>Worsening of symptoms from baseline to 2-years: Stress incontinence - hysterectomy = 11 (15%), ablation = 13 (16%) Urge incontinence - hysterectomy = 10 (14%), ablation = 12 (15%) Hot flushes - hysterectomy = 5 (7%),</p>	<p>Funding Source: Not stated</p> <p>Study summary: Bladder and ovarian symptoms do not differ between hysterectomy and ablation at 2-years follow-up.</p>

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							ablation = 14 (18%)	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Bongers 2005 <sup>341</sup>	Study Type: randomised; concealment  Evidence level: 1+	126 randomised. 83 to bi-polar ablation, 43 to balloon ablation. No loss to follow-up	Population characteristics: women; PBAC > 150; uterine cavity was 6 to 11cm; 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 radio-frequency endometrial ablation; thermal balloon ablation	12-months	Quality of life - SF-36, depression scale, Rotterdam symptom checklist, State-Trait Anxiety Inventory	SF-36 scores (at baseline (SD) and at 12-months (SD) for bipolar then balloon, with p-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), p < 0.001, p = 0.54 Role physical: 79 (SD 30) to 94 (SD 28), 73 (SD 27) to 89 (SD 24), p < 0.001, p = 0.56 Role emotional: 85 (SD 26) to 99 (SD 5), 80 (SD 26) to 95 (SD 15), p < 0.001, p = 0.97 Social functioning: 76 (SD 19) to 89 (SD 16), 76 (SD 21) to 86 (SD 21), p < 0.001, p = 0.86 Mental health: 72 (SD 18) to 80 (SD 15), 72 (SD 18) to 80 (SD 18), p < 0.001, p = 0.74 Energy/vitality: 56 (SD 19) to 73 (SD 18), 54 (SD 20) to 64 (SD 21), p < 0.001, p = 0.88 Pain: 62 (SD 20) to 76 (SD 24), 63 (SD 22) to 77 (SD 25), p < 0.001, p = 0.59 General health: 73 (SD 19) to 81 (SD 18), 76 (SD 21) to 75 (SD 23), p = 0.18, p = 0.84	Funding Source: Not stated  Study summary: Both methods of ablation significantly improve QoL



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							On differences between groups on Rotterdam symptom checklist or state-trait anxiety score.	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Bongers 2004 <sup>361</sup>	Study Type: randomised - 2:1 ratio; double-blind; intention-to- treat; allocation concealment - opaque envelopes  Evidence level: 1+	126 randomised. 83 to bi-polar ablation, 43 to balloon ablation. No loss to follow- up	Population characteristics: women; PBAC > 150; uterine cavity was 6 to 11cm; 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 radio- frequency 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 (p = 0.001), and bipolar reduce MBL more than balloon (p = 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: Bi-polar ablation is more effective than balloon ablation for treating menorrhagia. .

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Bongers 2000 <sup>366</sup>	Study Type: Cohort; comparative; prospective  Evidence level: 2-	152 of which 75 TCRE, 77 TBEA	Population characteristics: Women; menorrhagia; failed medical treatment; uterus < 12cm; no submucous fibroids or intra-uterine adhesions  Country: Netherlands	TCRE; TBEA  TCRE vs. TBEA	24 months	Patient satisfaction; Subsequent surgery; complications	<p>Patient satisfaction: Satisfied or better with TCRE: 3-months = 68 (91%), 6-months = 44 (64%), 12 months = 31 (54%), 24 months = 23 (49%)</p> <p>Satisfied or better with TBEA: 3-months = 66 (86%), 6-months = 45 (73%), 12 months = 48 (76%), 24 months = 30 (64%)</p> <p>Cumulative re-intervention rate at 3-years: TCRE = 26%, TBEA = 13%, NS</p> <p>Complications: 13 (17%) of TCRE had to be abandoned. 8 (10%) of TBEA had to be converted to TCRE</p>	<p>Funding Source: Not stated</p> <p>Study summary: TBEA is as effective as TCRE but with lower complications rates.</p>

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Boujida 2002 <sup>344</sup>	Study Type: randomised; concealed  Evidence level: 1-	120 - 61 (4 lost to follow-up by 5-years) rollerball ablation, 59 (3 lost to follow-up by 5-years) TCRE	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, TCRE = 44.8 Number with menorrhagia = 31, 30 Number with submucous fibroids = 13, 12  Country: Denmark	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 n = 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  Recommend to a friend: 49 in REA and 46 in TCRE would recommend (p > 0.05)  Complications: 1	Funding Source: West Zealand Health Authority

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Cooper 2002 <sup>346</sup>	Study Type: Randomised - 2:1 ratio; multicenter  Evidence level: 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 <6cm or >10cm.  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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Cooper 2004 <sup>347</sup>	Study Type: Prospective; multi-centre; randomised - 2:1 ratio; blinding not mentioned; concealment not mentioned  Evidence level: 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 3.75mg  Surgery versus baseline; surgery versus 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 to 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 versus 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	Funding Source: Not stated  Study summary: Microwave ablation is safe and efficacious treatment for menorrhagia

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							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).	
Cooper 2005 <sup>345</sup>	Study Type: randomised - 1:1 ratio, balanced blocks; concealment - opaque envelopes  Evidence level: 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 3.6mg	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 p-value of change since baseline, TCRE change, MEA p-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), p<0.01, 9.7 (25), p < 0.001. Role - physical: 56.5 (42.2), 62.9 (41.7), 17 (54), p < 0.01, 11 (43), p < 0.01.	Funding Source: Not stated  Study summary: Both treatments are safe and effective treatments for HMB, however, MEA is associated with greater patient satisfaction.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>Role - emotional: 61.8 (42.5), 62.6 (43.2), 19 (48), <math>p &lt; 0.001</math>, 20 (41), <math>p &lt; 0.001</math>.</p> <p>Mental health: 63.6 (18.8), 63.8 (21.7), 1.4 (21), ns, 1.2 (21), ns.</p> <p>Energy/fatigue: 44.3(22.6), 43.3 (24.3), 9.3 (25), <math>p &lt; 0.001</math>, 12 (23), <math>p &lt; 0.001</math></p> <p>Pain: 55.4 (28.2), 63.7 (26.1), 9.3 (35.0), <math>p &lt; 0.01</math>, 6.4 (31), <math>p &lt; 0.05</math>.</p> <p>General Health: 69.7 (21.7), 73.0 (19.4), -3.3 (26), ns, -2.4 (19), ns.</p> <p>Patient satisfaction: MEA = 100 (86%), TCRE = 87 (74%)</p> <p>Cure or acceptable improvement: MEA = 95 (83%), TCRE = 88 (75%)</p>	
Cooper 1999 <sup>246</sup>	<p>Study Type: Randomised; concealed</p> <p>Evidence level: 1++</p>	272 eligible, 187 recruited, 94 randomised to medical treatment, 93 to TCRE. By two years 86 medical and 87 TCRE patients remained in the study.	<p>Population characteristics: Women; referred due to HMB; completed family; &lt;10 weeks size uterus; normal uterine pathology; referred for surgery.</p> <p>Baseline characteristics (medical vs. TCRE):</p>	Medical treatment; TCRE	2 years	QoL (SF-36); patient satisfaction; menstrual status; bleeding score	<p>Outcomes for medical versus TCRE.</p> <p>QoL (SF-36):</p> <p>Baseline:</p> <p>Physical functioning = 78.67 vs. 82.33</p> <p>Social functioning = 68.35 vs. 70.03</p> <p>Role: physical = 53.01 vs. 56.98</p> <p>Role: emotional = 57.43 vs. 55.03</p> <p>Mental health = 58.20 vs. 59.43</p>	<p>Funding Source: Scottish Office Department of Health</p> <p>Study summary: The results at two 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</p>



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			<p>Age = 41.4 vs. 41.9</p> <p>Haemoglobin (g/dl) = 12.79 vs. 12.61</p> <p>Menstrual symptom rating = mild/moderate = 6 vs. 4</p> <p>Severe = 54 vs. 52</p> <p>Very severe = 26 vs. 32</p> <p>Bleeding score = 24.7 vs. 24.8</p> <p>Country: UK</p>				<p>Energy/fatigue = 40.36 vs. 41.49</p> <p>Pain = 53.55 vs. 58.14</p> <p>General health = 68.17 vs. 65.90</p> <p>Change by 2 years:</p> <p>Physical functioning = 3.73 vs. 5.00</p> <p>Social functioning = 3.94 vs. 10.59</p> <p>Role: physical = 12.95 vs. 18.60</p> <p>Role: emotional = 11.25 vs. 22.48</p> <p>Mental health = 7.17 vs. 9.98</p> <p>Energy/fatigue = 10.06 vs. 14.58</p> <p>Pain = 11.38 vs. 12.34</p> <p>General health = -0.67 vs. 1.69</p> <p>No significant difference between groups.</p> <p>patient satisfaction:</p> <p>Totally or generally satisfied with treatment = 48 (57%) vs. 68 (79%), p = 0.002</p> <p>Cure or acceptable improvement = 53 (61%) vs. 69 (81%), p = 0.017</p> <p>Treatment acceptable = 65 (77%) vs. 79 (93%), p = 0.004</p> <p>Menstrual status:</p> <p>No bleeding or light = 36 (42%) vs. 50 (58%), p</p>	in an effort to try alternative medical therapies.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							= 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 <sup>349</sup>	Study Type: randomised - 1:2 ratio; intention-to-treat  Evidence level: 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 = 10.5cm; history of HMB; failed medical treatment; no active pelvic inflammatory disease; intramural myoma <4cm; 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. :

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Corson 2000 <sup>348</sup>	Study Type: randomised - block  Evidence level: 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	Chaney 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.
Crosignani 1997 <sup>265</sup>	Study Type: randomised; open; prospective  Evidence level: 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	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).	Funding Source: National Research Council (Rome)  Study summary: LNG- IUS produces slightly less satisfactory results than resection at 12- months.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			<p>excluded; using hormonal treatment in last 3 months; serious concomitant condition excluded.</p> <p>IUD group - age 43.8, parity = 1.8, BMI = 25.3</p> <p>Endometrial resection group - age = 45.4, parity = 1.6, BMI = 24.0</p> <p>Country: Italy</p>				<p>Difference between LNG-IUS and resection <math>p = 0.015</math>.</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</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							other treatment.	
Duleba 2003 <sup>350</sup>	Study Type: Randomised - 2:1 ratio; concealment - sealed envelopes  Evidence level: 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 > 2cm, submucous myoma or polyps, previous ablation, pregnant, hyperplasia or malignancy.  Average age:	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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			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					
English 1998 402	Study Type: randomised; concealed; blinded - but method not mentioned Evidence level: 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 403	Study Type: randomised; blinded assessment Evidence level: 1+	163 screened for inclusion, 43 not randomised, 40 (32 at 12-months) in 200 mg Danazol group, 40 (32 at 12-months) in 600 mg Danazol group, and 40 (30 at 12-months) in placebo group	Population characteristics: Women; menorrhagia; scheduled for TCRE; failed medical treatment; uterine size < 10 weeks; no uterine scars Country: Australia	Pre-treatment with Danazol 200mg for 6 weeks; TCRE; post-surgery - Danazol 200mg, Danazol 600mg, placebo	12 months	menstrual blood loss; adenomyosis prevalence	12-month menstrual bleeding: Placebo (n=30) 100% had reduced bleeding Danazol 600mg (n = 32) 100% had reduced bleeding Danazol 200mg (n = 28) 100% had reduced bleeding Amenorrhoea rates higher in Danazol groups than placebo (p = 0.011)	Funding Source: Winthrop

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Garside 2004 <sup>339</sup>	Study Type: systematic review; meta-analysis; economic analysis  Evidence level: 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 where 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.	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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>Satisfaction with treatment: trials show high level of satisfaction (&gt;75%) with both MEA and TBEA.</p> <p>QoL: trials report improvement in QoL with both MEA and TBEA.</p> <p>Duration of procedure: trials show that MEA and TBEA both took less time to complete than first generation ablation techniques.</p> <p>Adverse effects: trial report that MEA was associated with greater equipment failure than first-generation ablation. No figures were available for TBEA.</p>	



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Gervaise 1999 <sup>367</sup>	Study Type: Prospective; cohort; matched  Evidence level: 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.  .

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Goldrath 2003 <sup>362</sup>	Study Type: Randomised - 2:1 ratio; multicentre  Evidence level: 1+	276 randomised, 269 received treatment. 177 (18 lost to follow-up, 24 had additional treatments) in HTA group, and 85 (14 lost to follow-up, 8 had additional treatments) in rollerball group	Population characteristics: Women; aged 30 to 50 years; completed families; menorrhagia - PBAC; uterine cavity between 4 and 10.5cm; failed or refused medical treatment; excluded if - pelvic inflammatory disease, intramural myomas > 4cm, submucous myomas, polyps or septate uterus.  Country: USA	Hydrothermal ablation (HTA); rollerball ablation (REA); pre- treatment of depot leuprolide acetate 7.5 mg.	12, 24, 36 months	Change in MBL (PBAC); Patient satisfaction; Additional treatment; Change in QoL	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) 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.	Funding Source: BEI medical systems  Study summary: HTA was a safe and effective method of treating HMB.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Grainger 2000 <sup>359</sup>	Study Type: randomised - 1:1; non-blinded; concealment not mentioned; ITT not mentioned; Sample size given  Evidence level: 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 10cm; 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Istre 2001 <sup>268</sup>	Study Type: Randomised  Evidence level: 1+	60: 30 LNG-IUS; 30 resection - 6 discontinued treatment by 12 months.	Population characteristics: women; menorrhagia (PBAC > 75); pre-menopausal; 30-49 yrs; regular uterine cavity <10cm; no pregnant or wanting to become so, breast feeding; large fibroid >40cm; 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Jack 2005 <sup>405</sup>	Study Type: Randomised - 1:1 ratio using block randomisation; concealment - opaque letters via telephone;  Evidence level: 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. 13 not randomised	Population characteristics: Women; complaining of HMB; normal endometrial pathology; family completed; uterine size 12 weeks or less; Submucous fibroids < 3cm  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 200mg bd, depot Gosealin 3.6mg 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 = 4.47mm (SD 2.67), Drug group = 2.6mm (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:	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 & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							Post-menses = 55.9%, Drug group = 61.9%	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Kriplani 2001 <sup>408</sup>	Study Type: randomised - computer generated  Evidence level: 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 mins, Control = 31.6 mins  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 <sup>404</sup>	Study Type: randomised - computer generated; no concealment; no blinding  Evidence level: 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	Danazol (as pre-treatment) 400-600mg a day for 4-6 weeks prior to surgery; TCRE - all patients  Pre-treatment versus 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.	Funding Source: Not stated  Study summary: Study shows that TCRE is an effective treatment for menorrhagia, with or without pre-treatment.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			years, no treatment = 3.8 years  Country: India				<p>No pre-treatment at 6-years (n = 31): 15 had amenorrhoea, 8 had spotting, and 8 had significant improvement.</p> <p>Later groups had smaller numbers as not all patients had reached that length of follow-up.</p> <p>Procedure differences (Danazol versus no pre-treatment):</p> <p>endometrial thickness - 3.43 (SD 1.02) vs. 11.45 (SD 1.89), <math>p &lt; 0.001</math></p> <p>Mean fluid used - 3630.30ml (SD 1378) vs. 5013.67 (SD 1779), <math>p &lt; 0.005</math></p> <p>Mean fluid deficit - 512.5 (SD 268.8) vs. 632.4 (SD 264.7), <math>p &lt; 0.05</math></p> <p>Mean duration of surgery - 25.7 mins (as 3.4) vs. 33.6 mins (SD 3.8), <math>p &lt; 0.001</math>.</p> <p>Repeat resection - 1 vs. 1</p> <p>Hysterectomy = 1 vs. 1</p>	
Lethaby <sup>340</sup>	Study Type: Systematic review; meta-analysis  Evidence level: 1++	19 studies included. 3285 pre-menopausal women included.	Population characteristics: Search on MEDLINE; EMBASE; Cochrane Library; PsycLit; CINAHL.	Any endometrial destruction technique: transcervical resection of the endometrium (TCRE); vaporising	n/a	Patient outcome - amenorrhoea rates; satisfaction; QoL. Operative time; re-operation rates;	Laser versus TCRE: Laser ablation took longer - 9 mins (WMD: 9.15) - and equipment more likely to fail - (OR = 6 [CI 1.7 to 20.9]. No difference between	Funding Source: No stated  Study summary: Newer ablation techniques have success and complications rates



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			<p>Article reference lists, hand-searching of journals and pharmaceutical companies contacted.</p> <p>Inclusion criteria: RCT only; Comparison of endometrial techniques only; HMB; no pathology - fibroids</p> <p>Country:</p>	<p>electrode; rollerball; thermal laser ablation; hydro-thermoblator; cryoablation; electrode ablation; microwave ablation; balloon; bi-polar electrode</p>		<p>complications.</p>	<p>methods for patient outcomes - amenorrhoea rates, satisfaction, QoL or complications.</p> <p>Vaporising electrode versus 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 mins [CI 0.35 to 2.65]. No difference between methods for patient outcomes - amenorrhoea rates, satisfaction, QoL.</p> <p>Rollerball versus TCRE: No difference between techniques on future hysterectomy or re-surgery at 2 and 5 years follow-up.</p> <p>Thermal laser versus 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</p>	comparable with 'gold standard' method of TCRE.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>in thermal group (OR = 0.7 units [CI 0.02 to 1.4]). No difference between groups for menorrhagia, re-surgery, complications or satisfaction.</p> <p>Hydro thermoblator versus 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]).</p> <p>Cryoablation versus rollerball: Cryo group less likely to have amenorrhoea at 1 year (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 &lt;75), menorrhagia rates, hysterectomy rates.</p> <p>Electrode ablation (balloon or mesh) versus</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>TCRE: Operative time with TCRE was longer (WMD = 18.7 mins [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 versus 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</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>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 versus 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 mins [CI 19.2 to 22.5]). Other outcomes showed no differences at 12, 24 and 36 months.</p> <p>Balloon versus 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 versus TCRE:</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>Balloon surgery quicker (WMD 13 mins [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 versus 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 versus 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</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							difference in satisfaction rates, except at 24-months. No difference in amenorrhoea rates or need for additional surgery.	
Lissak 1999 <sup>407</sup>	Study Type: randomised; blinding and concealment not mentioned  Evidence level: 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 fertility.  Average age: pre-treatment = 48.7, control = 45.6 Gravdiit: 4.9, 3.9  Country: Israel	Pre-treatment - intramuscular injection of decapeptyl 3.75mg 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	Duration of procedure: pre-treatment = 8.44 mins, control = 8.44 mins  Menstrual bleeding pattern (normal or no bleeding): pre-treatment = 17 (100%), control = 13 (100%)  Patient satisfaction: Pre-treatment = 15 (88%), control = 11 ((2%)  No major adverse events reported in either group.	Funding Source: Not stated  Reviewer comments: Small study size, plus lack of information on concealment and blinding, are likely causes of bias.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Loffer 2001 <sup>357</sup>	Study Type: Randomised - 1:1;  Evidence level: 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 4cm and 10cm; Patient had no desire for future fertility; willing to use same contraception for 3-years; minimum MBL score - PBAC  Country: USA & 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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Loffer 2002 <sup>358</sup>	Study Type: randomised - 1:1 ratio; non-blinded; concealment not mentioned; ITT not mentioned  Evidence level: 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 10cm; 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.



