National Institute for Health and Care Excellence

Draft

Heavy menstrual bleeding (update)

Evidence tables

NICE guideline TBC

Evidence reviews

August 2017

Draft for Consultation

These evidence reviews were developed by National Guideline Alliance

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive. All NICE guidance is subject to regular review and may be updated or withdrawn.

ISBN:

Contents

Diagnosis of heavy menstrual bleeding

What is the diagnostic accuracy of ultrasound and hysteroscopy for investigation of women presenting with heavy menstrual bleeding?

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>Full citation

Dasgupta, S., Chakraborty, B., Karim, R., Aich, R. K., Mitra, P. K., Ghosh, T. K., Abnormal uterine bleeding in peri-menopausal age: Diagnostic options and</td>
<td>Sample size

n=274

Only 252 patients analysed, 4 patients refused to undergo invasive procedure, 3 patients didn't allow hysteroscopy and D&C report showed inadequate sample in 9 patients. Ovarian neoplasm was detected in 6 patients during</td>
<td>Tests

Index test

2D transvaginal ultrasound scan (2D-TVUS)

Reference standard

Histopathology (hysteroscopy</td>
<td>Methods

After thorough history taking, clinical examination and exclusion of cervical malignancy by vaginal speculum & cervical Pap smear examination, informed written consent was taken from every eligible patient. Transvaginal ultrasonography was done followed by SIS in the same sitting. Endometrial cavity was examined from internal Os to fundus in both saggital and coronal planes. On the following day, hysteroscopy guidedtargeted biopsy followed by D & C was</td>
<td>Results

2D-TVUS versus histopathology (hysteroscopy-guided biopsy)

a) Polyp
<table>
<tr><td></td><td>Confirmed polyp</td><td>No polyp</td><td>Total</td></tr>
<tr><td>Polyp in index test</td><td>8*</td><td>11*</td><td>19</td></tr>
<tr><td>No polyp in index test</td><td>23*</td><td>210*</td><td>233</td></tr>
<tr><td>Total</td><td>31</td><td>221</td><td>252</td></tr>
</table>
Sensitivity 25% (95% CI 11.9%-44.6%*)

Specificity 95.2% (95% CI 91.3%-97.5%*)</td>
<td>Limitations

QUADAS-2 a quality assessment tool for diagnostic accuracy studies:

Patient Selection

A. Risk of Bias

Was a consecutive or random sample of patients enrolled? Unclear (not reported)

Was a case-control design avoided? Yes

Did the study avoid inappropriate exclusions? Yes</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>accuracy, Journal of Obstetrics and Gynecology of India, 61, 189-194, 2011

Ref Id

510607

Country/ies where the study was carried out

India

Study type

Prospective cohort study

Aim of the study</td>
<td>the investigation. These 22 patients were excluded from the result analysis.

Characteristics

Mean age of the study population was 46.2 years.

88.5% of the patients were multipara and 92% had history of normal delivery.

38.89% Pathological Endometrial abnormalities:

-4.76% Endometritis</td>
<td>guided biopsy)</td>
<td>done by different gynecologists. Each operator was unaware about the findings of the previous operators. All the tissue samples were examined by competent pathologists and the findings were recorded as follows:

Transvaginal ultrasound & saline infusion sonography: (Philips, image point-7.5 MHz endocavitary probe)

Endometrial thickness – Thickest part between the basal layers of both anterior and posterior uterine walls. Texture differentiation - Homogenous, heterogeneous and cystic.

Polyp - Intrauterine local overgrowth, hyper echoic</td>
<td>Positive likelihood ratio 5.18 (95% CI 2.26-11.58*)

Negative likelihood ratio 0.78 (95% CI 0.63-0.96*)

Prevalence of polyps 12.3%

b) Fibroids
<table>
<tr><th></th><th>Confirmed fibroids</th><th>No fibroids</th><th>Total</th></tr>
<tr><td>Fibroids in index test</td><td>30*</td><td>5*</td><td>35</td></tr>
<tr><td>No fibroids in index test</td><td>16*</td><td>201*</td><td>217</td></tr>
<tr><td>Total</td><td>46</td><td>206</td><td>252</td></tr>
</table>
Sensitivity 65.7% (95% CI 49.8%-78.7%*)

Specificity 97.4% (95% CI 94.4%-99.2%*)

Positive likelihood ratio 25.3 (95% CI 11.02-65.51*)

Negative likelihood ratio 0.35 (95% CI 0.24-0.53*)</td>
<td>Could the selection of patients have introduced bias? Unclear risk

B. Concerns regarding applicability:

The proportion of included patients with HMB is unclear. All included women had abnormal uterine bleeding but not specified further. The majority of women for a low socio-economic class where obesity and hypertension are rare.

Are there concerns that the included patients and setting do not match the review question? High concern</td>
</tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
Diagnostic accuracy of transvaginal sonography, saline infusion sonography and dilatation and curettage were compared with hysteroscopic guided biopsy to determine the etiology. **Study dates** September	-13.49% Simple Hyperplasia -7.14% Cystic Adenomatous hyperplasia -5.15% Atypical hyperplasia -12.30% Polyp -18.25% Fibroid **Inclusion Criteria** Patients belonging to the age group 40-50 years with AUB of at least 3 months duration **Exclusion Criteria** 1) Uterus >12 weeks size		relative to myometrium but echogenicity similar to endometrium, connected to endometrial wall by a stalk or forms an acute angle with the underlying endometrium. Fibroid- Heterogeneous echo texture, hypo echoic relative to myometrium with a broad base or forms an obtuse or right angle with the endometrial wall. Abnormal / pathological TVUS or SIS – double layered endometrial thickness >=5mm or presence of polyp / fibroid. Hysteroscopy guided biopsy: (rigid 30-degree hysteroscope and diagnostic sheath of 5mm diameter, Storz Endoscopy)	Prevalence of fibroids 18.25% *Calculated by the NGA technical team Numbers for "abnormal uterine pathology" (AUP) also reported, however, the definition of AUP not defined clearly, however, does not seem to mean 'any abnormal finding'. Due to unclarity it was not included in the review.	Index Test A. Risk of Bias Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified? Yes Could the conduct or interpretation of the index test have introduced bias? Low risk B. Concerns regarding applicability: The experience of the gynaecologist not reported Are there concerns