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
McClure 1992 <sup>351</sup>	Study Type: randomised  Evidence level: 1-	38 women assessed. 22 randomised. 12 to laser ablation, and 10 to electrocautery.	Population characteristics: Women; Menorrhagia (>80ml); 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 (mins): Laser = 114 mins, electro = 80 mins (P < 0.001).	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Meyer 1998 <sup>360</sup>	Study Type: randomised - 1:1 ratio; concealment not mentioned; non-blinded  Evidence level: 1-	275 randomised, 255 included in study, 250 treated as per protocol. Numbers randomised to each group not stated. Demographic data available on 128 in TBEA and 117 in REA.	Population characteristics: Women; menorrhagia; => 30 years of age; failed medical treatment for HMB; normal biopsy and pap smear; normal uterine cavity; excluded if - suspected 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	TBEA; REA	12 months	Satisfaction; MBL (menstrual diaries); Amenorrhoea rate; Procedure duration (minutes); Complications	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): = - 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	Funding Source: Gynecare Inc.  Study summary: In the treatment of dysfunctional uterine bleeding, uterine balloon therapy is as efficacious as hysteroscopic rollerball ablation and may be safer.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Mousa 2001 <sup>368</sup>	Study Type: Matched case-control  Evidence level: 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Pellicano 2002 <sup>363</sup>	Study Type: randomised; non-blinded; concealment not mentioned  Evidence level: 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 < 100kg; 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	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 & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							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 UTI = 1 vs. 0 Haemorrhage = 4 vs. 5 Blood transfusions = 0 vs. 2  Re-operation rate: 9 vs. 4  Bleeding recurrence: 17 vs. 6	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Perino 2004 <sup>352</sup>	Study Type: randomised - computer generated;  Evidence level: 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 3.75mg	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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Rauramo 2004 <sup>270</sup>	Study Type: randomised; open; equivalence  Evidence level: 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: 41.4yrs, 73.4kg. TCRE: 42.1 yrs, 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 & pain from resection, plus 1 stroke	Funding Source: Schering Ag  Study summary: Both treatments effectively reduced MBL.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Shawki 2000 <sup>337</sup>	Study Type:  Evidence level: 1-	131 randomised (D&C = 39, goserlin 3.6mg SC for 1 months = 23, geserlin 3.6mg SC for 3 months, Danazol 400- 600 mg PO per day for 3 months = 26 MPA 15 mg PO per day before procedure = 23)	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, goserlin 3.6mg SC for 1 months Geserlin 3.6mg 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 goserlin for 1 month (n = 23): 21, 9 goserlin 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) goserlin for 1 month (n = 23): 39 (SD 7) goserlin 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)  change in bleeding pattern by surgical technique: no difference between groups (THIS ANALYSIS IS NOT BASED ON RANDOMISED GROUPS)	Funding Source: Not stated



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Sowter 2002 <sup>401</sup>	Study Type: Systematic review; meta-analysis  Evidence level: 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, Goserlin, Leuprolide acetate, Danazol, progestins, progestogens.  Treatment versus treatment; treatment versus 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 versus placebo, and against one another. Only statistically significant differences reported here.  GnRH versus 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.	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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>GnRH vs. progestogens (n = 2): Endometrial thickness - WMD = -2.80 [-3.59 to -2.01]</p> <p>No other differences.</p> <p>Danazol vs. no pre-treatment (n = 2): Endometrial atrophy - RR = 3.15 [1.46 to 6.80]</p> <p>No other differences.</p> <p>Progestogens vs. no pre-treatment (n = 2) No differences</p> <p>Danazol vs. progestogens (n = 2)</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Soysal 2002 <sup>272</sup>	Study Type: randomised; blind  Evidence level: 1+	72: 36 ablation vs. 36 IUD. 1 ablation and 5 IUD not included in analysis due to treatment failure.	Population characteristics: Women; >40 yrs; completed family; menorrhagia; no pathology; no cancer.  LNG-IUS: 44.1 yrs. TBA: 43.8 yrs.  Country: Turkey	Thermal balloon ablation after GnRH- a; LNG IUD (20ug daily)  Treatment versus baseline; treatment versus 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Soysal 2001 <sup>353</sup>	Study Type: Prospective; randomised - computer generated; concealment - opaque envelopes  Evidence level: 1+	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 <5cm; active pelvic inflammatory disease; Submucous fibroids > 3cm 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	Thermal balloon ablation (TBA); Rollerball ablation (RBA); Pre- treatment in both groups of GnRH  Surgery versus surgery	3-, 6-, 12-months follow-up	MBL - PBAC; Duration of procedure; complications; pain score of surgery; Amenorrhoea rates	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 mins versus RBA = 37.3 mins (P<0.0001)  Intra-operative complication rates: TBA = 0 versus RBA = 3 (p<0.05)  No difference on other outcome measures.  No loss to follow-up	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Van Zon-Rabelink 2004 <sup>356</sup>	Study Type: random; blinded; concealment not outlined in detail  Evidence level: 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	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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							Procedure details and complications not stated.	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Van Zon-Rabelink 2003 <sup>355</sup>	Study Type: Randomised; blinded  Evidence level: 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Vercellini 1999 <sup>354</sup>	Study Type: randomised - 1:1; blinded; concealment - opaque envelopes  Evidence level: 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; 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	vaporising electrode; TCRE; pre-treatment with GnRH	12 months	Duration of operation (minutes); complications with operation; fluid deficit; MBL (PBAC); Menstrual pattern; Patient satisfaction; Haemoglobin levels (g/dl)	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 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	Funding Source: Not stated  Study summary: Endometrial ablation with the vaporizing electrode limited fluid absorption compared with resection by the standard cutting loop. Long-term effects on uterine bleeding were similar.



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Vihko 2003 <sup>364</sup>	Study Type: Randomised; blinding not mentioned; concealment not mentioned  Evidence level: 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 > 2cm 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 to 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 to 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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Zupi 2003 <sup>338</sup>	Study Type: Randomised; concealment and blinding not mentioned  Evidence level: 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 100kg; 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 (3.75mg) 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 mins, LSH = 71.5 mins, $p < 0.01$  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 (SD 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)	Funding Source: Not stated  Study summary: Laparoscopic hysterectomy may offer curative advantages of hysterectomy with operative advantages of ablation.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>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> <p>P &lt; 0.01 for change in general health score for both treatments, and for difference after treatment between groups in favour of hysterectomy.</p> <p>P &lt; 0.01 for change in emotional role in hysterectomy group</p> <p>P &lt; 0.01 for change in social function score for both treatments, and for difference after treatment between groups in favour of hysterectomy.</p> <p>P &lt; 0.01 for change in vitality score for hysterectomy treatments, and for difference after treatment between groups in favour of hysterectomy.</p>	

## Chapter 10 – Non-hysterectomy Surgery for HMB

### Endometrial ablation for treatment of HMB – Additional non-comparative studies

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Clarke 2005 <sup>369</sup>	Study Type: Cohort  Evidence Level: 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 <sup>370</sup>	Study Type: Case-series  Evidence Level: 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.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Donnez 2000 <sup>371</sup>	Study Type: Case-series  Evidence Level: 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 <sup>372</sup>	Study Type: Case-series  Evidence Level: 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 <sup>373</sup>	Study Type: Case-series  Evidence Level: 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 > 12cm, 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

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Erian 1994 <sup>374</sup>	Study Type: Prospective; case-series  Evidence Level: 3	Endoscopic laser ablation; Danazol 200mg tid 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.
Erian 1996 <sup>375</sup>	Study Type: Case-series  Evidence Level: 3	TCRE; Pre-treatment with Danazol 200mg tid 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 (n = 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 <sup>376</sup>	Study Type: Case-series  Evidence Level: 3	Thermal Balloon ablation (TBA)	141: 53 had completed 24 month follow-up	Women; referred due to heavy or prolonged menses; uterus size <10cm; Women with AUB associated with pathology were	Bleeding pattern; patient satisfaction; additional therapy	Bleeding patterns: Baseline - all had menorrhagia.  At 6-monhts: 32 had amenorrhoea, 63 had hypomenorrhoea, 27 had eumenorrhoea, 7 had menorrhagia, 11 had undergone hysterectomy.	Funding Source: Not stated  Study Summary: TBA is safe and efficient method to treat menorrhagia.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
				<p>excluded.</p> <p>47 women had ablation as first-line treatment.</p> <p>Country: USA</p>		<p>At 12 months: 25 had amenorrhoea, 47 had hypomenorrhoea, 22 had eumenorrhoea, 2 had menorrhagia, 15 had undergone hysterectomy.</p> <p>At 24-months: 15 had amenorrhoea, 19 had hypomenorrhoea, 14 had eumenorrhoea, 5 had menorrhagia, 19 had undergone hysterectomy.</p> <p>Patient satisfaction: 95% of patients were satisfied with TBA result.</p> <p>Subsequent treatment: 28 of 141 women underwent additional treatment: 1 myomectomy, 6 hormonal treatments, 21 hysterectomies (14 for menorrhagia).</p>	
<p>Ferry 1994 <sup>377</sup></p>	<p>Study Type: Case-series</p> <p>Evidence Level: 3</p>	TCRE	278	<p>Women; menstrual disorders; malignancy excluded; uterine size &lt; 12 weeks</p> <p>Country: UK</p>	<p>Patient satisfaction; complications</p>	<p>Patient satisfaction at 4-months: 90%</p> <p>Complications: 13 procedures not completed, 13 patient required overnight stay due to complications</p>	<p>Funding Source: Not stated</p>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Friberg 2000 <sup>378</sup>	Study Type: Case-series  Evidence Level: 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 (n = 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 (p < 0.001)  Subsequent hysterectomy: 10 women had hysterectomy - 7 for menorrhagia	Funding Source: Not stated
Gallinat 2001 <sup>379</sup>	Study Type: Case-series  Evidence Level: 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) (n = 122): amenorrhoea = 42%, hypomenorrhoea = 44%, Eumenorrhoea = 4%  Subsequent hysterectomies = 5	Funding Source: Not stated



Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Gallinat 2004 <sup>380</sup>	Study Type: Case-series; prospective  Evidence Level: 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 (n = 103): 65% had amenorrhoea 26% had spotting 3% had hypomenorrhoea 3% had eumenorrhoea 3% had menorrhagia  Additional treatment: 3 hysterectomies and 1 re-ablation	Funding Source: Not stated  Study Summary: NovaSure is a safe and effective treatment for menorrhagia.
Gandhi 1999 <sup>381</sup>	Study Type: Case-series  Evidence Level: 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.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Garry 1991 <sup>382</sup>	Study Type: Case-series  Evidence Level: 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 & 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 <sup>383</sup>	Study Type: Case-series  Evidence Level: 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 > 2cm; 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

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Lefler 2003 <sup>384</sup>	Study Type: Case-series  Evidence Level: 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 100ml, mean was 154ml (SD 289)	Funding Source: Not stated  Study Summary: RLR was associated with good long-term outcomes.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
McPherson 2005 <sup>385</sup>	Study Type: Cohort  Evidence Level: 3	TCRE; hysterectomy with or without BOS	Numbers responding at 5-year follow-up: TCRE = 3845, hysterectomy = 3397, hysterectomy & BOS = 2305	Women; undergone TCRE or hysterectomy.  Average age at 5-year follow-up: TCRE= 47.9, hysterectomy = 54.1, BOS = 50.6  Country: UK	Libido loss, difficult sexual arousal; vaginal dryness.	Adjusted Odds Ratio for loss of libido against TCRE (adjusted for age and HRT use): Some - Hysterectomy = 1.25 (1.13 to 1.39), BOS = 1.32 (1.16 to 1.51), p = 0.254 Severe - Hysterectomy = 1.29 (1.16 to 1.44), BOS = 1.68 (1.48 to 1.92), p < 0.001 Extreme - hysterectomy = 1.42 (1.22 to 1.65), BOS = 1.80 (1.51 to 2.14), p < 0.001  Adjusted Odds Ratio for difficulty of sexual arousal against TCRE (adjusted for age and HRT use): Some - Hysterectomy = 1.16 (1.05 to 1.29), BOS = 1.27 (1.11 to 1.44), p = 0.068 Severe - Hysterectomy = 1.28 (1.15 to 1.44), BOS = 1.79 (1.56 to 2.05), p < 0.001 Extreme - hysterectomy = 1.35 (1.15 to 1.58), BOS = 1.82 (1.52 to 2.19), p < 0.001.  Adjusted Odds Ratio for vaginal dryness against TCRE (adjusted for age and HRT use): Some - Hysterectomy = 1.28 (1.15 to 1.41), BOS = 1.17 (1.03 to 1.33), p = 0.057 Severe - Hysterectomy = 1.55 (1.36 to 1.78), BOS = 1.43 (1.22 to 1.69), p = 0.170 Extreme - hysterectomy = 1.50 (1.19 to 1.88), BOS = 1.69 (1.29 to 2.22), p = 0.195.	Funding Source: Department of Health & 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 BOS at the time of hysterectomy.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
McPherson 2005 <sup>386</sup>	Study Type: Prospective cohort  Evidence Level: 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	Odds Ratio of Urinary symptoms for hysterectomy compared to 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)	Funding Source: DoH & BUPA

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						<p>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)</p> <p>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)</p>	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
O'Connor 1996 <sup>387</sup>	Study Type: Case-series  Evidence Level: 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 > 5cm.  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) = 585ml 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

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Parkin 2000 <sup>388</sup>	Study Type: Case-series  Evidence Level: 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 26399}	Study Type: Case-series  Evidence Level: 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



Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Pooley 1998 <sup>390</sup>	Study Type: Case-series  Evidence Level: 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 S <sup>391</sup>	Study Type: Case-series  Evidence Level: 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% Early recovery of normal activity = 33% Less time off work = 30%	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						<p>Retain uterus = 18%            Avoid scar = 16%            Advised by GP = 8%            Early resumption of sexual activity = 8%</p> <p>What did you expect of surgery:            Lighter = 92%            No period = 6%            Shorter periods = 79%            Same length = 6%            Less painful = 46%            Same degree of pain = 12%            No pain = 18%</p> <p>Regression analysis of factors associated with satisfaction:            Age (&lt;40 or &gt;45) OR 6.66, p &lt; 0.001            Histology OR 2.11, p &lt; 0.05            Menstrual cycle (regular vs. irregular) OR 2.05, p &lt; 0.05.</p>	
Roushdy 1996 <sup>392</sup>	Study Type: prospective cohort  Evidence Level: 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:            108 had amenorrhoea and mean average uterine volume of 78.9ml.            8 had improved bleeding and mean average uterine volume of 98.7ml.            8 had persistent/recurring menorrhagia and mean average uterine volume of 112.8.</p> <p>No patient with uterine volume &lt; 110ml had recurring or persistent menorrhagia.</p>	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Seidman 2000 <sup>393</sup>	Study Type: Case-series  Evidence Level: 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.	Change in bleeding pattern with age: Decreased or amenorrhoea - <44 (n = 59) = 84.8%, 45 to 49 ( n = 72) = 95.5%, > 50 (n = 31) = 92.6%  Patient satisfaction: Satisfied or very satisfied - <44 = 81.4%, 45 to 49 = 92.5%, > 50 = 92.6%  Fluid overload requiring diuretics - <44 = 20.5%, 45 to 49 = 15.3%, > 50 = 25.8%  Blood transfusion - <44 = 6.8%, 45 to 49 = 5.6%, > 50 = 3.2%	Funding Source: Not stated
Sharma 2004 <sup>394</sup>	Study Type: Cohort; prospective  Evidence Level: 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 > 14cm  Average age: 40.2  Country: UK	Menstrual bleeding pattern	At 24 months: 70% had reduced menstrual blood loss pattern.  30 of original 115 had undergone hysterectomy due to recurrence of menorrhagia.	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Steffensen 1997 <sup>395</sup>	Study Type: Retrospective case-series, with follow-up  Evidence Level: 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	Amenorrhoea rates: 3 - months (n = 250) = 64% 12 - months (n = 232) = 55% 48 months (n = 25) = 81%  Hypomenorrhoea rates: 3 - months (n = 250) = 33% 12 - months (n = 232) = 35% 48 months (n = 25) = 11%  Additional surgery: 3 - months (n = 250) = 0 12 - months (n = 232) = 2 48 months (n = 25) = 13  Patient satisfaction: 3-months = 97%	Funding Source: Not stated  .

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Thijssen 1997 <sup>396</sup>	Study Type: Multi-centre; multi-national; case-series; prospective  Evidence Level: 3	Radiofrequency endometrial ablation (with and without pre-treatment)	1280	Women; subjective menorrhagia; aged 30 to 55 years; completed families; wish to retain uterus; no hyper- gonadotrophic; normal uterus size; normal cervical cytology; normal adnexa; no prolapse; no intrauterine abnormality; no history of bleeding disorders.  Recruited between 1990 and 1994.  Country: Worldwide: UK, Netherlands, South Africa, Australia, Spain, Denmark	Amenorrhoea rates, Hypomenorrhoea rates, Dissatisfaction rates.	Amenorrhoea rate = 184 of 1280 (14%) Hypomenorrhoea rate = 557 of 1280 (43.5%) Amenorrhoea/greatly reduced MBL/hypomenorrhoea = 78.5% Dissatisfied = 203 of 1280 (16%)  Complications: 19	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Tsaltas 1998 <sup>397</sup>	Study Type: Case-series; retrospective  Evidence Level: 3	Endometrial ablation - exact method not defined	232 questionnaires sent and 149 returned.	Women; undergone endometrial ablation  Country: Australia	Bleeding pattern; patient satisfaction	Bleeding patterns at follow-up:  No data for baseline  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.  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.	Funding Source: Not stated
Vilos 1997 <sup>398</sup>	Study Type: Prospective case-series  Evidence Level: 3	Thermal balloon ablation (thermablation); various forms of pre- treatment used	121 - 13 women had insufficient balloon pressure	Women; menorrhagia; major uterine pathology exclude; excluded if wanted future fertility.  Average age = 39 years  Country: USA	Menstrual bleeding pattern; additional surgical treatment	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  Additional surgery: 23 patients required additional surgery	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Vilos 1996 <sup>399</sup>	Study Type: Case-series  Evidence Level: 3	hysteroscopic endometrial ablation; pre-treatment with Danazol in 70% of cases	800 in 54 hospitals	women; menstrual symptoms requiring surgery.  618 (77.2%) had menorrhagia  Country: Canada	Complications	Peri-operative complications: 29 in total. 6 false passage, 7 uterine perforation, 8 excess fluid loss, 5 bleeding requiring tamponade, 3 incomplete surgery.  Long-term complications: 56 in total. 32 repeat ablation, 18 hysterectomies, 5 infections, 1 pregnancy.	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Wright 2003 <sup>400</sup>	Study Type: Case-control; after screening  Evidence Level: 3	Endometrial ablation - electrosurgical endometrial ablation	120 offered entry, 12 declined, 9 did not meet entry requirements (urgent hysterectomy required), 5 lost to follow-up, 7 withdraw after learning of normal MBL level. 87 were evaluable.	Women; referred for menorrhagia (subjective); fibroids < 5cm included, excluded if - endometrial neoplasia, FSH in menopausal range, hypothyroidism, or serious learning difficulties.  Average age: 42 years, Parity = 2  Country: UK	Present State Examination	63 of 108 women achieved 'caseness' with a Present State score $\leq 5$  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 versus control = 11.6 (3.3 to 40.2) 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%).	Funding Source: Not stated  Study Summary: Psychiatric outcome from endometrial ablation were linked to pre-surgical MBL levels and pre-surgical psychiatric scores.



## Chapter 11 – Interventions for Uterine Fibroids

### UAE for treatment of uterine fibroids – Comparative RCT & observational studies

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
417	Study Type: Randomised; open  Evidence level: 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 (mls) = 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 versus 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	Funding Source: Scottish Office

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>Vitality = 62 (21) vs. 67 (22), <math>p = 0.26</math>  Social function = 84 (23) vs. 87 (26), <math>p = 0.35</math>  Role - emotional = 81 (35) vs. 87 (30), <math>p = 0.22</math>  Mental health = 76 (17) vs. 76 (21), <math>p = 0.80</math></p> <p>EuroQoL at baseline  69.8 (15.8) vs. 62.9 (20.3)</p> <p>EuroQoL at 12 months  82 (16) vs. 83 (14), <math>p = 0.18</math></p> <p>pain score at 24 hours (0 to 10 scale, 10 is worst):  3.0 (2.1) vs. 4.6 (2.3), <math>p &lt; 0.001</math></p> <p>Symptom score at 12 months (-5 = worse to +5 score = better):  3.6 (2.0) vs. 4.3 (1.7), <math>p = 0.03</math></p> <p>Recommend to a friend at 12 months:  88% vs. 93%, <math>p = 0.32</math></p> <p>Complications:  Minor = 29 (27%) vs. 12 (23%)  Major = 8 (7%) vs. 3 (6%)</p> <p>Adverse events:</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							11 vs. 9  Treatment failure: UAE = 14  Subsequent treatment: 14 (13%) vs. 2 (4%)	
Broder <sup>455</sup>	Study Type:  Evidence level: 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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Goodwin 2006 <sup>426</sup>	Study Type: ITT; comparative cohorts; non- matched; multi- centre  Evidence level: 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 (n = 149) vs. myomectomy (n = 60)):  Mean age = 43.9 vs. 38.2 (p< 0.0001)	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)	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 & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			<p>Dominant symptom: AUB = 77 vs. 20 (<math>p = 0.02</math>) Bulk/pressure = 38 vs. 16 Pelvic pain = 29 vs. 18 Infertility = 0 vs. 2 Other = 5 vs. 4</p> <p>Duration of dominant symptom (months) = 145 vs. 60</p> <p>Number of fibroids (<math>p = 0.0001</math> for difference between groups). &lt;5 = 47 vs. 27 6 to 10 = 27 vs. 14 &gt;10 = 75 vs. 13</p> <p>Location of dominant fibroid (<math>p &lt; 0.0001</math> for difference between groups)</p> <p>Size of dominant fibroid (<math>\text{cm}^3</math>) = 182.12 (SD 208.978) vs. 226.92 (SD 196.394)</p>				<p>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)</p> <p>Significant improvement from baseline in both groups (<math>p &lt; 0.001</math>). No difference between groups.</p> <p>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</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			Uterine volume (cm <sup>3</sup> ): Baseline = 658.4 vs. 590.6 6-months = 404.3 vs. 251 (p<0.001 for change since baseline for both groups)				<p>Significant improvement from baseline in both groups (p &lt; 0.001). No difference between groups.</p> <p>Duration of hospital stay (hours): 23.8 vs. 61.6 (p &lt; 0.0001)</p> <p>At least 1 adverse event: 33 vs. 24 (p = 0.01)</p> <p>Total adverse events: 53 vs. 43</p> <p>Procedure related adverse events: 24 vs. 22</p> <p>Major adverse events: 6 vs. 1</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Gupta 2005 <sup>416</sup>	Study Type: Systematic review; meta-analysis  Evidence level: 1+	3 RCTs included.	Population characteristics: Searched the Cochrane Menstrual Disorders & 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 (mins); 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, Weighted Mean Difference (Fixed) 95% CI -16.40 [-26.04, -6.76] Intra-procedure blood loss (ml): 1, 156, Weighted Mean Difference (Fixed) 95% CI -405.20 [-512.71, -297.69] Intra-procedural complications: 2, 216, Odds Ratio (Fixed) 95% CI 2.02 [0.74, 5.47] Need for blood transfusion: 2, 216, Odds Ratio (Fixed) 95% CI 0.04 [0.00, 0.33] Length of hospital stay (days): 2, 213, Weighted Mean Difference (Fixed) 95% CI -3.27 [-3.77, -2.77] Unscheduled visits after discharge: 2, 217, Odds Ratio (Fixed) 95% CI 1.80 [0.98, 3.30] Readmission rates within 42 days: 2, 216, Odds Ratio (Fixed) 95% CI 6.00 [1.14, 31.53] Resumption to normal activities: 1, 59,	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 to 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>Weighted Mean Difference (Fixed) 95% CI -26.68 [-36.15, -17.21]</p> <p>Satisfaction with treatment: 1, 53, Odds Ratio (Fixed) 95% CI 0.47 [0.09, 2.48]</p> <p>UAE versus myomectomy (Outcome title; number of studies; number of participants; Statistical method; Effect size)</p> <p>Duration of procedure (minutes): 1, 63, Weighted Mean Difference (Fixed) 95% CI -34.50 [-48.74, -20.26]</p> <p>Febrile morbidity: 1, 63, Odds Ratio (Fixed) 95% CI 0.90 [0.24, 3.32]</p> <p>Need for antibiotics: 1, 63, Odds Ratio (Fixed) 95% CI 1.12 [0.25, 4.92]</p> <p>Need for blood transfusion: 1, 63, Odds Ratio (Fixed) 95% CI 0.21 [0.01, 4.48]</p> <p>Length of hospital stay (days): 1, 63, Weighted Mean Difference (Fixed) 95% CI -1.60 [-2.47, -0.73]</p> <p>Hospital stay 1 week: 1, 63, Odds Ratio (Fixed) 95% CI 0.11 [0.01, 2.08]</p> <p>Readmission to hospital:</p>	



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>1, 63, Odds Ratio (Fixed) 95% CI 2.29 [0.20, 26.58]</p> <p>Duration to full recovery (days): 1, 63, Weighted Mean Difference (Fixed) 95% CI -16.40 [-21.16, -11.64]</p> <p>Relief of fibroid-related symptoms at 6 months follow-up: 1 54 Odds Ratio (Fixed) 95% CI 0.50 [0.08, 3.27]</p> <p>Total relief of all fibroid-related symptoms at 6 months follow-up: 1, 54, Odds Ratio (Fixed) 95% CI 0.36 [0.12, 1.11]</p> <p>Fibroid-related symptoms same or worse at 6 months follow-up: 1 54 Odds Ratio (Fixed) 95% CI 2.00 [0.31, 13.06]</p> <p>Serum FSH levels at 6 months follow-up: 1, 63, Weighted Mean Difference (Fixed) 95% CI 0.79 [-0.24, 1.82]</p> <p>FSH levels 20 IU/l: 1, 63, Odds Ratio (Fixed) 95% CI 8.53 [0.42, 172.28]</p> <p>Fibroids detected by USS 4cm by at least 6 months follow-up: 1, 63, Odds Ratio (Fixed) 95% CI 5.88 [1.88, 18.44]</p> <p>Re-intervention rate: 1, 63, Odds Ratio (Fixed) 95% CI 8.97 [1.79,</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							44.95]	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Hehenkamp 2005 <sup>418</sup>	Study Type: randomised; multicentre; concealment and blinding not mentioned  Evidence level: 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	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), p = 0.024 Major complications = 3 vs. 1 (RR = 2.78 (0.3 to 26.13), p = 0.62  Unscheduled visits to	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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			vs. 89 Dysmenorrhoea = 47 vs. 50  Duration of symptoms = 24 vs. 24 Number of fibroids (median) = 2 vs. 2 Uterine volume (median, cm <sup>3</sup> ) = 321 vs. 313 Fibroid volume (median, cm <sup>3</sup> ) = 59 vs. 89  Country: Netherlands				health professionals: UAE = 45 vs. hysterectomy = 24  Readmission after UAE up to 6-weeks = 9  Duration of procedure (median): UAE = 75 mins vs. hysterectomy = 90 mins (p = 0.007 for comparison of means)  Blood loss (median, ml): UAE = 20 vs. hysterectomy = 300 (p < 0.01 for comparison of means)  Length of stay (days): UAE = 2 vs. hysterectomy = 5.1	
Hehenkamp 2006  <small>419</small>	Study Type: randomised; multicentre; concealment and blinding not mentioned  Evidence level: 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%	UAE; Hysterectomy		Pain; Return to daily activities	UAE (n = 72) vs. Hysterectomy (n = 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), p < 0.001 Voluntary work = 16.6 (8.9) vs. 46.6 (30.1), p =	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 & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			<p>within uterine cavity.</p> <p>UAE vs. hysterectomy: Age = 44.6 vs. 45.4 Parity =&gt; 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</p> <p>Symptoms: Menorrhagia = 88 vs. 89 Dysmenorrhoea = 47 vs. 50</p> <p>Duration of symptoms = 24 vs. 24 Number of fibroids (median) = 2 vs. 2 Uterine volume (median, cm<sup>3</sup>) = 471.9 vs. 483.5 Fibroid volume (median, cm<sup>3</sup>) = 121.5 vs. 159.0</p> <p>Country:</p>				<p>0.016</p> <p>Usual household activities = 12.0 (12.4) vs. 29.0 (30.1), p &lt; 0.001</p> <p>Heavy household activates = 20.7 (15.4) vs. 53.7 (30.8), p &lt; 0.001</p> <p>Buying groceries = 14.0 (12.1) vs. 35.0 (30.2), p &lt; 0.001</p> <p>Doing things around the house = 18.9 (14.4) vs. 39.8 (24.7), p &lt; 0.001</p> <p>Leisure time activities = 14.8 (13.3) vs. 40.4 (40.1), p &lt; 0.001</p> <p>Activities with children = 17.4 (14.2) vs. 30.3 (20.6), p = 0.001</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			Netherlands					

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Katsumori 2003 <sup>427</sup>	Study Type: retrospective; comparative  Evidence level: 2-	152 (fibroids > 10cm = 47, fibroids < 10cm = 105)	Population characteristics: Women; Undergone UAE;  Country: Japan	UAE in women with fibroids > 10cm; UAE in women with fibroids < 10cm;	Mean 17.5 months	Complication rates; duration of procedure (mins); Reduction in fibroid volume (%); reduction in uterine volume (%); Time to recovery (days); patient satisfaction	Fibroid > 10cm (n = 47), fibroid < 10cm (n = 105):  Complication rates: Major complications 3 vs. 2 Minor 9 vs. 16  Duration of procedure (mins): 55.3 (SD 15.8) vs. 46.6 (SD 14.3), p = 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), p = 0.004 1-year: 1.79 (SD 0.50) vs. 1.90 (SD 0.30) 2-year: 1.83 (SD 0.40)	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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							vs. 1.96 (SD 0.20)	
Pinto 2003 420	Study Type: randomised; concealed - sealed envelopes; blinding not mentioned  Evidence level: 1+	64 eligible. 57 randomised (38 in UAE group - 1 refused assignment and had hysterectomy, 19 in hysterectomy group - 3	Population characteristics: Women; bleeding associated with uterine fibroids; patient with fibroid > 10cm; contraindications to surgery; desire to maintain fertility	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:	Funding Source: Not stated  Study summary: Compared with hysterectomy, UAE is safe and effective treatment for bleeding fibroids, necessitates a shorter hospital stay, and



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
		refused assignment and had UAE, 1 of whom later had hysterectomy)	<p>and/or sensitivity to iodine were excluded from study.</p> <p>Baseline characteristics (UAE vs. hysterectomy):</p> <p>Age (years) 46.4 vs. 44.6</p> <p>No pregnancies = 2.6 vs. 3.2</p> <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 (cm<sup>3</sup>) = 72 vs. 113</p> <p>Symptoms:</p> <p>menorrhagia = 37 vs. 17</p> <p>Metrorrhagia = 19 vs. 9</p> <p>Country: Spain</p>				<p>UAE = 13, Hysterectomy = 4</p> <p>Intra-operative complications:</p> <p>Minor - UAE = 11 vs. 0</p> <p>Major - UAE = 0 vs. hysterectomy = 4</p> <p>Post-operative complications:</p> <p>Minor - UAE = 20 vs. hysterectomy = 3</p> <p>Moderate - UAE = 19 vs. hysterectomy = 2</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>	results in fewer major complications.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Prollius 2004 <sup>428</sup>	Study Type: Prospective case-control  Evidence level: 2-	64 (51 with normal uterus, 12 with large uterus)	Population characteristics: 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  Groups split based on uterus >780cm <sup>3</sup> or not  Country: South Africa	Uterine Artery Embolisation	6 weeks, 3 months and 12 months	Menstrual blood loss; pressure effects of fibroid; complications of procedure	Menstrual blood loss at 12-months (% improvement): Volume - Normal uterus = 85.1 Large uterus = 91.7 95% CI = -33.7 to 15.6  Clots - Normal uterus = 73.5 Large uterus = 66.7 95% CI = -17.9 to 37.2  Pressure effects of fibroid (% improvement): Discomfort - Normal uterus = 57.1 Large uterus = 83.3 95% CI = -54.8 to 4.5  Mass - Normal uterus = 40.8 Large uterus = 50 95% CI = -48.7 to 14.9  Deep dyspareunia - Normal uterus = 32.7 Large uterus = 50 95% CI = -43.6 to 13.8  Fibroid volume (cm <sup>3</sup> ): Normal uterus - Pre- treatment = 411, 12- months = 282 Large uterus - Pre- treatment 12 = > 780, 12-months 4 had uterus > 780  complications of procedure (including further treatment):	Funding Source: Not stated  Study summary: The large uterus does not decrease UAE's efficacy. Although 33.3% of the study group still had a uterus of > or =780 cm <sup>3</sup> , 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							Normal uterus = 30 Large uterus = 3	
Razavi 2003 575	Study Type:  Evidence level: 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 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	Funding Source: not stated  Study summary: UTE is less invasive and safer treatment than AM in women with symptomatic fibroids

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							activity: AM: 36 UTE: 8 (p<0.05)  Secondary intervention: AM: 10% UTE: 8% (NS)	
Society of Obstetricians and Gynaecologists of Canada.; 2005 429	Study Type: Guideline  Evidence level: 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-	Funding Source: SOGC funded

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>B)</p> <p>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)</p> <p>6. Genitourinary infection is the predominant cause of serious morbidity and mortality. Further research on the utility of prophylactic antibiotic therapy and 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>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<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>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Spies 2005 <sup>421</sup>	Study Type: randomised;  Evidence level: 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%) Incomplete infarction = 13 (92.9%) vs. 5 (45.5%) At least 90% infarction = 4 (28.6%) vs. 8 (72.2%) 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>

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Spies 2004 <sup>422</sup>	Study Type: randomised; single blinded  Evidence level: 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 <sup>3</sup> ): 648.7 (SD 326.7) vs. 603 (SD 343.3) Fibroid volume (cm <sup>3</sup> ): 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 <sup>3</sup> ); Fibroid volume (cm <sup>3</sup> ); complications	Tris-acryl vs. PVA  Procedure outcomes: Mean total embolic volume per patient: 9.4 vs. 3.0 (p = 0.0001) Frequency of catheter occlusion: 4 vs. 28 (p = 0.001)  No difference for fluoroscopy time, frequency of spasms, frequency of ovarian flow grade > 2 per artery.  In-hospital pain scores: No difference between groups for VAS pain, PCA dose, patient temperature, analgesia use or symptoms scores.  Symptom score/change;  Mean change in bleeding scores: 3.2 vs. 3.3 (ns)  Mean change in pressure symptoms: 3.3 vs. 3.4 (ns)  Mean fibroid specific symptoms: 21.3 (SD 14.8) vs. 23.4 (SD 18.5), p = 0.02)  Mean change in fibroid	Funding Source: Non-commercial  Study summary: No substantive difference were detected between outcomes of embolisation.



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>specific symptoms: -39.2 (SD 24.3) vs. -26.8 (SD 24.9), <math>p = 0.02</math></p> <p>Mean fibroid specific QoL: 81.9 (SD 15.7) vs. 80.9 (SD 18.8), <math>p = 0.02</math></p> <p>Percentage change in uterine volume (cm<sup>3</sup>); 35.1 vs. 30.2 (ns)</p> <p>Percentage change in fibroid volume (cm<sup>3</sup>): 56.5 (SD 22.2) vs. 42.5 (SD 25.8). <math>P = 0.01</math>.</p> <p>Frequency of uninfarcted dominant fibroid (%): 18 vs. 5, <math>p = 0.02</math></p> <p>No difference for other uninfarcted fibroids or presence of any uninfarcted fibroids or amenorrhoea rates</p> <p>Complications: 19 vs. 11</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Spies 2004 <sup>430</sup>	Study Type: Prospective; cohort  Evidence level: 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%	UAE; hysterectomy  UAE vs. Baseline UAE versus 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 = na  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 versus 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	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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			Country: USA				<p>(SD 6.1), +22.6% (SD 27.1), <math>p &lt; 0.001</math>  SF-12 physical for hysterectomy at baseline = 43.0 (SD 9.9), 12-months = 51.4 (SD 6.9), +25.4 (SD 32.7), <math>p &lt; 0.001</math>  SF-12 mental for UAE at baseline = 45.4 (SD 11.5), 12-months = 52.6 (SD 7.9), +23.4% (SD 37.7), <math>P &lt; 0.001</math>  SF-12 mental for hysterectomy at baseline = 40.6 (SD 11.1), 12-months = 51.1 (SD 11.2), <math>p &lt; 0.001</math></p> <p>Complications:  On SCVIR: UAE = 4 (3.9%), hysterectomy = 6 (12.0%)</p> <p>On ACOG: UAE = 15 (14.7%), Hysterectomy = 17 (34%)</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Vilos 2006 <sup>423</sup>	Study Type: Randomised  Evidence level: 1-	26 included, 14 UAE only, 12 UAE & GnRH- a. 10 UAE & 12 UAE & GnRH-a analysed. 7 UAE & 9 UAE & GnRH-a analysed at 12 months.	Population characteristics: Women; symptomatic uterine fibroids; no other gynaecological pathology  Country: Canada	UAE only; UAE & GnRH-a	12 months	Uterine volume (cm <sup>3</sup> ); Dominant fibroid volume (cm <sup>3</sup> )	Outcomes for UAE only vs. UAE & GnRH-a  Uterine volume (cm <sup>3</sup> ): 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 <sup>3</sup> ) 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.

## Chapter 11 – Interventions for Uterine Fibroids

### Radiological interventions for treatment of uterine fibroids – Additional non-comparative studies.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Bruno 2004 <sup>431</sup>	Study Type: Prospective; cohort; non- comparative  Evidence Level: 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 <sup>3</sup> ): 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,	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.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						temperature or symptoms scores found only one significant result for: African-American on symptom summary at weeks 2 to 4.	
Huang 2006 <sup>432</sup>	Study Type: Retrospective; cohort  Evidence Level: 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 (n = 22) vs. asymptomatic group (n = 211) Uterine volume (cm <sup>3</sup> ): 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 <sup>3</sup> ): 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.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Hutchins 1999 433	Study Type: Prospective case-series  Evidence Level: 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.  Patient satisfaction with treatment: 3-months: 155 of 185 6-months: 103 of 121 12-months: 51 of 59  Additional treatment: 2 arteriograms 6 hysterectomies 5 myomectomies	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.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Katsumori 2006 <sup>434</sup>	Study Type: Evidence Level: 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: Primary failure of symptom control = 0% Symptom recurrence = 10.5% Gynaecologic interventions = 10.5% Complication-related gynaecologic interventions = 2.1% Symptom control = 89.5% Overall failure of UAE = 12.7%</p> <p>Total number of complications = 25</p> <p>Major complications Sloughing fibroids = 2 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 <sup>435</sup>	Study Type: Case-series Evidence Level: 3	UAE	85	Women; undergone UAE  Country: France	Risk factors for recurrence	<p>Increase in fibroid size (<math>p &lt; 0.008</math>), size of largest fibroid (<math>p = 0.009</math>) and number of fibroids (<math>p = 0.02</math>) 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



Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
McLucas 2000 <sup>436</sup>	Study Type: Case-series  Evidence Level: 3	UAE	152	Women; undergone UAE  Baseline: Age = 43  Country: USA	Change in fibroid size; change in fibroid related symptoms	Change in fibroid size by 6-weeks (n = 115): Changed from 7.7cm to 6.0cm (-22%)  Change in fibroid size by 6-months (n = 115): Changed from 7.7cm to 4.9cm (-36%)  67% reported cessation of menorrhagia  74% reported relief from pain and pressure symptoms.  6 complications reported	Funding Source: Not stated
McLucas 1999 <sup>437</sup>	Study Type: Case-series  Evidence Level: 3	UAE	300	Women; menorrhagia secondary to uterine fibroids.  Average age =43  Country: USA	Success - symptom relief or fibroid shrinkage or no additional surgery	Success:  44 of 300 classified as failures.  Demographics and gynaecological conditions did not correlate with success of treatment.  Fibroid size > 8.5cm did correlate with success of treatment.	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
McLucas 2001 <sup>438</sup>	Study Type: Case-series  Evidence Level: 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	Change in uterine size (ml) and myoma size (cm) Baseline (n = 155): 1389 (range 117 to 8804); 7.8 (1.5 to 16.3) 6-weeks (n = 125): 864 (102 to 4640); 6.1 (1.1 to 14.2) 6-months (n = 98): 619 (75 to 3474); 5.4 (1.8 to 13.7) 12 months (n = 46): 608 (103 to 3716); 5.0 (1.4 to 11.0)  Change in symptoms: 123 of 150 reported improvement in menorrhagia  133 of 150 reported improvement in pressure and pain symptoms.  Complications: 7 were readmitted due to pain. 12 reported fever 8 reported passing of myoma  6 patients had had hysterectomy  21 of 167 were considered failures - had hysterectomy, no improvement or worsening of symptoms.	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Pelage 2000 <sup>439</sup>	Study Type: Prospective case-series  Evidence Level: 3	Uterine Artery Embolisation	80	<p>Women; menorrhagia; failed medical treatment to treat menorrhagia; uterine fibroids found via ultrasound.</p> <p>Mean average age: 44.7 years</p> <p>15 women had undergone myomectomy to treat fibroids</p> <p>Location of fibroids: Intramural = 79% Submucosal = 8% Mixed = 14%</p> <p>Number of fibroids: 1 = 31% 2 = 16% 3 = 21% &gt; 3 = 31%</p> <p>Country: France</p>	Menstrual bleeding pattern; completed procedure; Complications; Fibroid size	<p>In 76 of 80 women the procedure was completed.</p> <p>5 of 76 women reported no improvement in menstrual bleeding symptoms after treatment.</p> <p>Complications: 6 women complained of amenorrhoea.</p> <p>68 of 76 women complained of post-operative pain.</p> <p>Fibroid size: Pre-treatment fibroid = 58mm (range 21 to 100) At 6-months = 38mm (range 18 to 68)</p>	<p>Funding Source: Not stated</p> <p>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.</p>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Pron 2003 <sup>440</sup>	Study Type: Prospective; cohort  Evidence Level: 3	Uterine Artery Embolisation - polyvinyl alcohol articles	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 <sup>3</sup> ): 704 (SD 586)  Uterus size at 3-months (cm <sup>3</sup> ): 428 (SD 322)  Mean % change in uterus size: 27 (95% CI 23 to 32)  Baseline fibroid size (cm <sup>3</sup> ): 308 (SD 380)  Fibroid size at 3-months (cm <sup>3</sup> ): 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.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Pron 2003 <sup>441</sup>	Study Type: Prospective; cohort  Evidence Level: 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	<p>Baseline characteristics:</p> <p>Mean age = 43 (SD = 6.04; range 18 to 59). 167 of 539 were &lt; 40 years.</p> <p>General health: Excellent = 89 (17%) Very good = 215 (40%) Good 196 (37%) Not very good = 35 (7%)</p> <p>Menopausal status: pre-menopausal = 431 (80%) Peri-menopausal = 92 (17%) Postmenopausal = 14 (3%)</p> <p>Family intentions: No children = 168 (50%) decided not to have = 95 (18%) would like to have = 127 (24%) Unable to have = 35 (7%)</p> <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%) =&gt;5 = 125 (26%)</p> <p>Fibroid volume (cm<sup>3</sup>): 0 to 100 = 174 (35%) 101 to 200 = 114 (23%) 201 to 400 = 91 (18%) =&gt; 401 = 121 (24%)</p> <p>Mean average = 293 (95% CI 259 to 327)</p>	<p>Funding Source: Not stated</p> <p>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.</p>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						<p>Uterine volume (cm<sup>3</sup>):  0 to 250 = 106 (22%)  251 to 500 = 131 (27%)  501 to 1000 = 149 (31%)  =&gt; 1000 = 102 (21%)</p> <p>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):  &lt;1 = 20 (4%)  1 to 4 = 278 (54%)  5 to 9 = 122 (24%)  =&gt; 10 = 94 (18%)</p> <p>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>	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Pron 2003 <sup>442</sup>	Study Type: Prospective; cohort/single arm trial; multi-centre  Evidence Level: 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</p> <p>Numeric scale (0 to 10): 0 = 386 1.0 to 2.0 = 13 3.0 to 4.0 = 26 5.0 to 6.0 = 43 7.0 to 10.0 = 80</p> <p>Post-procedural pain; Categorical scale None = 44 Minor = 86 Uncomfortable = 103 Very uncomfortable = 188 Unbearable = 116</p> <p>Ineffective pain management = 24</p> <p>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</p> <p>Ineffective pain management = 57</p> <p>Length of stay: 1.3 days</p> <p>Complications: Pain/nausea/vomiting = 75 Pain/fever = 16 Hypertension = 3</p>	Funding Source: Boston scientific partially funded study

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						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)	



Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Rajan 2004 <sup>443</sup>	Study Type: Retrospective; case-series  Evidence Level: 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 <sup>444</sup>	Study Type: Prospective; cohort  Evidence Level: 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