Study details	Participants	Tests	Methods	Outcomes and results	Comments
2005-January 2008 **Source of funding** Not reported	2) Hormone therapy within the last 6 months 3) Previous abnormal endometrial biopsy 4) +ve pregnancy test 5) cervical pathology on speculum examination 6) abnormal cervical pap smear 7) history/evidence suggestive of active pelvic infection		Hyperplasia - Thick hyper-vascular friable mucosa, mammilated or polypoid in appearance, further classified as simple or atypical by the pathologists. Polyp - Soft intra-cavitary formation, which was easily mobilized and covered by mucosa with endometrial gland and no distended vascular network. Fibroid - Firm intra-cavitary formation with thin endometrial lining and superficial large blood vessels. Endometritis - Irregular proliferation of glands and the presence of chronic inflammatory cells e.g. plasma cells, macrophages, and lymphocyte in the		that the index test, its conduct, or interpretation differ from the review question? Unclear concern Reference Standard A. Risk of Bias Is the reference standards likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index tests? Yes Could the reference standard, its conduct, or its interpretation have introduced bias? Low risk B. Concerns

Study details	Participants	Tests	Methods	Outcomes and results	Comments
			endometrial stroma. Dilatation & Curettage: Polyp- soft mobile intracavitary mass with narrow base and hyperplastic endometrium. Fibroid- firm immobile mass with broad base distorting the shape of endometrial cavity. Abnormal/ pathological D & C - presence of hyperplasia, polyp or fibroid.		regarding applicability Are there concerns that the target condition as defined by the reference standard does not match the question? Low concern Flow and Timing A. Risk of Bias Was there an appropriate interval between index test and reference standard? Yes Did all patients receive the same reference standard? Yes Were all patients included in the analysis? No, 22/274 dropped out but all were explained.

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>Could the patient flow have introduced bias? Unclear risk

Other information</td></tr>
<tr><td>Full citation

Alborzi, S., Parsanezhad, M. E., Mahmoodian, N., Alborzi, S., Alborzi, M., Sonohysterography versus transvaginal sonography for screening of patients with</td><td>Sample size

N=81

Characteristics

Not reported.

Inclusion Criteria

Abnormal uterine bleeding.

Exclusion Criteria

Not reported.</td><td>Tests

Index test

2D transvaginal ultrasound scan (2D-TVUS)

Reference standard

Histopathological specime</td><td>Methods

Ultrasound

Transvaginal ultrasound (HS-2000, Honda-el., Toyohashi, Japan) was performed using a 7.5 MHz transvaginal transducer by the first author. The midline echo was considered to be normal when a straight endometrial lining with well defined margins and without echo dense foci was found.

Polyps were defined as echogenic masses with</td><td>Results

2D-TVUS versus histopathology (hysteroscopy-guided biopsies)

a) Polyps
<table><tr><td></td><td>Confirmed polyp</td><td>No polyp</td><td>Total</td></tr><tr><td>Polyp in index test</td><td>7*</td><td>3*</td><td>10</td></tr><tr><td>No polyp in index test</td><td>25*</td><td>46*</td><td>71</td></tr><tr><td>Total</td><td>32</td><td>49</td><td>81</td></tr></table>
Sensitivity 21.9% (95% CI 9%-40%)

Specificity 93.8% (95% CI 83%-99%)</td><td>Limitations

QUADAS-2 a quality assessment tool for diagnostic accuracy studies:

Patient Selection

A. Risk of Bias

Was a consecutive or random sample of patients enrolled? Unclear. (Not reported.)

Was a case-control design avoided? Yes

Did the study avoid inappropriate</td></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>abnormal uterine bleeding, International Journal of Gynaecology & Obstetrics, 96, 20-3, 2007

Ref Id

400994

Country/ies where the study was carried out

Iran

Study type

Prospective cohort</td>
<td></td>
<td>n from hysteroscopy</td>
<td>fairly homogenous texture, while submucosal myoma had a non homogenous texture. Location of myoma and its relation to endometrium and myometrium was detected.

Histopathology

During hysteroscopy the uterine cavity was evaluated and findings were recorded. All myomas and polyps were removed by a resectoscope (Karl Storz GmbH, Tuttlingen, Germany). In all patients a relatively deep specimen from the anterior and posterior wall of the uterus was resected and sent to a pathologist for the diagnosis of adenomyosis.</td>
<td>Positive likelihood ratio* 3.5 (95% CI 1.00-12.81*)

Negative likelihood ratio* 0.8 (95% CI 0.68-1.01*)

Prevalence of polyps 39.5%*

b) Myomas
<table>
<tr><th></th><th>Confirmed myoma</th><th>No myoma</th><th>Total</th></tr>
<tr><td>Myoma in index test</td><td>21*</td><td>2*</td><td>22</td></tr>
<tr><td>No myoma in index test</td><td>2*</td><td>56*</td><td>59</td></tr>
<tr><td>Total</td><td>23</td><td>58</td><td>81</td></tr>
</table>
Sensitivity 90.9%# (95% CI 72%-99%)

Specificity 96.6% (95% CI 88%-100%)

Positive likelihood ratio* 26.7 (95% CI 6.74-103.93*)

Negative likelihood ratio* 0.09 (95% CI 0.02-0.34*)</td>
<td>exclusions? Unclear. (No exclusions were reported. Inclusion criteria was not clearly defined either.)

Could the selection of patients have introduced bias? Unclear risk.

B. Concerns regarding applicability:

The proportion of included patients with HMB is unclear. All included women had abnormal uterine bleeding but not specified further.

Are there concerns that the included patients and setting do not match the review question?</td>
</tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
study **Aim of the study** To compare the accuracy of saline infusion sonohysterography (SIS) with transvaginal ultrasound scan (TVUS) for the screening of causes of abnormal uterine bleeding in outpatients. **Study**				Prevalence of myoma 28.4%* *Calculated by the NGA technical team. #Discrepancy in the reporting of sensitivity in the paper and according to the calculations made by the NGA technical team using the 2x2 reported in the paper. The sensitivity for TVUS detecting myomas according to the 2x2 table is 91.3%	High concern. Index Test A. Risk of Bias Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified? Yes. (Diagnostic criteria for polyp and myoma in the index test was defined.) Could the conduct or interpretation of the index test have introduced bias? Low risk. B. Concerns

Study details	Participants	Tests	Methods	Outcomes and results	Comments
dates June 2004 to November 2005. **Source of funding** Not reported					regarding applicability: The paper did not report who interpreted the index test or what was the level of experience of the person(s). Are there concerns that the index test, its conduct, or interpretation differ from the review question? Unclear concern. Reference Standard A. Risk of Bias Is the reference standards likely to correctly classify the target condition? Yes Were the reference standard results

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					interpreted without knowledge of the results of the index tests? Yes Could the reference standard, its conduct, or its interpretation have introduced bias? Low risk. B. Concerns regarding applicability Are there concerns that the target condition as defined by the reference standard does not match the question? Low concern. Flow and Timing A. Risk of Bias

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					Was there an appropriate interval between index test and reference standard? Yes Did all patients receive the same reference standard? Yes. Were all patients included in the analysis? Yes. Could the patient flow have introduced bias? Low risk.