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Roth; 2000 <sup>445</sup>	Study Type: Prospective; cohort/single arm trial  Evidence Level: 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 <sup>446</sup>	Study Type: Prospective; one-arm trial  Evidence Level: 3	UAE using PLE	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.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Spies 2001 <sup>44/</sup>	Study Type: Case-series  Evidence Level: 3	Uterine Artery Embolisation	200	<p>Women; uterine fibroids; symptoms associated with fibroids - menorrhagia, pelvic pain or pressure, urinary symptoms. Women excluded if - pregnant, primary aim was pregnancy.</p> <p>Average age = 43 Menorrhagia = 85% Pelvic pain or pressure = 83% Urinary symptoms = 54%</p> <p>Mean uterine volume (cm<sup>3</sup>) = 714 (SD 482) Mean fibroid volume (cm<sup>3</sup>) = 240 (SD 279)</p> <p>Location of primary fibroid: Submucosal = 19% Intramural = 59% Subserosal = 21%</p> <p>Country: USA</p>	Menstrual bleeding symptoms; bulk symptoms; satisfaction with symptoms; complications; completion of treatment; subsequent surgery; uterine and fibroid volume	<p>198 of 200 procedures were technically completed.</p> <p>97% discharged within 1 day of procedure.</p> <p>Mean average days until return to work = 8</p> <p>Menstrual symptoms (% improved) 3-months = 87, 6-months = 89, 12-months = 90</p> <p>Bulk symptoms (% improved): 3-months = 93, 6-months = 92, 12-months = 91</p> <p>Satisfaction with symptoms (%) 3-months = 93, 6-months = 93, 12-months = 92</p> <p>Uterine volume at 3-months (n = 174) was reduced by 27%, and by further 38% by 12-months (n = 116)</p> <p>Fibroid volume at 3-months was reduced by 44% and by 58% by 12-months</p> <p>Complications: minor = 13 Major = 1</p> <p>Subsequent surgery: 21 including 9 hysterectomies</p>	<p>Funding Source: Public and private funded (Boston Scientific)</p> <p>Study Summary: Uterine artery embolisation is safe and controls the symptoms caused by leiomyomata in most patients.</p>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Spies 2005 <sup>448</sup>	Study Type: Prospective; single arm- trial/cohort; non- comparative  Evidence Level: 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, n = 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:	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.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						- 57.8%	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Spies 2005 <sup>42b</sup>	Study Type: Cohort  Evidence Level: 3	Uterine Artery Embolisation	2112	Women; Undergone UAE  Country: USA	Symptoms score; QoL score; subsequent treatment	<p>Outcomes (baseline n = 2122, 6-months, n = 1798, 12-months, n = 1701)</p> <p>Symptom score (0 to 100; baseline, 6-months, 12-months; Mean (SD)): 58.61 (20.82), 19.87 (18.61), 19.23 (17.94)</p> <p>HRQOL score (0 to 100; baseline, 6-months, 12-months; Mean (SD)): 46.95 (23.03), 85.04 (20.06), 86.68 (18.15)</p> <p>Subsequent care: 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 HMB = -16.6 (-26.1 to -7.12) Bulk symptoms = -8.22 (-17.3 to 1.92) Pain = - 7.71 (-18.3 to 1.96)</p> <p>Fibroid size = 1.020 (0.60 to 1.44) Prior medication = -4.11 (-6.44 to -1.77) Fibroid morphology = -4.73 (-8.0 to -</p>	<p>Funding Source: Commercial and government sources</p> <p>Study Summary: Uterine embolisation results in substantial symptom improvement for most patients, with hysterectomy required in only 2.9% of patients in the first 12 months after therapy.</p>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						<p>1.46) Age = 0.21 (0.01 to 8.56)</p> <p>Multivariate analysis on change in QOL scores (adjusted):</p> <p>Predominant symptoms HMB = 17.94 (8.02 to 27.87) Bulk symptoms = 6.50 (-4.00 to 16.98) Pain = 7.07 (-2.98 to 17.12)</p> <p>Fibroid size = -0.937 (-1.37 to -0.51) Prior medication = 6.166 (3.77 to 8.56) Fibroid morphology = 4.87 (1.60 to 8.15) Age = -3.81 (-6.54 to -1.08)</p>	
Spies 2002 <sup>449</sup>	<p>Study Type: Prospective; one arm trial</p> <p>Evidence Level: 3</p>	UAE	200, 182 at 3-months, 184 at 12-months	<p>Women; UAE</p> <p>Country: USA</p>	Factors associated with fibroid volume change	<p>Factors associated with reduction in fibroid volume by 3-months: Submucosal, baseline uterine volume significant factors (<math>p &lt; 0.05</math>). 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: baseline uterine volume significant factors (<math>p &lt; 0.05</math>). Type of fibroid, number of fibroids, race, birth control use, GnRH, prior pregnancies, prior births, baseline uterine volume and age</p>	<p>Funding Source: Not stated</p> <p>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.</p>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Spies 2002 <sup>450</sup>	Study Type: Prospective; cohort  Evidence Level: 3	Uterine Artery embolisation	400	Women; uterine fibroids; undergoing UAE.  No demographic figures provided.  Country: USA	Complications	Complications after UAE: None = 358 Allergic reaction = 10 Leiomyoma passage = 10 Prolonged pain = 5 UTI = 4 Endometritis: 2 Femoral nerve injury = 3 Vessel injury = 2 Urinary retention = 2 Vaginal discharge = 1 DVT = 1 Drug reaction = 1 Thrush = 1 Clostridium difficile 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	Funding Source: Not stated  Study Summary: The short-term complication rate was low in women undergoing uterine embolisation.
Walker 1999 <sup>451</sup>	Study Type: Case-series  Evidence Level: 3	Uterine Artery Embolisation	200	Women; undergone UAE for symptomatic uterine fibroids  Country: UK	Menstrual symptoms; pressure symptoms; complications; failures; fibroid volume	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



Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Walker 2002 <sup>452</sup>	Study Type: Prospective case-series  Evidence Level: 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 & fibroid volume by ultrasound (cm <sup>3</sup> ): 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.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Watson 2002 <sup>453</sup>	Study Type: Case-series  Evidence Level: 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 <sup>424</sup>	Study Type: Prospective; cohort; non- comparative  Evidence Level: 3	UAE	3160	Women; Undergone UAE  baseline characteristics (n = 3005): Age = 43.5 (SD 5.6) Race: African-American = 48% White, non- Hispanic = 44.4% White, Hispanic = 3.6% Asian = 2.8% Other = 1.3%  Co-morbidities: Obesity = 12.1% Diabetes = 2.9% Hypertension = 12.8% Current smoker = 12.2%  Reproductive history:	Adverse events;	Adverse events (n = 3041)  In hospital events: None = 2952 1 event = 89 2 events = 5  Major event = 20 Nausea = 4 Prolonged pain = 6 Drug reaction = 1 Vessel injury = 3 Other complications = 4 Urinary retention = 1 Contrast reaction = 1  Minor events = 74 Contrast reaction = 3 Drug reaction = 5 Device related = 1 Groin haematoma = 22 Nausea = 0 Nontarget embolisation = 1 Prolonged pain = 0 Urinary retention = 11 Vessel injury = 13 Other = 18	Funding Source: Mixed commercial and non- commercial funding  Study Summary: Uterine embolisation for 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 & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
				<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>Post discharge adverse events (n = 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 (p &lt; 0.001)</p> <p>DVT prophylactic use: OR = 0.757 (p = 0.005)</p> <p>Duration of procedure: OR = 1.004 (p = 0.009)</p> <p>African-American: OR = 1.129 (p = 0.021)</p> <p>Current or recent smoker: OR = 1.141 (p = 0.039)</p>	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
				D&C = 18.7% Myomectomy = 13.7% Hysteroscopy = 5.6% Endometrial ablation = 1.4% Other = 4.0% UAE = 0.4%  Mean uterine volume = 677.7 (SD 520.4)  Number of uterine fibroids: Any demonstrate		were significant factors associated with adverse events.	

## Chapter 11 – Interventions for Uterine Fibroids

### Myomectomy for treatment of uterine fibroids – Comparative studies

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Agostini 2005  468	Study Type: randomised  Evidence level: 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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Broder 455	Study Type:  Evidence level: 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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Celik 2003 <sup>469</sup>	Study Type: Randomised; double-blind  Evidence level: 1-	25 randomised; 12 placebo pre-treatment; 13 vaginal misoprostol (400ug)	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 (mins); 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 (mins): 48.5 vs. 58  Length of stay (days): 4.2 vs. 4.2	Funding Source: Not stated

<b>Bibliographic Information</b>	<b>Study Type &amp; Evidence Level</b>	<b>Number of Patients</b>	<b>Patient characteristics</b>	<b>Intervention &amp; Comparison</b>	<b>Follow-up</b>	<b>Outcome measures</b>	<b>Effect Size</b>	<b>Source of funding &amp; additional comments</b>
Corson 1994  470	Study Type: Placebo; double-blind; randomised - double-blind  Evidence level: 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	Dilue vasopressin (20 units); placebo	Not stated	Blood loss (ml)	Minimal operative bleeding: 81% in vasopressin versus 42% in placebo (p = 0.0002)	Funding Source: Not stated



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Derman 1991  457	Study Type: Comparative case series - chart review  Evidence level: 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/menorrhagia, 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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Fedele 1990 <sup>471</sup>	Study Type:  Evidence level: 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 - 235ml (SEM 22) immediate myomectomy -275ml (SEM 35): NS  Post-operative morbidity (pyrexia <= 39 degrees 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-oestrogen prior to myomectomy may favour short-term recurrence of myomas, limiting the efficacy of surgery

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Fletcher 1996 <sup>472</sup>	Study Type: randomised  Evidence level: 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 Largest fibroid diameter = 6.6 vs. 9.4  Country: Jamaica	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 (no effect caused by transfusions)  Post-operative fever: 3 vs. 5, p = 0.703	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Frederick 1994 <sup>473</sup>	Study Type: Randomised; single blind  Evidence level: 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 (20ml)	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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Ginsburg 1993 <sup>474</sup>	Study Type: randomised  Evidence level: 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 <sup>3</sup> ) = 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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Jasonni 2001 <sup>475</sup>	Study Type: randomised  Evidence level: 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 <sup>3</sup> ); intra- operative blood loss (ml); LH, FSH and stradiol plasma levels	Long-term vs. short- term:  Uterine volume (cm <sup>3</sup> ); 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: Reduction in both groups, and no differences between groups	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Lethaby 2001 <small>467</small>	Study Type: Systematic review; meta-analysis  Evidence level: 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 versus placebo pre-treatment for hysterectomy: Uterine volume (mls)(n = 15, n = 978), WMD = -159.04 [-169.05 to -149.03] in favour of GnRH.  Duration of operation (mins): 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	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 & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>confidence intervals for all adverse events.</p> <p>GnRH versus 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 (mins)(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>	



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Liu 2004  458	Study Type: controlled study with no randomisation  Evidence level: 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	Symptoms resolution Menorrhagia Group 1: 79/94 (84%) Group 2: 194/194 (100%) Dysmenorrhoea Group 1: 31/36 (86%) Group 2: 104/106 (98%) Compression Group 1: 16/16 (100%) Group 2: 37/37 (100%) Total Group 1: 88/108 (82%) Group 2: 232/234 (99%)  Operation time Group 1: 55 min (40-85) Group 2: 68 min (48- 115)  Intra-operative mean blood loss Group 1: 250 +/- 133 ml (30-850) Group 2: 50 +/- 27 ml (20-350) (p<0.001)  Post-op hospital stay Group 1: 3.4 +/- 0.9 days Group 2: 3.2 +/- 1.0 days  Fibroid recurrence: Group 1: 21 (19%) recurrence at 16 month follow-up, 5 (24%) underwent second myomectomy Group 2: 0% (p<0.001)	Funding Source: Not stated  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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Loffer 2005 456	Study Type: Comparative study  Evidence level: 2+	177 women Hysteroscopic myomectomy without endometrial ablation (EA) (n=104) Hysteroscopic myomectomy with concomitant endometrial ablation (n=73)	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. Hysteroscopic myomectomy with concomitant endometrial ablation	up to 15 years	Control of bleeding  No of subsequent hysterectomy	Control of bleeding Women with EA: 96% bleeding was controlled at up to 15 years Women without EA: 81% bleeding was controlled at up to 15 years (OR 0.18, 85% CI 0.05 to 0.63)  In women who had complete removal of myoma: bleeding was controlled in 90% In women who had incomplete removal of myoma: bleeding was controlled in 76% (OR 0.39, 95% CI 0.16 to 0.99)  In women who had complete removal of myoma and EA: bleeding was controlled in 97% 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)  In women who had incomplete removal of myoma and EA: bleeding was controlled in 92%	Funding Source: Not stated  Study summary: Endometrial ablation at the time of hysteroscopic myomectomy improves results in the control of bleeding

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<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 In women with EA: 18% In women with no EA: 22% (NS)</p> <p>In women with complete resection: 18% In women with incomplete resection: 30% (NS)</p> <p>Complete myoma removal + EA: 18% Complete myoma removal with no EA: 17% (NS)</p> <p>Incomplete myoma removal + EA: 15% Incomplete myoma removal with no EA: 37% (NS)</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Palomba 2002  476	Study Type: randomised; open  Evidence level: 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 <sup>3</sup> ; 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 <sup>3</sup> ); fibroid volume (cm <sup>3</sup> ); fibroid symptoms; duration of surgery (minutes)	Tibolone vs. GnRH vs. Iron only  Hot flushes (pre-surgery): Tibolone group significantly less than placebo group (p < 0.05). (Data presented on weekly basis so not summarised.)  Uterine volume (cm <sup>3</sup> ): 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)  Reduction in volume significant for tibolone and GnRH groups, and no difference between groups.  Fibroid volume (cm <sup>3</sup> ): 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)  Reduction in volume significant for tibolone and GnRH groups, and no difference between	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>groups.</p> <p>Fibroid symptoms (10cm VAS): 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)</p> <p>Duration of surgery (minutes): 99.8 (SD 22.7) vs. 91.5 (SD 17.6) vs. 117.3 (SD 16.1)</p> <p>Intra-operative blood loss (ml): 186.8 (SD 62.2) vs. 171.2 (SD 64.3) vs. 245.8 (SD 53.0), <math>p &lt; 0.05</math> for iron versus other groups.</p>	
Phillips 1995 <sup>576</sup>	Study Type: Case-series; prospective  Evidence level: 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.	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	<p>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 (<math>p &lt; 0.05</math>)</p> <p>Bleeding patterns at 6-months (TSR vs. TSR-TEMR)</p>	<p>Funding Source: Not stated</p> <p>Study summary: TSR with or without TEMR is an effective and safe treatment for women with submucous leiomyomas suffering from chronic menorrhagia.</p>

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			Demographic information (TSR vs. TSR-TEMR) Mean age (years) = 37.9, 43.2 Mean leiomyoma diameter (cm <sup>3</sup> ) = 2.6, 3.2 Mean uterine size (gestational weeks) = 7.2, 6.8  Country: USA				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%)	
Razavi 2003 <sup>575</sup>	Study Type:  Evidence level: 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	Funding Source: not stated  Study summary: UTE is less invasive and safer treatment than AM in women with symptomatic fibroids

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							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 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)	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Sapmaz 2003  577	Study Type: Randomised  Evidence level: 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 (mins); Haemoglobin levels (g/dl)	Ligation (n = 26) versus tourniquet (n = 25)  Intra-operative blood loss (ml): 220 (SD 50) vs. 294 (SD 60)  Duration of operation (mins); 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



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Taylor 2005  578	Study Type: Randomised - computer generated; opaque envelopes; single blind?;  Evidence level: 1+	171 eligible; 28 randomised; 14 to control group; 14 to tourniquet group.	Population characteristics: Women; symptomatic fibroids; $\geq 14$ 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 (d/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 (mins) = 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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Vercellini 2003 <sup>477</sup>	Study Type: randomised - computer generated; concealed - opaque envelopes  Evidence level: 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 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	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 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.	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Zullo 2004  478	Study Type: randomised  Evidence level: 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 (n)	Therapy versus 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 (n): 4 vs. 7.6, p < 0.01	Funding Source: Not stated
Sawin 2000  454	Study Type:  Evidence level: 2+	394 women Abdominal myomectomy (AM): n=197 Abdominal hysterectomy (AH): n=197	Population characteristics: Mean age AM: 36 years AH: 44 years (p<0.0001)  Mean weight AM: 156 lb 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	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)	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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			bleeding (37%) or pain (39%), recurrent miscarriage, infertility  AH: vaginal bleeding (62%) or pain (31%)  Country: USA				Post op care Mean operative time (mins) 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)	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Gupta 2005 <sup>416</sup>	Study Type: Systematic review; meta-analysis  Evidence level: 1+	3 RCTs included.	Population characteristics: Searched the Cochrane Menstrual Disorders & 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 (mins); 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, Weighted Mean Difference (Fixed) 95% CI -16.40 [-26.04, -6.76] Intra-procedure blood loss (ml): 1, 156, Weighted Mean Difference (Fixed) 95% CI -405.20 [-512.71, -297.69] Intra-procedural complications: 2, 216, Odds Ratio (Fixed) 95% CI 2.02 [0.74, 5.47] Need for blood transfusion: 2, 216, Odds Ratio (Fixed) 95% CI 0.04 [0.00, 0.33] Length of hospital stay (days): 2, 213, Weighted Mean Difference (Fixed) 95% CI -3.27 [-3.77, -2.77] Unscheduled visits after discharge: 2, 217, Odds Ratio (Fixed) 95% CI 1.80 [0.98, 3.30] Readmission rates within 42 days: 2, 216, Odds Ratio (Fixed) 95% CI 6.00 [1.14, 31.53] Resumption to normal activities: 1, 59,	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 to 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>Weighted Mean Difference (Fixed) 95% CI -26.68 [-36.15, -17.21]</p> <p>Satisfaction with treatment: 1, 53, Odds Ratio (Fixed) 95% CI 0.47 [0.09, 2.48]</p> <p>UAE versus myomectomy (Outcome title; number of studies; number of participants; Statistical method; Effect size)</p> <p>Duration of procedure (minutes): 1, 63, Weighted Mean Difference (Fixed) 95% CI -34.50 [-48.74, -20.26]</p> <p>Febrile morbidity: 1, 63, Odds Ratio (Fixed) 95% CI 0.90 [0.24, 3.32]</p> <p>Need for antibiotics: 1, 63, Odds Ratio (Fixed) 95% CI 1.12 [0.25, 4.92]</p> <p>Need for blood transfusion: 1, 63, Odds Ratio (Fixed) 95% CI 0.21 [0.01, 4.48]</p> <p>Length of hospital stay (days): 1, 63, Weighted Mean Difference (Fixed) 95% CI -1.60 [-2.47, -0.73]</p> <p>Hospital stay 1 week: 1, 63, Odds Ratio (Fixed) 95% CI 0.11 [0.01, 2.08]</p> <p>Readmission to hospital:</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>1, 63, Odds Ratio (Fixed) 95% CI 2.29 [0.20, 26.58]</p> <p>Duration to full recovery (days): 1, 63, Weighted Mean Difference (Fixed) 95% CI -16.40 [-21.16, -11.64]</p> <p>Relief of fibroid-related symptoms at 6 months follow-up: 1 54 Odds Ratio (Fixed) 95% CI 0.50 [0.08, 3.27]</p> <p>Total relief of all fibroid-related symptoms at 6 months follow-up: 1, 54, Odds Ratio (Fixed) 95% CI 0.36 [0.12, 1.11]</p> <p>Fibroid-related symptoms same or worse at 6 months follow-up: 1 54 Odds Ratio (Fixed) 95% CI 2.00 [0.31, 13.06]</p> <p>Serum FSH levels at 6 months follow-up: 1, 63, Weighted Mean Difference (Fixed) 95% CI 0.79 [-0.24, 1.82]</p> <p>FSH levels 20 IU/l: 1, 63, Odds Ratio (Fixed) 95% CI 8.53 [0.42, 172.28]</p> <p>Fibroids detected by USS 4cm by at least 6 months follow-up: 1, 63, Odds Ratio (Fixed) 95% CI 5.88 [1.88, 18.44]</p> <p>Re-intervention rate: 1, 63, Odds Ratio (Fixed) 95% CI 8.97 [1.79,</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							44.95]	



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Seracchioli, R 2000 459	Study Type: RCT  Evidence level: 1-	131					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 ( $2.17 \pm 1.57$ vs. $1.33 \pm 1.23$ ; $p < 0.001$ ).	

## Chapter 11 – Interventions for Uterine Fibroids

### Myomectomy for treatment of uterine fibroids – Non-comparative studies

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
De 1995 <sup>463</sup>	Study Type: case-series; retrospective  Evidence Level: 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

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Marziani 2005 <sup>464</sup>	Study Type: case series  Evidence Level: 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 =ve 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

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Olufowobi 2004 <sup>465</sup>	Study Type: Retrospective chart review  Evidence Level: 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 $\geq$ 500 ml: 31% Hysterectomy due to bleeding: 4% bowel damage: 1% Pyrexia: 38% wound infection: 5% heamoperitoneum:1% Mean post-op stay: 4.8 days  IVF treatment: 17 women (2 pregnancy) Natural conception: 28 women (13 pregnancy)  No data on live births	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 embarking on myomectomy

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Reilly 1998 <sup>466</sup>	Study Type: case series (record review)  Evidence Level: 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 mins, median 91 mins  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 +/- 0.1  No hysterectomy performed	Funding Source: not stated  Study Summary: abdominal myomectomy a safe surgical procedure for uterine myoma

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Stringer 1997 460	Study Type: retrospective chart review (case series)  Evidence Level: 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

## Chapter 12 – Hysterectomy for treatment of HMB

### Indications for hysterectomy – Non-comparative studies

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
ACOG 1998 <sup>5/9</sup>	Study Type:  Evidence Level: 4	Hysterectomy for AUB	Consensus statement	Country: USA		<p>Confirmation of Indication:</p> <ol style="list-style-type: none"> <li>Excessive uterine bleeding evidenced by either of the following: <ol style="list-style-type: none"> <li>Profuse bleeding or repetitive periods lasting for more than 8 days</li> <li>Anaemia due to acute or chronic blood loss.</li> </ol> </li> <li>Failure to find uterine or cervical pathology that would cause abnormal bleeding</li> <li>Laboratory data <ol style="list-style-type: none"> <li>Endometrial biopsy negative for endometrial neoplasia</li> <li>Cytologic studies of cervix negative for malignancy</li> </ol> </li> <li>No documented evidence of pathology following D&amp;C, hysteroscopy, hysteroqram or ultrasonogram.</li> </ol> <p>Medical documentation:</p> <ol style="list-style-type: none"> <li>Consideration of patient's medical and psychologic risks concerning hysterectomy.</li> <li>Failure of attempted hormone treatment</li> <li>No history of a bleeding diathesis or use of medications that may cause bleeding</li> </ol>	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						<p>4. Pregnancy ruled out</p> <p>5. Assessment of surgical risk from anaemia and need for treatment</p> <p>6. Consideration of alternative therapeutic approaches.</p> <p>Contraindications:</p> <p>1. Desire to maintain fertility</p> <p>2. Medical or psychological risks that exceed benefits.</p>	
Bourdrez 2004 <sup>247</sup>	<p>Study Type: Prospective; cohort</p> <p>Evidence Level: 3</p>	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:</p> <p>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>



Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Hurskainen 2004 <sup>481</sup>	Study Type: randomised  Evidence Level: 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 (&gt;80ml 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>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Lefebvre 2002 <sup>4/9</sup>	Study Type: Guidelines  Evidence Level: 4	Indications for hysterectomy	Society of Obstetricians & 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): Investigate to exclude any pathology One or more medical treatments offered Health professional performing hysterectomy must be aware of alternatives and offer these to patient.</p> <p>Uterine leiomyomas (I-A; RCT evidence): Treatment based on myoma symptoms, size and growth No symptomatic patients do not require hysterectomy, unless myoma rapidly expanding Prophylactic use of hysterectomy where myomas likely to grow beyond 12-week size, due to increased complications If myomas associated with bleeding the endometrial biopsy required and testing for coagulation disorders GnRH agonists should be given as pre-treatment Myomectomy, myoma clips and UAE should be considered as alternatives to hysterectomy, but with associated problems.</p>	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Mingo 2000 <sup>483</sup>	Study Type: Focus groups  Evidence Level: 3	Women's experience of medicine during midlife	23 focus groups	Women; middle-age; various ethnic backgrounds  Country: USA		Hysterectomy: Women endure great pain to avoid hysterectomy. Hysterectomy seen as major surgery. Patients want minimally invasive surgery Patients tried alternative treatments to avoid hysterectomy - CAM If surgery undertaken then women were generally very satisfied. Women judge hysterectomy using much wider criteria than healthcare providers. Patients did not know that hysterectomy causes menopause.	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Nagele 1998 <sup>482</sup>	Study Type: Observational; cohort  Evidence Level: 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	Reasons for rejecting hysterectomy: Hysterectomy is a major operation Wanted to be back to normal quickly Wanted to be out of hospital as quickly as possible Would have more postoperative discomfort after hysterectomy Want to retain uterus Friends had taken a long time to recover from hysterectomy Hysterectomy can ruin sex life Do not want a scar Do not want to put on weight Too young for a hysterectomy Loss of femininity Friend had endometrial ablation and recommended it  Change in preference with 50/50 possible adverse outcomes: Period does not stop = approx. 85% Period flow not improved = 80% Period pain not decreased = 80% Repeat ablation needed = 40% Need a hysterectomy = 35% Developing cancer = 65%	Funding Source: Not stated  Study Summary: Women who choose ablation are willing to do so even if chances of success are potentially low.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Nathorst-Boos 1992 <sup>484</sup>	Study Type: Survey  Evidence Level: 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 <sup>480</sup>	Study Type: Consensus study  Evidence Level: 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 & treatment: confirm AUB, If meno / metrorrhagia exclude endometrial or cervical neoplasia, failed or refuse medical treatment.  Indications:	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						<p>pre-menopausal  Hb <math>\leq</math> 10 g/dl without major impairment = appropriate indication; hysterectomy not necessary  Hb <math>\leq</math> 10 g/dl with major impairment = Appropriate indication; necessary indication  Hb &gt; 10 g/dl without major impairment = uncertainty of appropriateness.  Hb &gt;10 g/dl with major impairment = Appropriate indication; not necessary indication</p> <p>Pre-menopausal women with leiomyomata causing bleeding, but no pain or discomfort:</p> <p>Investigations &amp; treatment:  Meno / metrorrhagia = exclude endometrial or cervical neoplasia  Estimate uterine weight  Confirmation of uterine bleeding  Failed or refused medical treatment.</p> <p>Indications  Estimated uterine weight &lt; 300g,  Hb &lt; = 10 g/dl = Appropriate indication; necessary indication.  Estimated uterine weight &lt; 300g,  Hb &gt;10 g/dl = Uncertainty about appropriateness.  Estimated uterine weight &gt; 300g,  Hb <math>\leq</math> 10 g/dl = Appropriate indication; necessary indication.  Estimated uterine weight &gt; 300g,  Hb &gt; 10 g/dl = Appropriate indication; Not necessary indication.</p> <p>Pre-menopausal women with</p>	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						<p>leiomyomata causing bleeding and pain or discomfort:</p> <p>Investigations &amp; treatment:  Meno / metrorrhagia = exclude endometrial or cervical neoplasia  Estimate uterine weight  Confirmation of uterine bleeding  Failed or refused medical treatment.</p> <p>Indications  Estimated uterine weight &lt; 300g, Hb &lt; = 10 g/dl, without major impairment = Appropriate indication; necessary indication.  Estimated uterine weight &lt; 300g, Hb &gt;10 g/dl, without major impairment = Uncertainty about appropriateness.  Estimated uterine weight &lt; 300g, Hb &lt; = 10 g/dl, with major impairment = Appropriate indication; necessary indication.  Estimated uterine weight &lt; 300g, Hb &gt;10 g/dl, with major impairment = Appropriate indication; not necessary indication.</p> <p>Estimated uterine weight &gt; 300g, Hb &lt;= 10 g/dl, without major impairment = Appropriate indication; necessary indication.  Estimated uterine weight &gt; 300g, Hb &gt; 10 g/dl, without major impairment = Appropriate indication; Not necessary indication.  Estimated uterine weight &gt; 300g, Hb &lt;= 10 g/dl, with major impairment = Appropriate indication; necessary indication.</p>	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						Estimated uterine weight > 300g, Hb > 10 g/dl, with major impairment = Appropriate indication; necessary indication.	
Sculpher <sup>248</sup>	Study Type: Cohort  Evidence Level: 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 & discomfort = 0.68 Hospital stay as short as possible = 0.59 Reduce periods = 0.42 Resume sex life as soon as possible = 0.59 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%	Funding Source: Not stated  Study Summary: Many women referred for surgery for menorrhagia have conflicting objectives from treatment. .



## Chapter 12 – Hysterectomy for treatment of HMB

### Hysterectomy for treatment of HMB – Comparative studies

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Aka 2004  514	Study Type: randomised;  Evidence level: 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, -antitrypsin - differences in favour of vaginal	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Benassi 2002 515	Study Type: randomised - computer generated  Evidence level: 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.  Uteri volume range from 200 to 1300ml  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 (mins); 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 (mins): 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	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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							Wound infection: 0 vs. 2 Wound dehiscence: 0 vs. 1 Total = 2 vs. 6 (p = 0.136) Fever (>38C): 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	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Bhattacharya 1996 <sup>365</sup>	Study Type: Groups based on RCT  Evidence level: 2+	204 - 99 (21 non-responders) in hysterectomy, 105 (23 non-responders) in ablation	Population characteristics: Women; part of previous RCT for ablation versus hysterectomy for HMB  Country: UK	Hysterectomy; Endometrial ablation - ELA or TCRE	2 years	Bladder function; ovarian function	<p>Cystometry findings: Total bladder dysfunction - hysterectomy = 14 (31%), Ablation = 17 (35%)</p> <p>Bladder symptoms: Stress incontinence - hysterectomy = 32 (44%), ablation = 35 (44%) Urge incontinence - hysterectomy = 15 (21%), ablation = 15 (19%)</p> <p>Ovarian function: FSH level &gt; 40 - hysterectomy = 3 (6%), ablation = 5 (10%) Patients on HRT - hysterectomy = 8 (16%), ablation = 5 (10%) Hot flushes - hysterectomy = 25 (35%), ablation = 35 (44%)</p> <p>Worsening of symptoms from baseline to 2-years: Stress incontinence - hysterectomy = 11 (15%), ablation = 13 (16%) Urge incontinence - hysterectomy = 10 (14%), ablation = 12 (15%) Hot flushes - hysterectomy = 5 (7%),</p>	<p>Funding Source: Not stated</p> <p>Study summary: Bladder and ovarian symptoms do not differ between hysterectomy and ablation at 2-years follow-up.</p>

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							ablation = 14 (18%)	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Casey 1994  580	Study Type: retrospective chart review of comparison of LAVH vs. VH vs. AH  Evidence level: 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)	Mean age: LAVH: 41yrs; VH 47 yrs ( $p<0.001$ ) LAVH: 41 yrs; AH:42 yrs (NS) Mean weight: range 73- 76 kg (NS between groups) Uterine wt: LAVH: 149g; AH: 280g ( $p<0.001$ ) LAVH: 149g; VH: 138g (NS) Body wt: NS between groups  Indications: LAVH chosen more frequently for abnormal uterine bleeding and CIN, less frequently for endometriosis and leiomyomas than AH  Adhesiolysis and adnexectomies more frequently done with AH than LAVH ( $p<0.0001$ ) vaginal repaired more frequently with VH than LAVH ( $p<0.0001$ )  Post-op complications: blood transfusion and leiomyomas sig associated with younger age in all groups ( $p<0.03$ )  No major complications (cystotomy, enterotomy,	Funding Source: not stated  Study summary: LAVH can be accomplished with low morbidity, short lengths of stay and little increase in operating time compared with VH and AH

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>laparotomy to control bleeding, transfusion, infection) in LAVH group, 9 in VH, 17 in AH</p> <p>Hospital care: (matched pair control: 28 LAVH/VH; 34 pairs LAVH/AH)</p> <p>Operating time: LAVH 112 mins; VH 91 mins (<math>p&lt;0.04</math>) LAVH 117 mins; AH 115 mins (NS)</p> <p>length of stay: LAVH 2.5 days; VH 3.3 days (<math>p&lt;0.003</math>) LAVH 2.2 days; AH 4.3 days (<math>p&lt;0.0001</math>)</p> <p>Accompanied by adnexectomy</p> <p>Fever: sig less with LAVH than AH or VH (<math>p&lt;0.05</math>)</p> <p>Anaemia: sig less with LAVH than with AH</p> <p>length of stay: sig less with LAVH than with VH or AH</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Cheng 2002 <sup>486</sup>	Study Type: randomised  Evidence level: 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 > 280g, 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	Laparoscopically assisted vaginal hysterectomy; total laparoscopic hysterectomy  LAVH vs. LTH	6 to 12 months	Operative duration; blood loss during surgery; Length of stay; Uterine weight; complications; sexual function	LAVH vs. TLH  Operative duration (mins): 115.1 (SD 38.3) vs 140.4 (SD 38.7)(p = 0.002)  Blood loss during surgery (m): 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.



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			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					
Darai 2001 <sup>487</sup>	Study Type: Randomised - computer generated  Evidence level: 1-	80 (40 to LAVH, 40 to vaginal hysterectomy)	Population characteristics: Women; uterine size > 280g 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	LAVH; vaginal hysterectomy  LAVH vs. vaginal hysterectomy	6 to 8 weeks	Complications; conversion to laparotomy; operating time (mins); 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)	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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			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 Adenxal mass: 2 vs. 4 Endometriosis: 3 vs. 2 Adnexectomy: 21 vs. 15  Uterine weight (g): 424 (SD 211) vs. 513 (SD 360)  Country: France				Operating time (mins): 108 vs. 160  Hospital stay (days): 5.3 vs. 5.7  Haemoglobin decrease: 2.0 vs. 2.1	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Ellstrom <sup>488</sup>	Study Type: Randomised  Evidence level: 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 (mins); Hospital stay (days); Outpatient visits	TLH vs. TAH  Operating time (mins): 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Ellstrom 1998  489	Study Type: Randomised  Evidence level: 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 to 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 to abdominal hysterectomy.
Ellstrom  490	Study Type: randomised;  Evidence level: 1+	854 eligible, 248 invited into study; 241 agreed to enter study (several studies?), 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	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 (SD 3.0) Total: 93.9 (SD 23.7) vs. 92.0 (SD 18.7)	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 & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			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				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) 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  491	Study Type: randomised  Evidence level: 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 < 2cm below umbilicus, concomitant incontinence or pelvic	LAVH; TAH  Surgery vs. surgery	6 weeks	Duration of operation (mins); estimated blood loss (ml); Uterine weight (g); postoperative complications; Length of stay; analgesia use	TAH vs. LAVH  Duration of operation (mins): 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	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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			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 = 129g LAVH = 199 AH = 478  Country: USA				(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.	hysterectomy.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Falkeborn 2000  581	Study Type:  Evidence level: 2-	17126 available, 1339 records assessed (207 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 myocardial infarction	Relative risk of MI by operation (95% CI): BOS 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) BOS 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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Ferrari 2000 <sup>492</sup>	Study Type: Randomised; concealed  Evidence level: 1+	108 assessed, 65 eligible, 62 agreed to randomisation (31 LAVH, 31 TAH)	Population characteristics: Women; uterine fibroids; between 500 and 1500ml 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  >500g vs. <500g; surgery vs. surgery		Operating time (mins); Uterine weight (g); Blood transfusions; Hospital stay (days); Post-operative analgesics	LAVH vs. TAH  Operating time (mins): 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 <500g and >500g 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 operating time than TAH and a 27% rate of conversion to laparotomy.



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Garry 2004 493	Study Type: randomised; concealed; ITT  Evidence level: 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	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 (mins); 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 Hehiscence: 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):	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 & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			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				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 (mins): 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	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							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 Other complications: 1 vs. 0  Minor complications: Minor haemorrhage: 2 vs. 8 Anaesthesia problems: 1 vs. 3 Fever: 12 vs. 18 Infection: 24 vs. 36 Haematoma: 10 vs. 14 DVT: 0 vs. 0 Other complications 17 vs. 24  At least 1 major complication: 16 vs. 33  QoL (SF-12, EQ-5D): SF-12 physical component Baseline (127 vs. 260): 47.0 (SD 11.3) vs. 47.4 (SD 11.1) 6-weeks (84 vs. 150): 46.3 (SD 9.6) vs. 46.2 (SD 9.6) 4-months (82 vs. 152): 53.5 (SD 6.7) vs. 53.9 (SD 6.7) 12 months (94 vs. 173): 53.7 (SD 7.3) vs. 54.6	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							(SD 6.3)  SF-12 mental component Baseline (127 vs. 260): 45.1 (SD 12.1) vs. 47.9 (SD 10.7) 6-weeks (84 vs. 150): 53.2 (SD 9.1) vs. 52.5 (SD 10.4) 4-months (82 vs. 152): 53.1 (SD 8.1) vs. 51.6 (SD 9.8) 12 months (94 vs. 173): 51.7 (SD 9.8) vs. 52.3 (SD 9.9)  Length of stay (days): 4.32 vs. 4.29  Duration of surgery (mins): 39 vs. 72	
Gimbel 2005 <sup>517</sup>	Study Type:  Evidence level: 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	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	Total hysterectomy; Sub-total hysterectomy	12-months	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	Lower urinary tract symptoms (total vs. sub-total): 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 All urinary incontinences at 12-months - 13 vs. 25, OR = 0.46 (0.23 to 0.95), p = 0.03.  Predictors of urinary	Funding Source: Public funded  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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
		PP analysis	<p>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</p> <p>Country: Denmark</p>			<p>incontinence; risk-factors for bother</p>	<p>incontinence at 12-months: Preoperative incontinence OR = 11.2 (5.1 to 25.9), <math>p &lt; 0.0001</math> Operative method OR = 0.43 (0.18 to 0.96), <math>p = 0.044</math> Size of uterus OR = 1.56 (1.00 to 2.49), <math>p = 0.051</math> Five other factors were not significant</p> <p>Multi-variate analysis of symptoms that cause 'bother': Urinary incontinence OR = 463 (69 to 3109), <math>p &lt; 0.001</math> Frequency OR = 29.2 (4.1 to 211), <math>p = 0.001</math> Incomplete bladder emptying OR = 20 (5.4 to 74.6), <math>p &lt; 0.001</math>. Other urinary symptoms were not significant.</p>	<p>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>

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Gimbel 2003  516	Study Type: randomised; concealed; non-blinded; multi-centre  Evidence level: 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	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 (n = 140) vs. subtotal (n = 136), OR, 95% CI, p-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, p = 0.043 Quality of life - physical score: 53.78 (8.81) vs. 52.92 (8.81), p = 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, p = 0.69 Prolapse: 0 vs. 3, 0.14, 0.01 to 2.67, p = 0.12 Satisfaction with sexual life: 95 vs. 85, 0.6, 0.31 to 1.16, p = 0.13	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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>Pelvic pain: 32 vs. 31, 1.01, 0.57 to 1.78, <math>p = 0.98</math></p> <p>Vaginal bleeding: 0 vs. 27 (2 normal, 25 slight).</p> <p>Complications:</p> <p>All = 64 vs. 54, 1.02, 0.55 to 1.88, <math>p = 0.95</math></p> <p>Serious adverse events (Rupture of wound): 22 vs. 21</p> <p>Severe adverse events (urinary tract infection): 7 vs. 8</p> <p>Moderate adverse events (wound infection): 19 vs. 12</p> <p>Mild adverse events (bleeding from surface of wound): 16 vs. 13</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Halmesmaki 2004 <sup>266</sup>	Study Type: randomised; prospective  Evidence level: 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	FSM levels increased from 8.4 iu/m at baseline to 13.8 iu/m at 12 months versus 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.



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Harkki-Siren 2000 <sup>494</sup>	Study Type: Randomised; concealed  Evidence level: 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 Prior Laparoscopy: 8 vs. 8 Uterine weight (g): 210.7 (SD 83.0) vs. 230 (SD 99.4)  Country: Finland	Laparoscopic hysterectomy; Abdominal hysterectomy	28 days	Operating time (mins); Estimated blood loss (ml); Haemoglobin drop (g/L); Hospital stay (days); Sick leave (days); Complications	LH vs. AH  Operating time (mins): 85.3 vs. 57.5 (p< 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 IL-6 at day 1 = 10.4 vs. 21.6 (p < 0.01) IL-6 at day 2 = .5.5 vs. 17.0 IL-6 at day 28 = 3.7 vs. 3.7  CRP at day 0 = 1.4 vs. 0.7 CRP at day 1 = 12.1 vs. 21.8 (p = 0.03) CRP at day 2 = 26.5 vs. 55.3 (P < 0.001) CRP at day 28 = 1.8 vs. 1.4  Same pattern for TATI,	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 & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							but not for CA 125.	
Harmanli 2004 582	Study Type:  Evidence level: 2-	288 (200 abdominal hysterectomy, 88 vaginal hysterectomy)	Population characteristics: Women; enlarged uterus > 250g; undergone hysterectomy for - uterine leiomyomata, endometriosis, uterine prolapse,	Vaginal hysterectomy; abdominal hysterectomy  Vaginal hysterectomy vs. abdominal hysterectomy	n/a	Complications	Vaginal versus abdominal complications: Post-operative febrile morbidity: 18 vs. 28 Bleeding requiring transfusion: 8 vs. 23 Urethral injury: 1 vs. 1 Bladder injury: 1 vs. 3 Venous	Funding Source: Not stated  Study summary: For women with a uterus weighing 250 g or more, vaginal hysterectomy shortens the hospital stay without significantly increasing peri-operative

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			<p>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)  Mean age: 44 vs. 44.1  Parity = 2.4 vs. 2.3  Mean uterine weight: 500.9 (SD 277.2)(250 to 1768) vs. 737.4 (SD 637.8)(250 to 5650), <math>p = 0.0006</math>  Adnexal removal: 19 vs. 67, <math>p = 0.049</math>  Indication for surgery: uterine fibroids - 84 vs. 188  Menometrorrhagia - 3 vs. 6  Other - 1 vs. 6  Country: USA</p>				<p>thromboembolism: 0 vs. 0  Ileus: 1 vs. 21 (<math>p = 0.006</math>)  Haematoma: 2 vs. 5  Urinary tract infection: 5 vs. 13  Readmission: 3 vs. 6</p>	morbidity when compared with the abdominal route.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Hehenkamp 2005 <sup>418</sup>	Study Type: randomised; multicentre; concealment and blinding not mentioned  Evidence level: 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	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), p = 0.024) Major complications = 3 vs. 1 (RR = 2.78 (0.3 to 26.13), p = 0.62)  Unscheduled visits to	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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			vs. 89 Dysmenorrhoea = 47 vs. 50  Duration of symptoms = 24 vs. 24 Number of fibroids (median) = 2 vs. 2 Uterine volume (median, cm <sup>3</sup> ) = 321 vs. 313 Fibroid volume (median, cm <sup>3</sup> ) = 59 vs. 89  Country: Netherlands				health professionals: UAE = 45 vs. hysterectomy = 24  Readmission after UAE up to 6-weeks = 9  Duration of procedure (median): UAE = 75 mins vs. hysterectomy = 90 mins (p = 0.007 for comparison of means)  Blood loss (median, ml): UAE = 20 vs. hysterectomy = 300 (p < 0.01 for comparison of means)  Length of stay (days): UAE = 2 vs. hysterectomy = 5.1	
Hehenkamp 2006  419	Study Type: randomised; multicentre; concealment and blinding not mentioned  Evidence level: 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%	UAE; Hysterectomy		Pain; Return to daily activities	UAE (n = 72) vs. Hysterectomy (n = 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), p < 0.001 Voluntary work = 16.6 (8.9) vs. 46.6 (30.1), p =	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			<p>within uterine cavity.</p> <p>UAE vs. hysterectomy: Age = 44.6 vs. 45.4 Parity =&gt; 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</p> <p>Symptoms: Menorrhagia = 88 vs. 89 Dysmenorrhoea = 47 vs. 50</p> <p>Duration of symptoms = 24 vs. 24 Number of fibroids (median) = 2 vs. 2 Uterine volume (median, cm<sup>3</sup>) = 471.9 vs. 483.5 Fibroid volume (median, cm<sup>3</sup>) = 121.5 vs. 159.0</p> <p>Country:</p>				<p>0.016</p> <p>Usual household activities = 12.0 (12.4) vs. 29.0 (30.1), p &lt; 0.001</p> <p>Heavy household activities = 20.7 (15.4) vs. 53.7 (30.8), p &lt; 0.001</p> <p>Buying groceries = 14.0 (12.1) vs. 35.0 (30.2), p &lt; 0.001</p> <p>Doing things around the house = 18.9 (14.4) vs. 39.8 (24.7), p &lt; 0.001</p> <p>Leisure time activities = 14.8 (13.3) vs. 40.4 (40.1), p &lt; 0.001</p> <p>Activities with children = 17.4 (14.2) vs. 30.3 (20.6), p = 0.001</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			Netherlands					
Hurskainen 2004 <sup>106</sup>	Study Type: randomised; allocation concealed; controlled  Evidence level: 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 versus baseline; treatment versus 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 in situ. 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	Funding Source: Government grant  Study summary: Study shows that at 5-years LNG-IUS offered effective alternative to hysterectomy.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							63, 62; role functioning - emotional - 65, 66; emotional - 61, 66. No data for entire population average.	
Hurskainen 2001 <sup>107</sup>	Study Type: randomised; allocation concealed  Evidence level: 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)	Funding Source: Government funded. IUD provided free by Leiras.  Study summary: Study shows LNG-IUS was effective alternative to hysterectomy at 12 months.