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>Other information

Inclusion and exclusion criteria were not reported clearly.
Characteristics of the included patients were not reported.</td></tr>
<tr><td>Full citation

Abd Elkhalek, Y. I., Kamel, O. F., El-Sabaa, H., Comparison of 3 dimensional sonohysterography and hysterosco</td><td>Sample size

n=50

Characteristics

Age range 24-45 years

20% nulliparous

80% multiparous

15 patients were diabetic, 18 patients were</td><td>Tests

Index test

Hysteroscopy (under general anaesthesia)

Reference standard</td><td>Methods

Hysteroscopy was done using a panoramic hysteroscopy length of 25cm, diameter of 4mm, having an outer sheeth about 5.5mm and a fiber optic lens of 30 degrees.

The proceedure was done in dorsal lithotomy position after evacuation of the urinary bladder. The uterine cavity was systematically explored by the hysteroscopy in order</td><td>Results

Hysteroscopy (under GA) versus histopathology (curettage of endometrium)

a) Endometrial polyp or submucosal fibroid
<table><tr><td></td><td>Confirmed polyp or fibroid</td><td>No polyp or fibroid</td><td>Total</td></tr><tr><td>Polyp or fibroid in index test</td><td>28</td><td>0</td><td>28</td></tr><tr><td>No polyp or fibroid in index test</td><td>4</td><td>18</td><td>22</td></tr></table></td><td>Limitations

QUADAS-2 a quality assessment tool for diagnostic accuracy studies:

Patient Selection

A. Risk of Bias

Was a consecutive or random sample of patients enrolled? Unknown (not reported)

Was a case-control</td></tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
py in Premenopausal women with abnormal uterine bleeding, Egyptian Journal of Radiology and Nuclear Medicine. (no pagination), 2016, Date of Publication, 2016 **Ref Id** 510879 **Country/ies where the study was carried**	hypertensive. 73% suffered from menorrhagia and 15% from menometrorrhagia and 12% from metorrhagia **Inclusion Criteria** Abnormal uterine bleeding in premenapausal women, along with normal endometrial lining on 2D transvaginal ultrasound. **Exclusion Criteria** Patients with	Histopathological specimen from curettage of endometrium	to identify the anomaly in the uterine walls and/or the right and left tubal ostia. The shape, size as well as the site of any pathology intrauterine were detected, and histopathology was done by curettage of the endometrium. The histopathological results were compared individually with the 3D-SIS as well as the hysteroscopy results. All cases were done under general anesthesia.	Total 32 18 50 Sensitivity 87.5% (95% CI 71.0%-96.5%*) Specificity 100% (95% CI 81.5%-100%*) Positive likelihood ratio* Inf Negative likelihood ratio* 0.12 (95% CI 0.05-0.31*) Prevalence of polyps or fibroids 64% *Calculated by the NGA technical team	design avoided? Yes Did the study avoid inappropriate exclusions? Yes Could the selection of patients have introduced bias? Unclear risk B. Concerns regarding applicability: All women with abnormal uterine bleeding, however, the proportion of women with HMB not reported; all women already undergone TVUS with no abnormal findings. Are there concerns that the included patients and setting do not match the review question? High concern

Study details	Participants	Tests	Methods	Outcomes and results	Comments
out Egypt **Study type** Prospective cohort study **Aim of the study** Compare the diagnostic accuracy of 3D sonohysterography and hysteroscopy in detection of intracavitary uterine abnormalities in	bleeding secondary to obvious pelvic infection, cervical and adnexal pathologies were excluded.				Index Test A. Risk of Bias Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified? Unclear (diagnostic criteria not reported for hysteroscopy only for SIS) Could the conduct or interpretation of the index test have introduced bias? Unclear risk B. Concerns regarding applicability: The paper did not report

Study details	Participants	Tests	Methods	Outcomes and results	Comments
premenapausal women with abnormal uterine bleeding. **Study dates** December 2010-October 2014 **Source of funding** None declared					who interpreted the index test or what was the level of experience of the person(s). Are there concerns that the index test, its conduct, or interpretation differ from the review question? Unclear concern Reference Standard A. Risk of Bias Is the reference standards likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					Could the reference standard, its conduct, or its interpretation have introduced bias? Unclear risk B. Concerns regarding applicability Are there concerns that the target condition as defined by the reference standard does not match the question? Low concern Flow and Timing A. Risk of Bias Was there an appropriate interval between index test and reference standard? Yes Did all patients receive the same

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>reference standard? Yes

Were all patients included in the analysis? Yes

Could the patient flow have introduced bias? Low risk

Other information</td></tr>
<tr><td>Full citation

Abe, M., Ogawa, H., Ayhan, A., The use of non-three-layer ultrasound in biopsy recommendation for premenop</td><td>Sample size

n=213

Characteristics

Mean age of women 39 years (38.0 + 7.7), with an age range of 17-49

147 (69%) had an endometrila pathological</td><td>Tests

Index test

2D transvaginal ultrasound scan (2D-TVUS)

Reference standard</td><td>Methods

2D-TVUS

Transvaginal ultrasonography was performed on all patients on the day of admission. If the admission was during the secretory phase of the cycle or the phase was unknown because of abnormal bleeding, the patient was requested to attend once again during</td><td>Results

2D-TVUS versus histopathology (simultaneuous vacuum aspiration biopsy)

a) Any endometrial abnormality
<table><tr><td></td><td>Confirmed abnormality</td><td>No abnormality</td><td>Total</td></tr><tr><td>Abnormality in index test</td><td>139</td><td>15</td><td>154</td></tr><tr><td>No abnormality in index test</td><td>8</td><td>51</td><td>59</td></tr></table></td><td>Limitations

QUADAS-2 a quality assessment tool for diagnostic accuracy studies:

Patient Selection

A. Risk of Bias

Was a consecutive or random sample of patients enrolled? Unclear (not reported)</td></tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
ausal women, Acta Obstetricia et Gynecologica Scandinavica, 87, 1155 **Ref Id** 510881 **Country/ies where the study was carried out** Japan **Study type** Retrospective cohort study	abnormality. 7 cases of endometrial carcinoma, 5 cases of hyperplasia with or without atypia, 4 cases of polyp with atypia, 106 cases of endometrial polyp, 4 cases of endometritis and 13 cases of cell cycle discrepancy. **Inclusion Criteria** Premenopausal status, age <50 years and the presenting symptom of abnormal bleeding. **Exclusion**	Histopathology (simultaneuous vacuum aspiration biopsy)	the proliferative phase of her cycle or after withdrawal bleeding induced by progestin or estrrgen/progestin, to repeat the transvaginal ultrasonography examination. Target conditions defined as 'abnormal endometrium' were endometrial carcinoma, endometrial hyperplasia with or without atypia, endometrial polyps including atypical polypoid adenomyoma and polyps with atypia, endometriosis and dysfunctional uterine bleeding. All transvaginal ultrasonography examinations were carried out by one of the authors using Sonovista-C 3000 and SSD 4000 ultrasound machines. For examinations conducted during the proliferative	<table><tr><td>Total</td><td>147</td><td>66</td><td>213</td></tr></table> Sensitivity 94.6% (95% CI 91%-98%) Specificity 77.2% (95% CI 67%-87%) Positive likelihood ratio 4.16 (95% CI 2.66-6.50) Negative likelihood ratio 0.07 (95% CI 0.04-0.14) Prevalence of any endometrial abnormality 69% *Calculated by the NGA technical team Further results stratified by cycle phase (proliferative and secretory) were reported by the authors but not considered relevant for this review was this was not defined in the protocol.	Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions? Unclear (Participants with indeterminate TVUS results were excluded.) Could the selection of patients have introduced bias? Unclear risk B. Concerns regarding applicability: The proportion of included patients with HMB is unclear. All included women had abnormal uterine bleeding but not specified further. Are there concerns

Study details	Participants	Tests	Methods	Outcomes and results	Comments
Aim of the study Evaluate the diagnostic accuracy of our defined abnormal transvaginal ultrasonographic criteria, based on echo patterns and line irregularities for selection of premenapausal patients with abnormal	**Criteria** Exclusion criteria were the presence of cervical polyps or neoplasm, the use of hormone replacement therapies and cases of transvaginal ultrasonography with indeterminate results		phase, a three-layer pattern of normal endometrium was defined as hypoechoic endometrium, lined by a triple-line appearance with bright lines of the central ad outer basalis layers. Accordingly, we have decided that an abnormal patter is of either diffuse or focal hyperechoic texture, regardless of a three-layer, three-layer-like, or non-laminar appearance, and linear (especially in the central line) irregularities. For patients in the secretory phase or unknown phase due to irregular bleeding, a normal endometrium phase was defined as <15mm, measured by double-layered thickness in the sagittal plane. As the triple line gradually		that the included patients and setting do not match the review question? High concern Index Test A. Risk of Bias Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified? Yes Could the conduct or interpretation of the index test have introduced bias? Low risk B. Concerns regarding applicability: Level of

Study details	Participants	Tests	Methods	Outcomes and results	Comments
uterine bleeding for endometrial biopsy, and to assess the proper timing for this procedure. **Study dates** January 2005-2007 **Source of funding** None declared			disappears and the endometrium becomes hyperechoic and thickens to between 10 and 14mm, the measurement of thickness is easy and reproducible, however, the evaluation for texture is difficult during the secretory phase. For that reason, an abnormal pattern was defined as >15 in our study without evaluating the texture. For each patient, the cyclic phase, endometrial thickness, presence of a three-layer pattern and presence of a focal or diffuse hyperechoic pattern were recorded, and the data were photographed. Histopathology Together with TVUS, a simultaneous vacuum aspiration biopsy was		experience of author who conducted the test not stated. Are there concerns that the index test, its conduct, or interpretation differ from the review question? Unclear concern Reference Standard A. Risk of Bias Is the reference standards likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index tests? Yes (examined and reviewed by 2 pathologists, where as investigations

Study details	Participants	Tests	Methods	Outcomes and results	Comments
			taken using suresample type aspiration device. The histopathologic results of endometrial biopsy served as the reference standard. All biopsies were histopathologically examined and reviewed by two pathologists, one of whom had special training in gynaecological pathology. The histopathologists were blinded to the results of the ultrasonography. The evaluation of all material from vacuum biopsy was based on multiple serial sections. Not only the presence or absence of malignancy, but also the dating and accuracy of diagnosis of the underlying disease causing abnormal uterine bleeding was attempted. Diagnosis of the polyp		were done by gynaecologists) Could the reference standard, its conduct, or its interpretation have introduced bias? Low risk B. Concerns regarding applicability Are there concerns that the target condition as defined by the reference standard does not match the question? Low concern Flow and Timing A. Risk of Bias Was there an appropriate interval between index test and reference standard? Yes Did all patients

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td>was based on the presence of spindle stroma, abnormal vascularisation patterns and glandular distortion. Dysfunctional uterine bleeding included anovulation and abnormal folliculogenesis and histologically characterized by specific histologic described elsewhere.</td><td></td><td>receive the same reference standard? Yes

Were all patients included in the analysis?Yes

Could the patient flow have introduced bias? Low risk

Other information</td></tr>
<tr><td>Full citation

Dasgupta, S., Sharma, P. P., Mukherjee, A., Ghosh, T. K., Ultrasound assessment of</td><td>Sample size

n=100

(Only 83 were analysed. 17 excluded - 3 refused to undergo transvaginal imaging, 5 women refused to undergo</td><td>Tests

Index test

2D transvaginal ultrasound scan (2D-TVUS)</td><td>Methods

Patients were selected from those attending the gynaecology outpatient department. After thorough history taking, clinical examination and haemoglobin estimation, those fulfilling the inclusion criteria were sent for a transvaginal ultrasound. All sonological</td><td>Results

2D-TVUS versus histopathology (hysteroscopy guided biopsy)

a) Any endometrial abnormality
<table><tr><td></td><td>Confirmed abnormality</td><td>No abnormality</td><td>Total</td></tr><tr><td>Any abnormality in index test</td><td>40</td><td>13</td><td>53</td></tr></table></td><td>Limitations

QUADAS-2 a quality assessment tool for diagnostic accuracy studies:

Patient Selection

A. Risk of Bias

Was a consecutive or random sample of patients enrolled?</td></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>endometrial cavity in perimenopausal women on oral progesterone for abnormal uterine bleeding: comparison of diagnostic accuracy of imaging with hysteroscopy-guided biopsy, The journal of obstetrics and gynaecology research, 37, 1575</td>
<td>hysteroscopy under local anaesthesia, in 3 women SIS produced inadequate images, and an adnexal mass was detected in 6 women during TVUS)

Characteristics

Age years: 46.7 (43.6-49.8) BMI: 23.2 (20.4-26.0)

Mean Parity: 1.77

History of caesarean section: 15

History of hormone use: 29

History of</td>
<td>Reference standard

Histopathology (hysteroscopy-guided biopsy)</td>
<td>evaluations were done by a consultant sonologist. The endometrial cavity was examined from the internal os to the fundus in both sagittal and coronal planes. On the following day the patient was admitted and a hysteroscopy followed by a guided biopsy from the endometrium or any endometrial lesion was performed by a consultant gynaecologist blinded to the findings of the imaging study.The ultrasound was performed with an image point-7.5MHz endocavity probe. Endometrial thickness was measured by measuring the thickest part between the basal layer of both anterior and posterior uterine walls. Hysteroscopy was done by a rigid 30 degree hysteroscope with a diagnostic sheath of 5mm</td>
<td>
<table>
<tr><td>No abnormality in index test</td><td>14</td><td>16</td><td>30</td></tr>
<tr><td>Total</td><td>54</td><td>29</td><td>83</td></tr>
</table>
Sensitivity 74% (95% CI 61%-84%)

Specificity 55% (95% CI 37%-71%)

Positive likelihood ratio 1.65 (95% CI 1.07-2.55)

Negative likelihood ratio 0.47 (95% CI 0.27-0.82)

Prevalence of any abnormality 65.1%

b) Polyp
<table>
<tr><td></td><td>Confirmed polyp</td><td>No polyp</td><td>Total</td></tr>
<tr><td>Polyp in index test</td><td>5</td><td>6</td><td>11</td></tr>
<tr><td>No polyp in index test</td><td>6</td><td>66</td><td>72</td></tr>
</table>
</td>
<td>Unclear (not reported)

Was a case-control design avoided? Yes

Did the study avoid inappropriate exclusions? Yes

Could the selection of patients have introduced bias? Unclear risk

B. Concerns regarding applicability:

The proportion of included patients with HMB is unclear. All included women had abnormal uterine bleeding but not specified further. The majority of women for a low socio-economic class. All patients were on oral</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>Ref Id
511120
Country/ies where the study was carried out
India
Study type
Prospective cohort study
Aim of the study
To investigate the effect of oral progesterone on the accuracy</td>
<td>diabetes: 15
History of hypothyroidism: 10
Clinically enlarged uterus: 17
Duration of hormone use: 26 days (+12)
Dose of hormone use:
Medroxyprogesterone (mg): 22.75 (+4.5)
Norethisterone (mg): 20.4 (+6.4)
Inclusion Criteria
Women belonging to the 40- to 55-year</td>
<td></td>
<td>diameter. Guided biopsy of abnormal endometrium or from any visible endometrial mass was taken and sent for histopathological examination. Comparison between the results of a test with the standard was done by defining normal and abnormal results for each as follows:
-Abnormal TVUS was defined as a double-layered endometrial thickness > 10mm or the presence of an endometrial polyp or submucosal fibroid
-Abnormal hysteroscopy and guided biopsy was defined as the presence of hyperplasia (simple or atypical), an endometrial polyp or submucosal fibroid and the presence of infective changes on</td>
<td>
<table>
<tr><td>Total</td><td>11</td><td>72</td><td>83</td></tr>
</table>
Sensitivity 45% (95% CI 21%-72%)
Specificity 92% (95% CI 83%-96%)
Positive likelihood ratio 5.45 (95% CI 0.76-7.8)
Negative likelihood ratio 0.6 (95% CI 0.34-1.02)
Prevalence of polyp 13.2%
c) Submucosal fibroid
<table>
<tr><td></td><td>Confirmed submucosal fibroid</td><td>No submucosal fibroid</td><td>Total</td></tr>
<tr><td>Submucosal fibroid in index test</td><td>8</td><td>8</td><td>16</td></tr>
<tr><td>No submucosal fibroid in index test</td><td>5</td><td>62</td><td>67</td></tr>
</table>
</td>
<td>hormones.
Are there concerns that the included patients and setting do not match the review question? High concerns
Index Test
A. Risk of Bias
Were the index test results interpreted without knowledge of the results of the reference standard? Yes
If a threshold was used, was it pre-specified? Yes
Could the conduct or interpretation of the index test have introduced bias? Low risk
B. Concerns</td>
</tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
of imaging studies performed to detect endometrial pathology in comparison to hysteroscopy-guided biopsy in perimenopausal women on progesterone treatment for abnormal uterine bleeding **Study dates** 1 July	age group (perimenopausal age) with a complaint of AUB and who had been on oral progesterone therapy for at least 10 days were included in the study. **Exclusion Criteria** Women with a uterus larger than 12 weeks gestation or a previous endometrial biopsy were excluded from the study. Women with a cervical lesion on speculum examination,		histopathology In cases where there was a simultaneous presence of hyperplasia along with an endometrial polyp or submucosal fibroid, the final diagnosis was decided according to the biopsy report. If the hyperplasia was benign, the final diagnosis was given as an endometrial polyp or submucosal fibroid, but if the hyperplasia was atypical then the diagnosis of atypical endometrial hyperplasia was given precedence.	<table><tr><td>Total</td><td>13</td><td>70</td><td>83</td></tr></table> Sensitivity 61% (95% CI 35%-82%) Specificity 88% (95% CI 79%-94%) Positive likelihood ratio 5.38 (95% CI 0.93-5.52) Negative likelihood ratio 0.43 (95% CI 0.22-0.87) Prevalence of submucosal fibroid 15.7%*# Sub population results of endometrial hyperplasia (28.9%), atypical hyperplasia (3.6%), and endometritis (2.4%) were not reported. *Calculated by the NGA technical team #Discrepancy in reporting of prevalence of submucosal fibroids and diagnostic accuracy of TVUS in detecting submucosal fibroids in the text and in the table in the paper. Text says 14 women had submucosal fibroids (16.8%) whereas table in the paper shows that 13 women had fibroids (15.7%), sensitivity, specificity, LR+ and LR-	regarding applicability: Are there concerns that the index test, its conduct, or interpretation differ from the review question? Low concern Reference Standard A. Risk of Bias Is the reference standards likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index tests? Yes Could the reference standard, its conduct, or its interpretation

Study details	Participants	Tests	Methods	Outcomes and results	Comments
2008-30 June 2009 **Source of funding** Not reported	abnormal pap smear, active pelvic infection, adnexal mass on clinical examination or during ultrasound scan, and a positive pregnancy test were excluded from the study.			reported in the paper correspond with the latter reporting.	have introduced bias? Low risk B. Concerns regarding applicability Are there concerns that the target condition as defined by the reference standard does not match the question? Low concern Flow and Timing A. Risk of Bias Was there an appropriate interval between index test and reference standard? Yes Did all patients receive the same reference standard? Yes Were all patients included in the

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>analysis? No, 17/100 dropped out but all were explained.