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<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</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>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>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Hwang 2002 495	Study Type: Randomised; blinding not mentioned; envelope concealed  Evidence level: 1+	90 (30 LAVH, 30 TAH, 30 VTH)	Population characteristics: Women; myoma > 6cm, 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 (cc): 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Iversen 2005  583	Study Type: Comparative cohort  Evidence level: 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  485	Study Type: Systematic review - meta-analysis  Evidence level: 1++	27 RCTs involving 3643 women undergoing abdominal hysterectomy (AH), vaginal hysterectomy (VH), laparoscopic	Population characteristics: MDSG Specialised registered for controlled trials, CENTRAL, MEDLINE, EMBASE, Biological	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 surgery) or 6-12 months	Operation time Intra-operative complications Short-term: Bladder, ureteric, bowel and vascular injuries blood loss infections/febrile episodes	Operation time: 1) AH operation significantly shorter than LH (WMD 10.6 mins, 95% CI 7.4 to 13.8) 2) LAVH operation significantly shorter than AH (WMD 7.6 mins, 95% CI 3.0 to 12.2)	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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
		hysterectomy (LH) for benign diseases including fibroids	Abstracts, National Research Register  Country: NA		after surgery	Hospital stay Long-term: fistula formation urinary and sexual dysfunction patient satisfaction - QOL (SF12)	<p>3) VH operation significantly shorter than LH (WMD 41.5 mins, 95% CI 33.7 to 49.4)</p> <p>4) LAVH operation significantly shorter than LH(a)(WMD 25.3 mins, 95% CI 10.0 to 40.6)</p> <p>Intra- and post-operative complications</p> <p>1) No significant difference between VH vs. AH; LH vs. AH; LH vs. VH; LH(a) vs. LAVH in bladder, ureteric and bowel injuries</p> <p>2) No significant difference between LH vs. AH, LH vs. VH or LH(a) vs. LAVH in vascular injury</p> <p>3) No significant difference between VH vs. AH in mean blood loss</p> <p>4) No significant difference between the no of women with substantial bleeding between LH vs. AH and LH vs. VH</p> <p>5) No significant difference between LH vs. VH, or LH(a) vs. LAVH in unintended laparotomy</p> <p>6) Significant fewer unspecified</p>	<p>AH. However, the length of surgery for LH needs to be considered.</p> <p>Surgical approach to hysterectomy should be decided by the woman after discussing the relative benefits and hazards with her surgeon.</p>

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>infections/febrile episodes between VH vs. AH (OR 0.42, 95% CI 0.21 to 0.83)</p> <p>7) 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:</p> <p>Need for blood transfusion for VH vs. AH, LH vs. VH, LH(a) vs. LAVH</p> <p>(LH associated with significantly lower mean blood loss (WMD 45.3 mls, 95% CI 17.9 to 72.7) and smaller drop in Hgb (WMD 0.55g/L, 95% CI 0.28 to 0.82));</p> <p>Occurrence of pelvic haematoma for VH vs. AH, LH vs. AH, or LH(a) vs. LAVH;</p> <p>UTI for VH vs. AH, LH vs. AH, LH vs. VH;</p> <p>Other unspecified infection or pyrexial illness for LH vs. VH, or LH(a) vs. LAVH;</p> <p>thrombo-embolic events for LH vs. AH, LH vs. VH</p> <p>Hospital stay</p> <p>Shorter hospital stay (WMD 1.0 day, 95% CI</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>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</p> <p>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</p> <p>No significant differences in hospital stay and return to normal activities for LH vs. VH</p> <p>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</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							the statistical significance of any meta-analysis results.  Data expressed as medians were not included in the meta-analysis results.	
Kung 1996 584	Study Type: Prospective cohort  Evidence level: 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	LAVH; TAH	No follow-up	Completed surgery; Operative time; Blood loss; complications; Length of stay; post-operative haemoglobin	Comparison of LAVH versus TAH  Completed surgery: LAVH = 138 of 144, TAH = 157 of 157 (NS) Operative time = 134.5 (SD 31.2) versus 112 (SD 21.7)(p < 0.001) Estimated blood loss (ml) = 260 versus 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.	Funding Source: Not stated



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			Adenomyosis = 38 Combination = 13 Normal sized uterus = 20  Pre-operative haemoglobin = 117 g/l  Country: Taiwan				109 (NS)	
Kupperman 2004 <sup>331</sup>	Study Type:  Evidence level: 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%	Hysterectomy; expanded medical treatment  treatment vs. treatment; treatment vs. baseline	24 months	SF-36; Body image & 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	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 & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			<p>&lt; high school education = 39%, 38%</p> <p>&lt;\$25000 income = 42%, 53%</p> <p>Uterine fibroids = 65%, 63%</p> <p>Pervious treatment: hysterectomy = 39%, Prostaglandin inhibitors 13%, GnRH-a 10%, D&amp;C 19%, myomectomy 6%, endometrial ablation 3%</p> <p>Medicine = COC 50%, Prostaglandin inhibitors 19%, GnRH-a 6%, D&amp;C 38%, myomectomy 0%, endometrial ablation 0%</p> <p>Country: USA</p>				<p>22), Medicine = 39 (SD 24)</p> <p>Change in QoL scores from baseline to 6-months using intention to treat (hysterectomy, medicine, p-value for difference between groups):</p> <p>SF-36 MCS score: hysterectomy = 8, Medicine = 2, p = 0.04</p> <p>SF-36 PCS score: hysterectomy = 6, Medicine = 3, p = 0.21</p> <p>Body image score: hysterectomy = 15, Medicine = 5, p = 0.07</p> <p>Satisfaction with sex: hysterectomy = 20, Medicine = 10, p = 0.19</p> <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 &lt; 0.001</p> <p>Satisfaction with symptom level: hysterectomy = 44, medicine = 7, p &lt; 0.001</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<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</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>symptom level: hysterectomy = 46, medicine = 40, <math>p = 0.36</math></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>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Kuppermann 2005 <sup>519</sup>	Study Type:  Evidence level: 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 +ve pregnancy test Desire for future childbearing Known cervical or genital tract cancer Complex endometrial hyperplasia 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	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	Sexual functioning SCH: higher mean score the TAH group on orgasm frequency at 6 months (likely due to better sexual functioning at baseline)  Reported problems with sexual functioning (on a 0-100 scale with 100 indicating the absence of problems) SCH: 82 TAH: 80 (Mean difference 2, 95% CI -8 to 11)(  but no significant differences in both groups at 2 years ( mean scores above 90)	Funding Source: funded by a grant from the Agency for Health Care Research and Quality  Study summary: SCH and TAH resulted in similar sexual functioning and health-related quality of life at 2 years follow-up

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Langebrekke 496	Study Type: Randomised; concealed  Evidence level: 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 (mins); Hospital stay (days); Resumption of work (days); Postoperative pain; Estimated blood loss (ml); Complications	LAVH vs. TAH:  Median operation time (mins): 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 121	Study Type: randomised - block; non-blinded; concealment  Evidence level: 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	medical treatment; hysterectomy  treatments versus 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%	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 & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			<p>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.</p> <p>Average age: hysterectomy = 42, medicine = 40 Health insurance = 65%, 81% &lt; high school education = 39%, 38% &lt;\$25000 income = 42%, 53% Uterine fibroids = 65%, 63%</p> <p>Pervious treatment: hysterectomy = COC 39%, Prostaglandin inhibitors 13%, GnRH-a 10%, D&amp;C 19%, myomectomy 6%, endometrial ablation 3%</p> <p>Medicine = COC 50%,</p>				<p>Continued vaginal bleeding at 6-months was 87% for medicine and 11% for hysterectomy (<math>p &lt; 0.001</math>).</p> <p>Continued vaginal bleeding at 24-months was 37% for medicine and 7% for hysterectomy (<math>p &lt; 0.001</math>).</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>Change in symptom frequency fro baseline at 6-months (intention-to-treat) Pelvic pain: hysterectomy = -2.3, medicine = -0.7, <math>p &lt; 0.01</math> Urinary urgency: hysterectomy = -0.7, medicine = 0.0, <math>p = 0.03</math></p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			Prostaglandin inhibitors 19%, GnRH-a 6%, D&C 38%, myomectomy 0%, endometrial ablation 0%  Country: USA				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	



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							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 <sup>497</sup>	Study Type:  Evidence level: 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 +ve 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	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	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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			variables Country: USA				(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 mins TAH: 123 +/- 46 mins (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 TAH: 8.8 +/- 18.8 days	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							(NS)  Cut down on activities SCH: 9.3 +/- 15.7 days TAH: 6.0 +/- 14.6 days (NS)  Rate of patients hospital admission (0-2 years) SCH: 31% TAH: 16% (Relative hazard 2.05, 95% CI 0.99 to 4.2)(NS)  During 1st year SCH: 7.4% TAH: 6%  Baseline body weight >100kg associated with hospital re-admission (by multivariate analysis) for all cause (RR 2.18, 95% CI 1.06 to 4.48) for readmission related to hysterectomy (RR 2.83, 95% CI 0.86 to 9.36)  2 deaths (1 from stroke and 1 from Ca breast)	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Lethaby 2004 335	Study Type: systematic review; meta-analysis  Evidence level: 1++	5 RCTs included with 752 patients	Population characteristics: Searches undertaken on Cochrane library, MEDLINE, EMBASE, PsychLIT; Web of Science; CINAHL. Searches of bibliographies.  Search designed to identify studies comparing ablation and hysterectomy.  Free-text and MESH headings used as search terms.  Search date 1999  Country:	Transcervical Resection of the Endometrium (TCRE); Laser ablation; electrocautery ablation; radiofrequency ablation; hysterectomy - any route.  Resection/ablation versus hysterectomy		MBL - subjective and objective; QoL; Length of stay; Duration of procedure; Patient satisfaction; Adverse events; mortality; further surgery	Comparison of improvement in MBL between ablation/resection and hysterectomy: At 12 months (3 studies, n = 440) peto odds ratio = 0.12 (0.06 to 0.25)  Comparison of satisfaction between ablation/resection and hysterectomy: At 12 months (3 studies, n = 519) peto odds ratio = 0.46 (0.24 to 0.88)  At 24 months (3 studies, n = 354) peto odds ratio = 0.31 (0.16 to 0.59)  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.  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	Funding Source: Not stated - Cochrane review usually unfunded.  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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<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>Thirteen 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 odds ratio = 7.33 (4.18 to 12.86).</p>	
Lumsden 498	Study Type: Randomised  Evidence level: 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 &gt; 14 weeks included, Need oophorectomy included; HRT inappropriate excluded.</p> <p>TAH vs. LAVH: Age: 42.7 vs. 41.1 BMI: 26.6 vs. 26.3</p>	TAH; LAVH	12 months	<p>Length of operation (mins); 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 (mins): 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:</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 operation and patient satisfaction were not affected by the route chosen. It is unlikely that LAVH represents an efficient use of NHS resources.</p>

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & 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: Menstrual problems - 55% vs. 59%</p> <p>Pelvic pain - 17% vs. 22%</p> <p>Country: UK</p>				<p>8 vs. 6</p> <p>Blood transfusions: 2 vs. 1</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>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							12-months - 15.9 (21) vs. 12.6 (25)	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Marana 1999  499	Study Type: Randomised; multi-centre  Evidence level: 1-	116 (58 in LAVH group, 58 in Abdominal Hysterectomy)	Population characteristics: Women; contraindications to vaginal surgery - uterine size > 280g, 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 700g.  Baseline (LAVH vs. AH): Age: 49.2 vs. 49.1 Parity: 1.67 vs. 1.78 Uterine weight: 326.4 (SD 125.8) vs. 352.3 (SD 165.9)  Country: Italy	Laparoscopically assisted vaginal hysterectomy; abdominal hysterectomy  LAVH vs. AH	3 days	Operating time (mins); Estimated blood loss; postoperative haemoglobin drop (g/100 ml); Complications; Postoperative pain levels; Length of stay (days)	LAVH vs. AH  Operating time (mins): 91.1 vs. 01.8  Estimated blood loss; 264.7 (SD 194.4) vs. 353.9 (SD 254.6)  postoperative haemoglobin drop (g/100 ml): 1.09 vs. 1.55  Complications: Conversions to AH from LAVH = 0 Bladder laceration: 1 vs. 0 Febrile morbidity: 2 vs. 0 Vaginal cuff haematoma: 0 vs. 1 Pelvic bleeding: 0 vs. 1 Post-operative fever: 0 vs. 5  Length of stay (days): 4 vs. 5.9 (P < 0.001)  Postoperative pain levels: day 1 = 5.2 vs. 6.3 (P < 0.05) day 2 = 2.3 vs. 4.4 (P < 0.001) day 3 = 1.3 vs. 2.8 (P < 0.005)	Funding Source: Not stated  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.



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Martel 1995  585	Study Type: Matched case-control study  Evidence level: 2-	212 (106 had LAVH, 106 had TAH)	Population characteristics: Women; matched for age and uterine weight  Country: Canada	LAVH; TAH	No follow-up	Operative time; Length of stay; Narcotic use; Complications	Operative time (minutes) LAVH = 146 vs. TAH = 61.9 (p = 0.00001) Length of stay: 3.5 vs. 6.4 days (p = 0.00001) Narcotic use (mg): 527 vs. 983 (p = 0.00001)  Complications (LAVH vs. TAH): 24 vs. 15 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	Funding Source: Not stated  Study summary: There was no difference in the complication rate between the two groups.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Mehra 1999  586	Study Type: Case-series  Evidence level: 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 (mins); Recovery time (days); Length of stay (days); complications	VH vs. TAH vs. LAVH  Operating time (mins): 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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Meikle 1997  523	Study Type: Systematic review  Evidence level: 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	<p>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%)</p> <p>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%)</p>	<p>Funding Source: Not stated</p> <p>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.</p>

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Miskry 2003 <sup>500</sup>	Study Type: randomised - sealed envelopes; blinded; concealed  Evidence level: 1+	120 assessed, 57 eligible, 36 randomised (AH = 18, VH = 18). All completed trial.	Population characteristics: Women; scheduled for hysterectomy; excluded if - genital tract malignancy, adnexal pathology, uterine size > 14-weeks 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	Abdominal hysterectomy; Vaginal hysterectomy  AH vs. VH	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.  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) =	Funding Source: Not stated  Study summary: Vaginal 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			vs. 5 Country: UK				<p>131.4 (58.2) vs. 75.4 (29.7), <math>p = 0.002</math>  Bowels open (days): 3.7 vs. 2.6, <math>p = 0.002</math>  Postoperative stay (days) = 5.0 (1.49) vs. 3.6 (1.42), <math>p = 0.01</math>  Time to domestic activity (weeks): 8.5 (4.1) vs. 4.6 (1.9), <math>p = 0.01</math>  Time to fitness to work = 13.9 (9.5) vs. 7.0 (2.9), <math>p = 0.005</math>  Time to full recovery (weeks) = 16.9 (10.1) vs. 7.9 (4.5), <math>p = 0.02</math>.</p> <p>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</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Mousa 2001  368	Study Type: Matched case-control  Evidence level: 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  587	Study Type:  Evidence level: 2-	451 women who had had a hysterectomy for reasons of meno/menorrhagia or dysmenorrhoea /dyspareunia  Control 110 women who had had a laparoscopic cholecystectomy	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 mins (p=0.01) Blood loss 252 vs. 303 vs. 137ml (p=0.01) Sig longer hospital stay in AH group  Bladder injury 1 in supra-cervical H	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 reviewed over time

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
		y, excluding nulliparous					<p>0 in AH 7 in VH</p> <p>Urinary symptoms Pre-op Women in supra-cervical H group experienced sig more bothersome incontinence than AH, VH and cholecystectomy</p> <p>de novo urinary symptoms post-op Women in supra-cervical H group experienced sig urge, urgency and feeling of hygienic problem than AH, VH and cholecystectomy</p> <p>de novo cure sig more common than in cholecystectomy group</p> <p>Use of devices and feeling of having a hygiene problem more associated with women after supra-cervical H than AH</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Olsson 1996 <sup>501</sup>	Study Type: randomised; concealed  Evidence level: 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	Laparoscopic hysterectomy; abdominal hysterectomy		Anaesthesia (mins); Duration of surgery (mins); Hospital stay (days); Convalescence (days); Complications	LH vs. AH  Anaesthesia (mins); 190 (range 125 to 305) vs. 125 (range 65 to 275)  Duration of surgery (mins); 148 (range 70 to 240) vs. 85 (45 to 225)  Hospital stay (days): 2.0 vs. 4.0  Convalescence (days): 16.0 (0 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	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.