Could the patient flow have introduced bias? Unclear risk

Other information</td></tr>
<tr><td>Full citation

Erdem, M., Bilgin, U., Bozkurt, N., Erdem, A., Comparison of transvaginal ultrasonography and saline infusion sonohysterography in</td><td>Sample size

n=133

(only n=122 were analysed, no explanation of what happened to 11 patients no included)

Characteristics

Age range 44.5 + 7.3 years.</td><td>Tests

Index test

2D transvaginal ultrasound scan (2D-TVUS)

Reference Standard

Pathological</td><td>Methods

Both the TVUS ans SIS procedures were performed on all study participants blindly in the same session by the same investigator with a 5.0-MHz vaginal probe.

No prophylactic antibiotics or analgesics were used before the procedure.

After informing all the women about the procedure, their uterus and ovaries were</td><td>Results

2D-TVUS versus histopathology (D&C, hysteroscopy, or hysterectomy)

a) Endometrial polyp
<table><tr><td></td><td>Confirmed polyp</td><td>No polyp</td><td>Total</td></tr><tr><td>Polyp in index test</td><td>43*</td><td>6*</td><td>49</td></tr><tr><td>No polyp in index test</td><td>18*</td><td>55*</td><td>73</td></tr><tr><td>Total</td><td>61</td><td>61</td><td>122</td></tr></table></td><td>Limitations

QUADAS-2 a quality assessment tool for diagnostic accuracy studies:

Patient Selection

A. Risk of Bias

Was a consecutive or random sample of patients enrolled? Unclear (not reported)

Was a case-control design avoided? Yes</td></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>evaluating the endometrial cavity in pre- and postmenopausal women with abnormal uterine bleeding, Menopause, 14, 2007

Ref Id

511194

Country/ies where the study was carried out

Turkey

Study</td>
<td>78% of population premenopausal

22% of population postmenopausal

Inclusion Criteria

Premenopausal women older than 35 years of age who suffered from abnormal uterine bleeding symptoms, such as menorrhagia, metorrhagia, menometrorrhagia, and polymenorrhea.

Bleeding after a minimum of 1 year without any</td>
<td>specimen</td>
<td>evaluated longitudinally first with TVUS, and the findings were recorded. A measured by TVUS, endometrial thickness of 8mm or less in the proliferative phase, 14mm or less in the luteal phase or premenopausal women, and 5mm or less in the postmenopausal period, and symmetric and flat endometrium were considered normal. Otherwise, and endometrial thickness that measured more than the above-cited figures without showing any specific focal intracavitary lesions (i.e. endometrial polyps or sub-mucous fibroids) were considered abnormal. Lesions entirely within the uterine cavity and observed as hyperechogenic were considered abnormal. Lesions entirely within the</td>
<td>Sensitivity 70.49% (95% CI 57.4%-81.5%*)

Specificity 90.16% (95% CI 79.8%-96.3%*)

Positive likelihood ratio 7.17* (95% CI 3.30-15.59)

Negative likelihood ratio 0.33* (95% CI 0.22-0.49)

Prevalence of endometrial polyp 50%*

b) Submucosal fibroid
<table>
<tr><th></th><th>Confirmed submucosal fibroid</th><th>No submucousal fibroid</th><th>Total</th></tr>
<tr><td>Submucosal fibroid in index test</td><td>14</td><td>2</td><td>16</td></tr>
<tr><td>No submucosal fibroid in index test</td><td>5</td><td>101</td><td>106</td></tr>
</table>
</td>
<td>Did the study avoid inappropriate exclusions? Yes

Could the selection of patients have introduced bias? Unclear Risk

B. Concerns regarding applicability:

The proportion of included patients with HMB is unclear. All included women had abnormal uterine bleeding but not specified further. Furthermore, includes 22% of postmenopausal women

Are there concerns that the included patients and setting do not match the</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>type

Prospective cohort study

Aim of the study

Evaluate the accuracy of TVUS and SIS in the diagnosis of abnormal uterine bleeding by comparing them with invasive procedures such as hysteroscopy and hysterectomy.</td>
<td>menstrual bleeding was considered postmenopausal bleeding.

Exclusion Criteria

Women with bleeding due to pregnancy or pelvic infections were excluded by history, measurement of serum Beta-human chorionic gonadotrophin level, and vaginal and bimanual pelvic examination.</td>
<td></td>
<td>uterine cavity and observed as hyperechogenic were considered to be endometrial polyps, where as those related to the myometrium, reaching the cavity by pushing the endometrium and being isoechogenic or hypoechogenic when compared with myometrium, were considered to be uterine fibroids.

After the women were evaluated by TVUS and SIS, surgical proceedures were performed within 1 month. The pre-diagnosis achieved with pathological results of the specimens obtained with D&C, Hysteroscopy, or Hysterectomy.</td>
<td>
<table>
<tr><td>Total</td><td>19</td><td>103</td><td>122</td></tr>
</table>
Sensitivity 73.7% (95% CI 48.8%-90.9%*)

Specificity 98.1% (95% CI 93.2%-99.8%*)

Positive likelihood ratio 37.95 (95% CI 9.37-153.65*)

Negative likelihood ratio 0.27 (95% CI 0.13-0.57*)

Prevalence of submucosal fibroid 15.6%*

c) Abnormally endometrial thickness/endometerial hyperplasia
<table>
<tr><td></td><td>Confirmed endometrial hyperplasia</td><td>No confirmed endometrial hyperplasia</td><td>Total</td></tr>
<tr><td>Abnormal endometrial thicness in index test</td><td>3</td><td>9</td><td>12</td></tr>
</table>
</td>
<td>review question? High concern.

Index Test

A. Risk of Bias

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? Yes

Could the conduct or interpretation of the index test have introduced bias? Low risk

B. Concerns regarding applicability:

The paper did not report who interpreted the index</td>
</tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
Study dates July 1999 - July 2002 **Source of funding** Not reported.				<table><tr><td>No abnormal endometrial thickness in index test</td><td>1</td><td>109</td><td>110</td></tr><tr><td>Total</td><td>4</td><td>118</td><td>122</td></tr></table> Sensitivity 75.0% (95% CI 19.4%-99.4%*) Specificity 92.4% (95% CI 86.0%-96.5%*) Positive likelihood ratio 9.83 (95% CI 4.22-22.90*) Negative likelihood ratio 0.27 (95% CI 0.05-1.48*) Prevalence of endometrial hyperplasia 3.3% *Calculated by the NGA technical team	test or what was the level of experience of the person(s) Are there concerns that the index test, its conduct, or interpretation differ from the review question? Unclear concern Reference Standard A. Risk of Bias Is the reference standards likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear Could the reference standard, its conduct,

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					or its interpretation have introduced bias? Unclear risk B. Concerns regarding applicability Are there concerns that the target condition as defined by the reference standard does not match the question? Low concern Flow and Timing A. Risk of Bias Was there an appropriate interval between index test and reference standard? Unclear (1 month interval, possible disease progression?) Did all patients receive the same

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					reference standard? Yes, however different methods of obtaining the histology samples, a mix of D&C, hysteroscopy, and hysterectomy was used as reference standard. Were all patients included in the analysis? No, 11/133 dropped out, no explanations for the dropouts were given. Could the patient flow have introduced bias? High risk **Other information**
Full citation	**Sample size**	**Tests**	**Methods**	**Results**	**Limitations**

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>Fakhar,S., Mahmud,G., Validity of hysteroscopy and histopathology in patients with menstrual irregularity, Journal of Ayub Medical College, Abbottabad: JAMC, 22, 129-132, 2010

Ref Id

152826

Country/ies where the study was</td>
<td>Original sample N=290

However, 21 patients were excluded due to non availability of histopathology results. Furthermore, only n=223 analysed for sensitivity and specificity, after excluding n=46 cases of fibroid diagnosed at hysteroscopy and no match pf histopathology was available for them.

Characteristics

Mean age of the</td>
<td>Index test

Hysteroscopy (mostly outpatient)

Reference standard

Histopathology (sharp curettage)</td>
<td>Evaluated in gynae OPD by detailed history and clinical examination. Investigations include complete blood picture, urine analysis, random blood sugar, renal function tests, hepatitis B & C screening and routine pelvic ultrasound. Hysteroscopy was performed mostly on out patient basis in a separate setting reserved for the procedure. A trained staff nurse was available for assistance and instrumental care. After maintaining I/V line with lactated ringer, patient put in lithotomy position. Injection sosegon 10mg and phenergan was used for sedation. Hysteroscopy was performed by using rigid hysteroscope—Karl storz, with 30 degree tilt and</td>
<td>Hysteroscopy (mostly outpatient) versus histopathology (direct curettage)

a) Adenocarcinoma
<table>
<tr><td></td><td>Confirmed adenocarcinoma</td><td>No adenocarcinoma</td><td>Total</td></tr>
<tr><td>Adenocarcinoma in index test</td><td>2</td><td>4</td><td>6</td></tr>
<tr><td>No adenocarcinoma in index test</td><td>0</td><td>217</td><td>217</td></tr>
<tr><td>Total</td><td>2</td><td>221</td><td>223</td></tr>
</table>
Sensitivity 100% (95% CI 15.8%-100%*)

Specificity 98% (95% CI 95.4%-99.5%*)

Positive likelihood ratio* 55.2 (95% CI 20.92-145.91)

Negative likelihood ratio* 0</td>
<td>QUADAS-2 a quality assessment tool for diagnostic accuracy studies:

Patient Selection

A. Risk of Bias

Was a consecutive or random sample of patients enrolled? Unclear (not reported)

Was a case-control design avoided? Yes

Did the study avoid inappropriate exclusions? Yes

Could the selection of patients have introduced bias? Unclear risk

B. Concerns regarding applicability:</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>carried out

Pakistan

Study type

Prospective cohort study

Aim of the study

The purpose of this study was to know the different pathologies associated with menstrual irregularity which can be diagnosed</td>
<td>patients was 47.1 + 8.36 years, mean age at menarche was 13.3 + 1.66, and mode of parity was 4. Various indications for hysteroscopy included menorrhagia (39.4%), polymonorrhagia (26.8%), irregular bleeding (25.3%) and postmenapausal bleeding (8.6%).

Inclusion Criteria

35 years of age and above presenting with menorrhagia,</td>
<td></td>
<td>5mm diagnostic sheath(Olympus office system).Normal saline with Ashcroft pressure cuff or CO2 were used as distention medium with pressure between 50-75mmHg & flow rate 40-60ml/min.After performing pelvic examination, anterior lip of cervix was held with tenacullum. Cervical dilatation upto hegar 6 was usually required. Light source and distention media were attached to hysteroscope which was then introduced into the os. Further advancement was done under direct vision to perform a systematic inspection of uterine cavity including fundus, ostia, all the four walls and cervical canal. Hysteroscopy was followed by sharp curettage and specimen sent for histopathology.</td>
<td>Prevalence of adenocarcinoma 0.9%

b) Retained products of conception (RPOCs)
<table>
<tr><td></td><td>Confirmed RPOCs</td><td>No RPOCs</td><td>Total</td></tr>
<tr><td>RPOCs in index test</td><td>5</td><td>1</td><td>6</td></tr>
<tr><td>No RPOCs in index test</td><td>0</td><td>217</td><td>217</td></tr>
<tr><td>Total</td><td>5</td><td>218</td><td>223</td></tr>
</table>
Sensitivity 100% (95% CI 47.8%-100%*)

Specificity 100% (95% CI 97.5%-100%*)

Positive likelihood ratio* 218 (95% CI 30.85-1540)

Negative likelihood ratio* 0

Prevalence of RPOCs 1.9%</td>
<td>66.2% of patients with HMB

Are there concerns that the included patients and setting do not match the review question? High concern

Index Test

A. Risk of Bias

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? Unclear

Could the conduct or interpretation of the index test have introduced bias? Unclear risk</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>by hysteroscopy and curettage and, to know the sensitivity, specificity, positive predictive value and negative predictive value of hysteroscopy against histopathology.