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			Uterine fibroids: 22 vs. 20 Endometrial hyperplasia: 21 vs. 25 dysmenorrhoea Mechanical symptoms: 4 vs. 6 Endometriosis: 2 vs. 7 Adnexal mass: 0 vs. 4 Country: Sweden				Blood transfusions: 5 vs. 9 Blood units given: 11 vs. 23 (P < 0.001)	
Ottosen 2000 <sup>502</sup>	Study Type: Randomised; concealed; ITT Evidence level: 1+	120 (40 VH, 40 AH, 40 LAVH)	Population characteristics: Women; indications of menorrhagia, uterine fibroids < 15cm 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	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	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 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			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 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				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 Abdominal wall infection: 1 vs. 0 vs. 0 Prolonged catheter time: 0 vs. 0 vs. 1 Converted to TAH: 0 vs. 1 vs. 4	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Perino 1999 <sup>503</sup>	Study Type: Randomised  Evidence level: 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 = 368g (SD 125.3)  abdominal group: age = 47.6, parity = 2.4, uterine weight = 389g (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 (mins)	Operating time (mins): Laparoscopic - first 15 = 129.2 mins (SD 22.3), last 36 = 93.6 (SD = 21.4)  Abdominal - first 15 = 87.9 mins (SD = 20.3), last 36 = 87.8 mins (SD = 20.7)  Blood loss (ml) Laparoscopic = 140ml (SD = 41.5) Abdominal = 406ml (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 <sup>420</sup>	Study Type: randomised; concealed - sealed envelopes; blinding not mentioned  Evidence level: 1+	64 eligible. 57 randomised (38 in UAE group - 1 refused assignment and had hysterectomy, 19 in hysterectomy group - 3	Population characteristics: Women; bleeding associated with uterine fibroids; patient with fibroid > 10cm; contraindications to surgery; desire to maintain fertility	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:	Funding Source: Not stated  Study summary: Compared with hysterectomy, UAE is safe and effective treatment for bleeding fibroids, necessitates a shorter hospital stay, and

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
		refused assignment and had UAE, 1 of whom later had hysterectomy)	<p>and/or sensitivity to iodine were excluded from study.</p> <p>Baseline characteristics (UAE vs. hysterectomy):</p> <p>Age (years) 46.4 vs. 44.6</p> <p>No pregnancies = 2.6 vs. 3.2</p> <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 (cm<sup>3</sup>) = 72 vs. 113</p> <p>Symptoms:</p> <p>menorrhagia = 37 vs. 17</p> <p>Metrorrhagia = 19 vs. 9</p> <p>Country: Spain</p>				<p>UAE = 13, Hysterectomy = 4</p> <p>Intra-operative complications:</p> <p>Minor - UAE = 11 vs. 0</p> <p>Major - UAE = 0 vs. hysterectomy = 4</p> <p>Post-operative complications:</p> <p>Minor - UAE = 20 vs. hysterectomy = 3</p> <p>Moderate - UAE = 19 vs. hysterectomy = 2</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>	results in fewer major complications.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Raju 1994 504	Study Type: randomised; concealed  Evidence level: 1+	80 (40 abdominal hysterectomy; 40 LAVH)	Population characteristics: Women; scheduled for hysterectomy and bilateral oophorectomy for benign condition; excluded if - uterus > 14 weeks in size, morbidly obese, uterine prolapse.  Baseline characteristics (LAVH vs. TAH): Indication - 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  Maximum uterus	Laparoscopic-assisted bilateral salpingo-oophorectomy and vaginal hysterectomy; total abdominal hysterectomy with bilateral salpingo-oophorectomy  Surgery versus surgery	6 weeks	Operating time (mins); estimated blood loss (ml); Length of stay; duration of post-operation analgesia (days); recovery from pain (days); time for recovery (days)	LAVH vs. TAH  Operating time (mins): 100 (61 to 180) vs. 57 (25 to 151) (p < 0.0001)  Estimated blood loss (ml): 260 (70 to 700) vs. 220 (50 to 500)  Length of stay: 3.5 (1 to 6) vs. 6 (3 to 13) (p < 0.0001)  Duration of post-operation analgesia (days): 6.6 vs. 13.3 (p < 0.0001)  Recovery from pain (days): 13 vs. 26 (p < 0.0001)  Time for recovery (days): restricted physical activity - 16 (6 to 35) vs. 27 (5 to 47) (p < 0.001)	Funding Source:  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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			size: 12 weeks vs. 14 weeks.  Country: UK					
Ribeiro 2003 505	Study Type: randomised  Evidence level: 1-	60 consecutive patients (20 AH, 20 VH, 20 LAVH)	Population characteristics: Women; suitable for hysterectomy; excluded if - uterine volume > 400 cm <sup>3</sup> , use of anti-inflammatory drugs in past 3 months; diabetes mellitus; coagulation disorders; autoimmune diseases.  Average uterine weight: TAH = 189.50, VH = 155.65, LH = 154.50  Patient age: range 34 to 76 (mean average = 42.33) HMB = 57 Myoma = 41 Adenomyosis = 19  Country: Brazil	Abdominal hysterectomy; vaginal hysterectomy; LAVH	2 days	Operative time; complications; blood loss; C-reactive protein levels; interleukin 6 levels	Operative time (mins): TAH = 109, VH = 78, LH = 119  Blood loss: VH had lower levels of haemoglobin than TAH and LH ( $p < 0.05$ )  Inflammatory response: TAH different from VH and LH ( $p < 0.05$ )	Funding Source: Not stated  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 hysterectomy.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Richardson 1995 506	Study Type: randomised  Evidence level: 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 (n = 22) vs. VH (n = 23)  Operating time: 131.4 vs. 76.7  Opioid 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	Study Type:	394 women Abdominal	Population characteristics:	AM vs. AH	Chart review over a period of 2	Morbidity Post op care	Morbidity Overall morbidity	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
454	Evidence level: 2+	myomectomy (AM): n=197 Abdominal hysterectomy (AH): n=197	<p>Mean age AM: 36 years AH: 44 years (p&lt;0.0001)</p> <p>Mean weight AM: 156 lb AH: 174 lbs (p&lt;0.0001)</p> <p>Mean parity AM: 0.5 AH: 1.6 (p&lt;0.0001)</p> <p>Pre-op uterus size (weeks equivalent) AM: 14 AH: 16 (p&lt;0.0001)</p> <p>Indications AM: vaginal bleeding (37%) or pain (39%), recurrent miscarriage, infertility</p> <p>AH: vaginal bleeding (62%) or pain (31%)</p> <p>Country: USA</p>	AM vs. AH	years		<p>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)</p> <p>Post op care Mean operative time (mins) AM: 201 AH: 176 (p&lt;0.00002) Estimated blood loss (mL) AM: 227 AH: 484 (p&lt;0.00001) Length of hospital stay (days) AM: 4 AH: 4.4 (p&lt;0.048) Max drop in hgb AM: 2.5 AH: 4 (NS) Transfusion (no.)</p>	Study summary: No clinical difference in peri-operative morbidity between myomectomy and hysterectomy. Myomectomy should be considered a safe alternative to hysterectomy



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							AM: 9% AH: 13% (NS)	
Schutz 2002 507	Study Type: Randomised; concealed  Evidence level: 1+	48 (28 LAVH, 20 AH)	Population characteristics: Women; Uterine weight > 200g; 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) vs. 369 (254 to 595)  Country: Germany	Laparoscopically assisted vaginal hysterectomy; Abdominal hysterectomy  LAVH vs. AH	12 months	Duration of operation (mins); Estimated blood loss (ml); number of blood transfusions; Additional procedures; uterine weight (g); complications; Haemoglobin levels; pain index (WHO); length of stay (days); Recovery time (days)	LAVH vs. AH (median, 25 to 75 percentile)  Duration of operation (mins): 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 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)	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 acceptance.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							to 11) Recovery time (days): 42 vs. 42	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Seracchioli 2003  588	Study Type: Randomised  Evidence level: 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 11.25mg) for 3 month; no treatment	3 months prior to surgery and 2 months after surgery	Preoperative haemoglobin (gr/dl); Preoperative uterine volume (ml); Uterine weight (g); operating time (mins); Drop in haemoglobin; number of transfusions; Mean hospital stay (hrs)	GnRH vs. no treatment  Pre-treatment uterine volume (ml): 528 (SD 275) vs. 579 (SD 337)  Preoperative haemoglobin (gr/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 (mins): 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 (hrs): 76.2 vs. 80.4  7 in GnRH and 8 in no treatment group had BOS.  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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Seracchioli 2002 <sup>508</sup>	Study Type: Randomised; concealed  Evidence level: 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 (mins); Estimated blood loss (ml); number of transfusions; Number of with fever; Lapro-conversions; Length of stay (hrs); length of recovery (days)	TLH vs. TAH  Operating time (mins): 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) Lapro-conversions: 1 vs. 0 Length of stay (hrs): 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 <sup>509</sup>	Study Type: Randomised  Evidence level: 1-	80 (LAVH = 40 - 3 had AH, VH = 40)	Population characteristics: Women; Inclusion criteria - uterine size > 280mg and one of following - previous pelvic surgery, history of pelvic disease,	Vaginal hysterectomy; Laparoscopic assisted vaginal hysterectomy	1 day	Operative time (mins); haemoglobin drop in day 1; NSAID (g); Paracetamol (g); Opioid (mg); Gas and stool (day); Length of stay (day); Conversion to	VH vs. LAVH  Operative time (mins): 108 (SD 35) vs. 160 (SD 50) (p< 0.001)  Haemoglobin drop in day 1: 2.0 vs. 2.2	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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			<p>endometriosis, concomitant adnexal masses. Exclusion criteria were - suspicious adnexal mass, anaesthetic contraindications, contra-indications to pain relief.</p> <p>baseline (VH vs. LAVH)  Age: 49.1 vs. 49.3  Gravidity: 3.7 vs. 2.4  Parity: 2.7 vs. 1.6  Vaginal delivery: 33 vs. 32  Previous caesarean: 7 vs. 0  Previous pelvic surgery: 5 vs. 8</p> <p>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</p> <p>Uterine weight</p>			<p>abdominal hysterectomy</p>	<p>NSAID (g): 137 vs. 137</p> <p>Paracetamol (g): 10.1 vs. 11.1</p> <p>Opioid (mg): 8.7 vs. 6.8</p> <p>Gas and stool (day): 1.3 vs. 1.5</p> <p>Length of stay (day): 5.3 vs. 5.7</p> <p>Conversion to abdominal hysterectomy: 0 vs. 3</p>	<p>hysterectomy. No advantage was found performing laparoscopic assisted vaginal hysterectomy in comparison with the standard vaginal hysterectomy.</p>

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			(g): 424 (SD 211) vs. 481 (SD 329)  Country: France					
Spies 2004  430	Study Type: Prospective; cohort  Evidence level: 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	UAE; hysterectomy  UAE vs. Baseline UAE versus 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 = na  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 versus 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	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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			treatment: None = 52%, 70% Hormonal = 39%, 24% Surgery = 53%, 20%  Country: USA				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%)	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Summitt 1992 510	Study Type: randomised;  Evidence level: 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 - 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.  baseline (VH vs. LAVH)	Vaginal hysterectomy; LAVH  Surgery vs. surgery	6 weeks	Duration of operation (mins); Uterine weight; Intra-operative complications; postoperative complications; surgery completed; post-operative pain relief use.	LAVH vs. VH  Duration of operation (mins): 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: LAVH = 1 laceration, 1 cystotomy VH = none  5 (2 VH and 3 LAVH) patients underwent oophorectomy  Postoperative complications: LAVH = 1 readmitted for pain control VH = 1 vaginal cuff infection, 1 vesicovaginal fistula.  Post-operative pain relief use: Day of surgery: 3.13 vs. 3.82 Day 1: 3.67 vs. 3.61 Day 2: 2.71 vs. 1.57 (p = 0.027)	Funding Source: Not stated  Study summary: Other than cost, laparoscopy-assisted vaginal hysterectomy and standard vaginal hysterectomy appear comparable in patients who could otherwise undergo a vaginal hysterectomy.



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			Age: 37.5 vs. 37.7 Parity: 2.5 vs. 2.4 Indication: Leiomyomata uteri: 18 vs. 16 Recurrent CIN: 2 vs. 1 Abdominal bleeding 3 vs. 4 Adenomatous hyperplasia: 1 vs. 2 Chronic pelvic pain: 3 vs. 6 Country: USA					

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Summitt 1998 <sup>511</sup>	Study Type: Randomised; concealed  Evidence level: 1-	65 (34 LAVH, 31 TAH)	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	Laparoscopic-assisted vaginal hysterectomy; total abdominal hysterectomy  LAVH vs. TAH	6 weeks	Operating time (mins); Estimated blood loss (ml); Uterine weight (g); Hematocrit levels; Length of stay (days); Convalescent (days); complications	TAH vs. LAVH  Operating time (mins): 146 (SD 69.9) vs. 179.8 (SD 56.4)  Estimated blood loss (ml): 660.5 (SD 610.0) vs. 568 (SD 394.0)  Uterine weight (g): 383.9 (SD 227.8) vs. 336.8 (SD 276.0)  Hematocrit levels: Pre-surgery - 35.8 vs. 36.9 Day 2 - 29.3 vs. 29.3  Length of stay (days): 4.13 vs. 2.12 (p < 0.001)  Convalescent (days): 38 vs. 28 (p = 0.002)  Complications: Cystotomies: 0 vs. 2 Artery damage: 0 vs. 1 Intra-operative haemorrhage > 100ml: 2 vs. 2  Need for IM narcotics: 26 of 34 vs. 30 of 31 (p = 0.018)	Funding Source: US surgical corporation  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. 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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			<p>major operation, major medical condition requiring monitoring, Fibroid or pelvic mass &gt; 18 weeks, intolerant to anaesthesia, severe bleeding disorder, acute peritonitis of the upper abdomen, midline abdominal hernia.</p> <p>Baseline (TAH vs. LAVH)  Age: 41.5 vs. 38.3  Gravidity: 2.4 vs. 3.1  Parity: 1.7 vs. 2.3  Weight (lbs): 178.1 vs. 168.8</p> <p>Indications for surgery:  Endometriosis: 1 vs. 1  Adhesions: 2 vs. 0  Uterine fibroids: 23 vs. 23</p>					

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Thakar <sup>518</sup>	Study Type: double-blind  Evidence level: 1+	N=279 Subtotal hysterectomy STH (n=133) Total hysterectomy TH (n=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% (p<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 (p=0.03 for the change over time within each group; p=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 (P<0.01) Frequency of orgasm, and sexual relationship: NS between both groups post-op Deep dyspareunia: Pre-op: STH 46%; TH	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

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>39% Post-op: STH 7%); TH 14% (P&lt; 0.001 for change over time in each group)</p> <p>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</p> <p>Post-op complications: Before discharge STH 13 (10%) TH 40 (27%) (p&lt;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;</p>	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							TH 3) Ileus (STH 0; TH 1) vaginal bleeding (STH 0; TH 1)  at 12 months STH 14 (11%) TH 9 (6%) (p<0.001)  bowel obstruction (STH 0; TH 2) cyclical vaginal bleeding (STH 9; TH --) cervical prolapse (STH 2; TH --) persistent pain (STH 3; TH 7)	
Tsai 2003 512	Study Type: randomised  Evidence level: 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 syphilis; 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	Laparoscopic assisted vaginal hysterectomy plus light-endorsed transvaginal section; total abdominal hysterectomy	1 day	Estimated blood loss (ml); Operating time (mins); Weight of uterus (g); Complications; Length of stay (day); Number of meperidine ampules	Estimated blood loss (ml): 202 vs. 238  Operating time (mins): 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)	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			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 in situ: 5 vs. 8 Endometrial atypia: 3 vs. 1  Country: Taiwan				Number of meperidine ampules: 1.2 (SD 0.7) vs. 3.7 (SD 1.3) ( $p < 0.05$ )	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Unger 2002 <sup>589</sup>	Study Type: Comparative case-series; retrospective  Evidence level: 2-	318 (group 1 uteri < 500g = 208, group 2 uteri between 500 = 63 and 999g, group 3 uteri >1000g = 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 (mins); Blood transfusions; At least one complication - blood loss > 500ml, 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 (mins): 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.



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Wattiez 2002 590	Study Type: Matched case-control  Evidence level: 2+	283 admitted for hysterectomy for benign conditions. 240 were appropriate for TLH. 34 had uteri 500g>, and 68 matched controls had uteri < 300g	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 (>500g vs. <300g) 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	Total laparoscopic hysterectomy with or without Burch operation and/or adnexectomy.	6 to 6 weeks	Operating time (mins); oral analgesia use (mg); Opioid administration (mg); Hospital stay (days); Complications	Operating time (mins): 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 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	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 certain surgical steps to ensure optimal exposure of the operative field and more effective and safer excision of the uterine vascular pedicle.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Weeks 2000 <sup>527</sup>	Study Type: Randomised; Double-blind; concealment  Evidence level: 1-	51 - 26 (2 withdrawals due to side- effects) in Leuprorelin 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 > 2.5cm present; excluded if malignancy present.  Average age: leuprorelin = 39, placebo = 40 No pathology: 15, 13 Abdominal hysterectomy: 14, 20  Country: UK	Leuprorelin acetate or placebo pre- treatment; hysterectomy	120 days	Operative outcome4s; complications; patient outcomes - return to normal activity	Operative blood loss: Leuprorelin = 183, placebo = 285, p = 0.27 Operative difficulty: Leuprorelin = 2.4, placebo = 3.2, p = 0.09 Length of operation: Leuprorelin = 39, placebo = 49, p = 0.64  No statistically significant differences for post-operative outcomes between groups - analgesia use, day of discharge, transfusions.  Complications: Leuprorelin = 11, placebo = 14  Patient return to normal health: Leuprorelin = 37 days, placebo = 64 days, p = 0.06	Funding Source: Wyeth- Lederle UK  Study summary: Leuprorelin pre-treatment before hysterectomy in non-fibroid patients had no operative or post- operative benefits.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Ylikorkala 1995 526	Study Type: randomised; double-blind  Evidence level: 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 200ug 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 513	Study Type: randomised  Evidence level: 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)	Laparoscopic hysterectomy; abdominal hysterectomy  LH vs. AH	3 days	Trauma response (IL-6, C-reactive protein, cortisol) Operating time (mins); Anaesthetic time (mins); 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.	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.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
			Country: Hong Kong				44.2 (p = 0.02) White blood cell: 59.5 vs. 69.8 (p = 0.009)  Operating time (mins): 95 vs. 105  Anaesthetic time (mins): 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: Febrile: 3 vs. 11 UTI: 2 vs. 3 Vault haematoma: 4 vs. 1 Wound infection: 1 vs. 0	

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Zupi 2003 338	Study Type: Randomised; concealment and blinding not mentioned  Evidence level: 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 100kg; 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 (3.75mg) 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 mins, LSH = 71.5 mins, $p < 0.01$  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)	Funding Source: Not stated  Study summary: Laparoscopic hysterectomy may offer curative advantages of hysterectomy with operative advantages of ablation.

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							<p>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> <p>P &lt; 0.01 for change in general health score for both treatments, and for difference after treatment between groups in favour of hysterectomy.</p> <p>P &lt; 0.01 for change in emotional role in hysterectomy group</p> <p>P &lt; 0.01 for change in social function score for both treatments, and for difference after treatment between groups in favour of hysterectomy.</p> <p>P &lt; 0.01 for change in vitality score for hysterectomy treatments, and for difference after treatment between groups in favour of hysterectomy.</p>	

## Chapter 12 – Hysterectomy for treatment of HMB

### Hysterectomy for treatment of HMB – Non-comparative studies

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Clarke 2005 <sup>369</sup>	Study Type: Cohort  Evidence Level: 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.

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Cravello 1999 <sup>461</sup>	Study Type: case series  Evidence Level: 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



Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
De Meeus 1997 <sup>591</sup>	Study Type: retrospective study  Evidence Level: 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: 47years Mean parity: 1.59 6.5% menopausal 40% previous surgery 5% previous laparoscopy  Country: France	Uterine weight Intra-operative events	Uterine weight: Mean wt VH: 236 +/- 137g AH: 608 +/- 432g (p<0.0001) wt >280g VH: 32% AH: 77% (p<0.01) wt+myomas VH: 267g AH: 879g (p<0.0001)  Intra-operative events Bleeding (mean vol.): VH: 140+/- 119ml AH: 384 +/- 283ml (p<0.0001) Duration of procedure: VH: 50.6+/-16 mins AH: 90 +/- 34.4mins (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

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Erian 2005 <sup>592</sup>	Study Type: case series, prospective  Evidence Level: 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 7 pelvic adhesiolysis 2 excision of implants 2 ovarian cystectomy 1 cystoscopy  59% of laparoscopic subtotal hysterectomy performed on an outpatient basis  Country: UK	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 0 anaesthetic complications  Operating time 45.5 mins (15-90) Hospital stay Median 3 days (2-5)  Satisfaction 100% satisfaction with operation and would recommend to friends	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, reduced operating time and high patient satisfaction
Gath 1982 <sup>108</sup>	Study Type: Cohort; prospective  Evidence Level: 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 =	Funding Source: Not stated  Study Summary: Hysterectomy reduces level of psychiatric morbidity. Hysterectomy did not cause psychiatric morbidity. Psychiatric

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						<p>9% vs. 85% (<math>p&lt;0.001</math>), tension = 33% vs. 77% (<math>p&lt;0.001</math>), irritability = 17% vs. 62% (<math>p&lt;0.001</math>), situational anxiety = 28% vs. 55% (<math>p&lt;0.001</math>), lack of energy = 8% vs. 53% (<math>p&lt;0.001</math>), simple depression = 16% vs. 47% (<math>p&lt;0.001</math>), social unease = 23% vs. 43% (<math>p&lt;0.001</math>), anxiety = 6% vs. 40% (<math>p&lt;0.001</math>), loss of concentration = 12% vs. 31% (<math>p&lt;0.001</math>).</p> <p>Patients after vs. patients before surgery (p-values for after surgery figures versus general population figures:  Worry = 61% vs. 89% (<math>p&lt;0.01</math>), Somatic features of depression = 37% vs. 85%, (<math>p&lt;0.001</math>), tension = 64% vs. 77% (<math>p&lt;0.001</math>); irritability = 22% vs. 62% (ns), situational anxiety = 48% vs. 55% (<math>p&lt;0.001</math>), lack of energy = 27% vs. 53% (<math>p&lt;0.001</math>), simple depression = 24% vs. 47% (ns), social unease = 28% vs. 43% (ns), anxiety = 22% vs. 40% (<math>p&lt;0.001</math>), loss of concentration = 22% vs. 31% (<math>p&lt;0.05</math>).</p>	morbidity higher in patient group than general population.
Gath 1995 <sup>593</sup>	<p>Study Type: case series (last of a series of 3 studies by the same authors)</p> <p>Evidence Level: 3</p>	hysterectomy	239 women undergoing hysterectomy for menorrhagia of benign origin	<p>Study 1 - mean age: 42 years  Study 2 - mean age: 38 years  Study 3 - mean age: 39 years</p> <p>Country: UK</p>	<p>Levels of psychiatric morbidity</p> <p>Association between psychiatric morbidity and demographic factors</p> <p>psychotropic medication</p> <p>past psychiatric illness</p> <p>women's</p>	<p>Levels of psychiatric morbidity</p> <p>Pre-op level of PSE drop:  Study 1: 58%  Study 2: 28%  Study 3: 9% (<math>p&lt;0.001</math>)</p> <p>Post-op level of PSE drop:  Study 1: 26%  Study 2: 7%  Study 3: 4% (<math>p&lt;0.001</math>)</p> <p>Demographic factors:  Study 1 women sig older than</p>	<p>Funding Source: MRC</p> <p>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</p>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
					understanding and expectation of the operation	<p>women in Study 2 and 3 no significant differences between the 3 groups in social class, marital status and menstrual symptoms</p> <p>Medication Anti-menorrhagic drugs prescribed more frequently in Study 3 than in Study 1 and 2 (<math>p&lt;0.001</math>) Psychotropic medication prescribed more frequently in Study 1 than in Study 2 and 3 (<math>p&lt;0.001</math>)</p> <p>Past psychiatric illness Sig. fall in 'neuroticism' across the 3 studies (<math>p&lt;0.001</math>)</p> <p>Women's understanding and expectation of the operation Satisfaction with GP's explanation: Study 1: 65% Study 3: 49% NS</p> <p>Satisfaction with gynaecologists' explanation: Study 1: 64% Study 3: 60% NS</p> <p>Books and magazines as source of information for women: Study 1: 51% Study 3: 42% NS</p> <p>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</p>	reassurance

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Harkki-Siren 1997 <sup>594</sup>	Study Type: Survey  Evidence Level: 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 (mins); Estimated blood loss (ml); Hospital stay; Recovery time; Complications	Duration of operation (mins): 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 Urethral 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 <sup>595</sup>	Study Type: Case series  Evidence Level: 3	LAVH  Concomitant procedures: 67 appendicectomy 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: 1.2g/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

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Hurskainen 2004 <sup>481</sup>	Study Type: randomised  Evidence Level: 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 (&gt;80ml 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>

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Johns 1994 <sup>59b</sup>	Study Type: case series  Evidence Level: 3	LAVH	119 women undergoing LAVH  82 concomitant oophorectomy	mean age: 39.2 +/- 0.7years 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 mins Mean blood loss: 135 +/- 10 ml (25-500) Mean length of hospital stay: 59 hrs (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 <sup>524</sup>	Study Type: Prospective case series study,  Evidence Level: 3	hysterectomy  30% had concomitant surgery fro 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	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	In-hospital complications: 21% no complications 67% =>1 mild complications 11% =>1 moderate complications 0.7% =>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	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

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
				3% cancer 3% adnexal condition 2% infectious condition  Country: USA	Predictors of lack of symptom relief	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 $\leq$ 35,000 sig. associated with lack of symptom relief (OR 0.37, 95% CI 0.24 to 0.59) at 2 years	



Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Malzoni 2004 <sup>59/</sup>	Study Type: Case-series; retrospective  Evidence Level: 3	LAVH	1020 (series 1 = 396, series 2 = 624)	Women; symptomatic myomas or uterine fibroatosi; not suitable for vaginal hysterectomy.  baseline (Series 1, Series 2): Age: 50.1, 49.8 BMI: 25.2, 24.8 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	Operating time (mins); Hospital stay (days); Recovery time (days); complications; Postoperative haemoglobin drop (g/dl)	Series 1 (1997 to 1999) vs. series 2 (2000 to 2002)  Operating time (mins): 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  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	Funding Source: Not stated  Study Summary: Laparoscopic hysterectomy is a safe, effective, and reproducible 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. .

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Maresh 2002 <sup>521</sup>	Study Type: Clinical audit of a group of hysterectomy cases in a multi-centre cohort study  Evidence Level: 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 $\geq 50$ 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

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
McPherson 2005 <sup>385</sup>	Study Type: Cohort  Evidence Level: 3	TCRE; hysterectomy with or without BOS	Numbers responding at 5- year follow-up: TCRE = 3845, hysterectomy = 3397, hysterectomy & BOS = 2305	Women; undergone TCRE or hysterectomy.  Average age at 5- year follow-up: TCRE= 47.9, hysterectomy = 54.1, BOS = 50.6  Country: UK	Libido loss, difficult sexual arousal; vaginal dryness.	Adjusted Odds Ratio for loss of libido against TCRE (adjusted for age and HRT use): Some - Hysterectomy = 1.25 (1.13 to 1.39), BOS = 1.32 (1.16 to 1.51), p = 0.254 Severe - Hysterectomy = 1.29 (1.16 to 1.44), BOS = 1.68 (1.48 to 1.92), p < 0.001 Extreme - hysterectomy = 1.42 (1.22 to 1.65), BOS = 1.80 (1.51 to 2.14), p < 0.001  Adjusted Odds Ratio for difficulty of sexual arousal against TCRE (adjusted for age and HRT use): Some - Hysterectomy = 1.16 (1.05 to 1.29), BOS = 1.27 (1.11 to 1.44), p = 0.068 Severe - Hysterectomy = 1.28 (1.15 to 1.44), BOS = 1.79 (1.56 to 2.05), p < 0.001 Extreme - hysterectomy = 1.35 (1.15 to 1.58), BOS = 1.82 (1.52 to 2.19), p < 0.001.  Adjusted Odds Ratio for vaginal dryness against TCRE (adjusted for age and HRT use): Some - Hysterectomy = 1.28 (1.15 to 1.41), BOS = 1.17 (1.03 to 1.33), p = 0.057 Severe - Hysterectomy = 1.55 (1.36 to 1.78), BOS = 1.43 (1.22 to 1.69), p = 0.170 Extreme - hysterectomy = 1.50 (1.19 to 1.88), BOS = 1.69 (1.29 to 2.22), p = 0.195.	Funding Source: Department of Health & 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 BOS at the time of hysterectomy. :

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
McPherson 2004 520	Study Type: Case series  Evidence Level: 3	Women undergoing abdominal hysterectomy (67% AH, 30% VH, 3% LAVH)  72% received antibiotic prophylactic  58% carried by consultants Hysterectomies by non-consultants (34% supervised) <2% by un-supervised SHO  152/194 consultants performed LHs 11% LH by non-consultants (65% unsupervised, 3% supervised)	37295 cases of hysterectomies	Median age: 45 years (12-95) 46% DUB 19% fibroids 19% prolapse 5% endometriosis/adenomyosis 3% pelvic mass 8% misc  Country: UK	Peri- and post-op complications, association between these complications and age, comorbidity, indications, pre-op use of antibiotics, grade of surgeon, grade of supervisors and types of hysterectomy	14 deaths (0.38/1000)(No death in LH group)  Operative complications in: 3% overall Age 20-39 (NS) 40-49 (Reference category) 50->=60 (NS)  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)  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)  History of serious illness No (ref category) Yes (4.8% vs. 3.4%, adjusted OR 1.47, 95%CI 1.18 to 1.82)  Method AH (ref category) VH (NS) LAVH (6.1% vs. 3.6%, adjusted OR 1.92, 95%CI 1.48 to 2.50)  Reduction in risk associated with increasing age in women with fibroids but not DUB	Funding Source: DOH BUPA  Study Summary: Younger women, with more 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 & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						<p>Post-op complications 1% overall Age 20-39 (NS) 40-49 (Reference category) 50-&gt;=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) Yes (NS)</p> <p>Operative complications No (ref category)</p>	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						Yes (adjusted OR 8.39, 95% CI 6.53 to 10.77)	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
McPherson 2005 <sup>386</sup>	Study Type: Prospective cohort  Evidence Level: 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	Odds Ratio of Urinary symptoms for hysterectomy compared to 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)	Funding Source: DoH & BUPA

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						<p>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)</p> <p>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)</p>	



Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Nathorst-Boos 1992 <sup>484</sup>	Study Type: Survey  Evidence Level: 3	Hysterectomy	678	<p>Women; aged &lt; 55; Hysterectomy for benign conditions.</p> <p>Indication: Leiomyoma = 78.9% Endometriosis = 10.8%</p> <p>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</p> <p>Country: Sweden</p>	Patient opinions on positive and negative aspects of hysterectomy	<p>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%</p> <p>Disadvantages: Hot flushes = 6.1% Ugly scar = 3.4% Dry sore mucous membranes = 4.0% Weight gain = 3.5% Incontinence = 2.9%</p>	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Panici 2005 <sup>59B</sup>	Study Type: case series  Evidence Level: 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 mins (34-88) 0 intra-operative complication 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

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Parkar 2004 <sup>599</sup>	Study Type: Retrospective case analysis  Evidence Level: 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) Parity: 0 ->5 (92% </+ parity 3_  Country: Kenya	Operation time Hospital stay Intra- and post-op complications	Operation time 45-245 mins (58% between 91 -120 mins) 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

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Riza 1997 <sup>600</sup>	Study Type: Case-series  Evidence Level: 3	LAVH	209 (1090 records available for review)	<p>Women; LAVH for benign condition</p> <p>Endometriosis = 52.2%  Leiomyomas = 30.2%  Endometriosis &amp; Leiomyomas = 8.8%  Menorrhagia = 5%  Adenocarcinoma = 1.1%  Squamous = 1.1%  Ca in situ = 0.5%  Other = 1.1%</p> <p>Average age = 41.3  Gravidity = 2.7  Weight (lbs) = 159.6  Uterine weight (g) = 178.6</p> <p>Country: USA</p>	Operative time; operative blood loss; complications; Length of stay	<p>Average operative time = 117.3 minutes  Postoperative length of stay = 0.7 days  Average intra-operative blood loss = 242.3ml</p> <p>Complications = Fever = 6, transfusion = 3, UTI = 2, Vaginal cuff cellulitis = 1</p>	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Schofield 1991 <sup>601</sup>	Study Type: retrospective survey by telephone interview and postal questionnaire  Evidence Level: 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 & 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

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Takamizawa 1999 <sup>602</sup>	Study Type: Case-series  Evidence Level: 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 <sup>603</sup>	Study Type: Retrospective chart audit  Evidence Level: 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  Rate of concurrent oophorectomy	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)	Funding Source: not stated  Study Summary: Significant reduction in LOS with the VH when compared with AH

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
				<p>Indications:  26.4% abnormal uterine bleeding  16% leiomyomas  11.4% pelvic mass, neoplasm or cyst  11% endometrial/ovarian /cervical cancer  10.6% Chronic dysmenorrhoea  8.9% endometrial hyperplasia, dysplasia or family history of cancer  7.6% pelvic prolapse/incontinence  5.1% endometriosis  2.9% chronic salpingitis, hydro- and pyo-salpinx</p> <p>16% had diagnosis of cancer pre-op  20% had diagnosis of cancer post-op</p> <p>Country: Canada</p>		<p>35% in women with dysfunctional uterine bleeding</p> <p>71.4% in women with leiomyomas</p> <p>AH vs. VH:  Age - NS  BMI - 29.2 (7.8) vs. 25.8 (4.6) (p&lt;0.01)  LOS in days - 5.2 (4.8) vs. 3.0 (1.6) (p&lt;0.01)  Length of surgery in minutes - 106.3 (48.7) vs. 84.7 (34.6)  Infection - NS  Readmission - NS  Excessive bleeding or complication - NS</p> <p>Logistic regression:  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&lt;0.001); 1.7 times more likely to have VH with each additional child</p>	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Varol 2001 <sup>522</sup>	Study Type: retrospective review of medical records  Evidence Level: 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	VH: Mean age: 57 years Mean parity: 3.1 6.5% Leiomyomas 19.5% DUB 0% endometriosis 1.7% adenomyosis 67.3% uterovaginal prolapse 2.6% cervical dysplasia 0% adenal mass 0% PID 0.2% endometrial hyperplasia 0.9% pelvic pain 1.3% others  AH: Mean age: 45.3 years Mean parity: 2.5 34% Leiomyomas 26.5% DUB 5.4% endometriosis 11% adenomyosis 0.4% uterovaginal prolapse 4.9% cervical dysplasia 7.6% adenal mass 1.7% PID 4.3% endometrial hyperplasia 2.6% pelvic pain 1.5% others  LAVH: Mean age: 44.4 years Mean parity: 1.8	Post-op complications and injuries to adjacent organs	Post-op complications: Mortality rate: 1.5/1000 women  VH: 27.3% overall complication rates 10.2% febrile morbidity 9.7% infections 5% haemorrhage requiring transfusion 1% unintended major surgical procedure 0% life threatening event 2.4% re-hospitalisation 3.4% minor complications (retention, incontinence, ileus etc) 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)  AH: 44% overall complication rates 15.9% febrile morbidity 12.6% infections 6.5% haemorrhage requiring transfusion 3% unintended major surgical procedure 0.4% life threatening event 2% re-hospitalisation 14.4% minor complications (retention, incontinence, ileus etc) Injuries to adjacent organs (1-2% bladder, 0.1-0.5% ureter, 0.1-0.5% bowel, 0.1-0.2% vesicovaginal fistula)  LAVH: 22.2% overall complication rates 5.5% febrile morbidity 0% infections	Funding Source: Victoria Medical Foundation  Study Summary: Higher complication in AH than VH



Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
				25% leiomyomas 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% app		5.5% haemorrhage requiring transfusion 2.8% unintended major surgical procedure 0% life threatening event 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)	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Walker 2006 <sup>6U4</sup>	Study Type:  Evidence Level: 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	<p>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</p> <p>164 women were pre-menopausal at time of treatment</p> <p>Vaginal discharge: 83 women complained of vaginal discharge post-treatment.</p> <p>Sexual function: Improved = 31 Same = 64 Worse = 12</p> <p>Subsequent treatment for fibroids: 28 (16%) had further treatment.</p> <p>Satisfaction with UAE: Very satisfied = 104 Satisfied = 48 Dissatisfied = 5 Very dissatisfied = 2</p> <p>Quality of life: Better = 146 Not improved = 8</p>	Funding Source: Not stated

## Chapter 13 – Oophorectomy at time of hysterectomy

### Oophorectomy undertaken at time of hysterectomy – Comparative studies

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Ballard 1996 539	Study Type: Chart review  Evidence level: 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	<p>There was not statistical difference between groups on any of the outcome measures.</p> <p>Only difference was age of groups (66.4 for BOS vs. 71.1 or non-BOS)</p> <p>Of the 61 women where ovaries were not removed:</p> <p>In 48 cases women wanted BOS, but ovaries were found to be normal or could not be removed vaginal.</p> <p>In 12 cases women opted not to have BOS.</p> <p>In 1 case women had already had BOS.</p>	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Davies 1996  540	Study Type: Prospective cohort  Evidence level: 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 (mins) 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

## Chapter 13 – Oophorectomy at time of hysterectomy

### Oophorectomy undertaken at time of hysterectomy – Non-comparative studies

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Bhavnani 2003 541	Study Type: Qualitative interviews  Evidence Level: 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</p>	Funding Source: NHS R&D programme

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						<p>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>	
Fry 2001 256	Study Type: Survey  Evidence Level: 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: Reducing risk of ovarian cancer, reducing cancer worry, Age, worries about effectiveness of screening, partner's attitude, loss of periods. All at <math>p &lt; 0.05</math></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 538	Study Type: Interviews  Evidence Level: 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> <ul style="list-style-type: none"> <li>-Oophorectomy will lead to menopause</li> <li>-What menopausal symptoms to expect</li> <li>-The need to use HRT</li> <li>-Risks and benefits of HRT</li> <li>-Financial cost of long-term prescriptions</li> <li>-Type of surgery being undertaken</li> <li>-Convalescence</li> <li>-Inherited genetic mutations</li> </ul>	Funding Source: Not stated

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Parker 2005 <sup>605</sup>	Study Type: Modelling  Evidence Level: 3	Oophorectomy or no oophorectomy; without or with oestrogen 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	Ovarian conservation and no ET vs. oophorectomy and no ET vs. ovarian conservation and ET vs. oophorectomy and ET.  Proportion of women aged 50 to 54 alive at age 80 (%): Ovarian conservation and no ET = 62.46 Oophorectomy and no ET = 53.88 Ovarian conservation and ET = 62.75 Oophorectomy and ET = 62.15	Funding Source: No stated  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.
Wagner 2000 <sup>537</sup>	Study Type: Survey  Evidence Level: 3	Opinions on prophylactic oophorectomy and/or mastectomy	138 individuals in 35 families	Women; BRCA1 or BRCA2 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 favour of surgery.	Women's views about oophorectomy (both affected and non-affected carriers) agree vs. disagree: Willingness to undergo surgery - 30 vs. 0; attitude to surgery 15 vs. 14; surveillance vs. surgery - 25 vs. 4 feelings associated with surgery anxiety = 15 vs. 8 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	Funding Source: Not stated

## Chapter 14 – Competencies

### Surgical Competencies in HMB

Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
Arndt 1995 547	Study Type: Case-series  Evidence level: 2+	2220 Total abdominal hysterectomies; total cholecystectomy = 4370; transurethral prostatectomy = 2851; Intervertebral disc excision = 1764.	Population characteristics: 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	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.  Effect of surgeon volume on length of stay: beta-coefficient = 0.021, T-statistic = 2.98 (P<0.05). Length of stay more influenced by age and severity  All other procedures show stronger volume outcome relationships. Total cholecystectomy: beta-coef = -0.128 and t-statistic = 20.38; transurethral prostatectomy - beta-coef = -0.49 and t-statistic = 8.13; Intervertebral disc excision - beta-coef = -0.091 and t-statistic =	Funding Source: Not stated



Bibliographic Information	Study Type & Evidence Level	Number of Patients	Patient characteristics	Intervention & Comparison	Follow-up	Outcome measures	Effect Size	Source of funding & additional comments
							20.48.	

## Chapter 14 – Competencies

### Surgical Competencies in HMB

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Abramovich 1995 <sup>543</sup>	Study Type: Audit  Evidence Level:	Endometrial ablation	978	Women; undergone endometrial ablation  Country: UK	Complication rates; satisfaction levels	Operative complications: Fluid overload = 61 Uterine perforation = 11 Excessive bleeding = 35 Immediate surgery = 12 Death = 1  Satisfaction at 12 months Very satisfied = 283 (53%) Satisfied = 167 (31%) Dissatisfied = 65 (12%) Very dissatisfied = 22 (4%)  Further treatment for failed EA by 24 months: Repeat ablation = 84 Hysterectomy = 73 Drug treatment = 107 HRT = 60  No association between operator experience and outcomes.	Funding Source: Clinical Response & Audit Group : .
Altgassen 2004 <sup>548</sup>	Study Type: Case-series  Evidence Level: 3	Laparoscopic-assisted vaginal hysterectomy	929 patients - 33 surgeons	Laparoscopic-assisted vaginal hysterectomy  Split into 3 groups:	Volume-outcome assessment	Change in duration, intraoperative complications and postoperative complications with experience: 1 to 10 (n=273) - 145.8 mins,	Funding Source: Not stated .

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
				<p>O, A, B</p> <p>O = surgeons doing fewer than 30 procedures A = Procedures 1 to 30 for surgeons doing more than 30 B = Procedures &gt;30 for surgeons doing more than 30 procedures.</p> <p>Country: Germany</p>		<p>7, 22</p> <p>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 (m=98) - 117.3, 0, 8 &gt;100 (n = 46) - 120.8, 0, 0</p> <p>Analysis showed reduction in complication rates ater 30 procedures.</p> <p>Group O (&lt;30 procedures): Intraoperative compications = 5 (1.9%) Postopative complications = 17 (6.5%)</p> <p>Group A (Procedures 1 to 30 in surgeons undertaking &gt;30): Intraoperativecomplications = 10 (4.2%) Postopative complications = 31 (12.9%)</p> <p>Group B (Procedures &gt;30 in surgeons undertaking &gt;30): Intraoperative Complications = 2 (0.5%) Postopative complications = 30 (7.0%)</p> <p>Significant difference between A and B, and between A and O. Not difference between O and B.</p>	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
Luft 1987 <sup>549</sup>	Study Type: Evidence Level: 3	Volume-outcome relationship	20249	Country:		actual versus 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 <sup>542</sup>	Study Type: Audit Evidence Level: 3	Endometrial ablation	18641 cases	Women; undergone endometrial ablation Country: UK	Complications rates; Operator experience	<p>Peri-operative complications:</p> <p>Loop &amp; ball = 171 (4.20%)  Loop alone = 229 (6.40%)  Laser = 46 (2.70%)  Ball alone = 13 (2.10%)  Total = 474 (4.44%)</p> <p>Intra-operative emergency surgical procedures.</p> <p>Loop &amp; ball = 50 (1.36%)  Loop alone = 69 (2.39%)  Laser = 6 (0.34%)  Ball alone = 6 (1.11%)  Total = 135 (1.26%)</p> <p>Immedaite complication by opertaor experience:</p> <p>&lt;100 = 107 (8.1%)  101-200= 26 (4.0%)  201-300 = 36 (5.6%)  301-400 = 9 (4.1%)  401-500 = 12 (5.0%)  &gt;500 = 7 (4.8%)  p &lt; 0.005 for trend</p> <p>Uterine perforations by experience</p> <p>&lt;100 = 53 (4.0%)  101-200 = 4 (0.6%)  201-300 = 11 (1.7%)  301-400 = 3 (1.4%)  401-500 = 2 (0.8%)  &gt;500 = 1 (0.7%)  p &lt; 0.00005)</p>	

Bibliographic Information	Study Type & Evidence Level	Aim of Study	Number of Patients	Population Characteristics	Outcomes	Results	Study Summary
						Operative haemorrhage by experience <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 > 0.040 for trend	
Overton 1995 <sup>606</sup>	Study Type: Audit/Survey  Evidence Level: 3	Endometrial ablation	7426	endometrial ablation.  Part of MISTLETOE survey  Country: UK	Training standards of those performing endometrial ablation	Training standards for TCRE: 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.  Training standards for Laser ablation: 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.	Funding Source: Not stated
Roos 1986 <sup>550</sup>	Study Type:  Evidence Level: 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)	

<b>Bibliographic Information</b>	<b>Study Type &amp; Evidence Level</b>	<b>Aim of Study</b>	<b>Number of Patients</b>	<b>Population Characteristics</b>	<b>Outcomes</b>	<b>Results</b>	<b>Study Summary</b>
Spies 2001 <sup>544</sup>	Study Type: Training guideline  Evidence Level: 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 <sup>546</sup>	Study Type: Consensus statement  Evidence Level: 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