Study dates

Not reported

Source of funding

Not reported</td>
<td>polymenorrhagia, irregular periods or post menopausal bleeding.

Exclusion Criteria

Patients unwilling for the proceedure, incomplete follow-up, positive pregnancy test, recent cervicitis, vaginitis, endometritis, pelvic infection and uterine perforation were excluded from this study.</td>
<td></td>
<td>Patients monitored in recovery room for 4–6 hours and discharged home on the same day if there was no complication. A predesigned proforma was filled at the same time with detailed record of hysteroscopic findings, which were later compared with histopathology reports.</td>
<td>c) Polyps
<table><tr><td></td><td>Confirmed polyp</td><td>No polyp</td><td>Total</td></tr><tr><td>Polyp in index test</td><td>21</td><td>14</td><td>35</td></tr><tr><td>No polyp in index test</td><td>3</td><td>185</td><td>188</td></tr><tr><td>Total</td><td>24</td><td>199</td><td>223</td></tr></table>Sensitivity 88% (95% CI 67.6%-97.3%*)

Specificity 93% (95% CI 88.5%-96.1%*)

Positive likelihood ratio* 12.44 (95% CI 7.34-21.07)

Negative likelihood ratio* 0.13 (95% CI 0.05-0.39)

Prevalence of polyps 8.6%

d) Hyperplasia</td>
<td>B. Concerns regarding applicability:

The paper did not report who interpreted the index test or what was the level of experience of the person(s).

Are there concerns that the index test, its conduct, or interpretation differ from the review question?
Unclear concern

Reference Standard

A. Risk of Bias

Is the reference standards likely to correctly classify the target condition? Yes

Were the reference standard results</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td></td><td></td><td></td><td></td>
<td>
<table>
<tr><td></td><td>Confirmed hyperplasia</td><td>No hyperplasia</td><td>Total</td></tr>
<tr><td>Hyperplasia in index test</td><td>20</td><td>16</td><td>36</td></tr>
<tr><td>No hyperplasia in index test</td><td>12</td><td>175</td><td>187</td></tr>
<tr><td>Total</td><td>32</td><td>191</td><td>223</td></tr>
</table>
Sensitivity 63% (95% CI 43.7%-78.9%*)
Specificity 92% (95% CI 86.8%-95.1%*)
Positive likelihood ratio* 7.46 (95% CI 4.35-12.81)
Negative likelihood ratio* 0.41 (95% CI 0.26-0.64)

Prevalence of hyperplasia 11.9%

e) Endometritis
<table>
<tr><td></td><td>Confirmed endometritis</td><td>No endometritis</td><td>Total</td></tr>
</table>
</td>
<td>interpreted without knowledge of the results of the index tests? Yes
Could the reference standard, its conduct, or its interpretation have introduced bias? Low risk
B. Concerns regarding applicability
Are there concerns that the target condition as defined by the reference standard does not match the question? Low concern
Flow and Timing
A. Risk of Bias
Was there an appropriate interval between index test and reference</td>
</tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
				<table><tr><td>Endometritis in index test</td><td>19</td><td>2</td><td>21</td></tr><tr><td>No endometritis in index test</td><td>27</td><td>175</td><td>202</td></tr><tr><td>Total</td><td>46</td><td>177</td><td>223</td></tr></table> Sensitivity 41% (95% CI 27.00-56.77 95% CI*) Specificity 99% (95% CI 95.98-99.86 95% CI*) Positive likelihood ratio* 36.55 (95% CI 8.83-151.30 95% CI) Negative likelihood ratio* 0.59 (95% CI 0.47-0.76 95% CI) Prevalence of endometritis 20.1 % *Calculated by the NGA technical team	standard? Yes Did all patients receive the same reference standard?Yes Were all patients included in the analysis? No, 67/290 dropped out/were excluded from analysis, but all dropouts were explained (see below). Could the patient flow have introduced bias? Unclear risk **Other information** With regards to inclusion of all patients in the analysis, 21 patients were excluded due to non availability of histopathology

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					reports. A further 46 patients were excluded from the analysis due to the discrepancy between the hysteroscopy and histopathology results (46 of uterine fibroids diagnosed at hysteroscopy for which histopathology results were normal endometrium 27 cases, hyperplasia 2 cases, endometritis 8 cases, and hormonal imbalance 9 cases) - 23% of the population at the start were not included in the analysis.
Full citation Mukhopadhayay, S.,	**Sample size** n=85 **Characteristics**	**Tests** Index test	**Methods** In this tertiary hospital, outpatient facilities for hysteroscopy and	**Results** 1) 2D-TVUS versus histopathology (hysteroscopy with D&C)	**Limitations** **QUADAS-2** a quality assessment tool for diagnostic accuracy

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>Bhattacharyya, S. K., Ganguly, R. P., Patra, K. K., Bhattacharya, N., Barman, S. C., Comparative evaluation of perimenopausal abnormal uterine bleeding by transvaginal sonography, hysteroscopy and endometrial biopsy, Journal of</td>
<td>Age range 40-55 years old.

38.9% of population were in the age group of 40-43 years and 88.23% of population were between para 1 and 4.

TVUS finding showed 68.23% had normal myometrium and rest had some lesion in myometrium. Those who had anatomical lesion in the myometrium, fibroid was most common (21.18%) followed by myoperplasia (7.06%) and</td>
<td>2D transvaginal ultrasound scan (2D-TVUS)

Reference standard

Histopathology (hysteroscopy followed by D&C)</td>
<td>endometrial biopsy are not available. Therefore, all selected patients were advised to get admission one day prior to hysteroscopy. After admission a detailed clinical history of each patient was taken and special emphasis was given on mestrual history, general, systemic and gynaecological examinations performed. Lab investigations like complete haemogram, postprandial blood sugar, urea, creatinine, bleeding time, coagulation time, platelet count, TSH, T3, T4 estimations were performed. TVUS was performed in the radiology department. Hysteroscopy and dilatation and currettage (DC) operation for endometrial biopsy were performed in the OT under IV sedation.</td>
<td>a) Hyperplasia
<table>
<tr><th></th><th>Confirmed hyperplasia</th><th>No hyperplastia</th><th>Total</th></tr>
<tr><td>Hyperplasia in index test</td><td>7</td><td>3</td><td>10</td></tr>
<tr><td>No hyperplasia in index test</td><td>9</td><td>66</td><td>75</td></tr>
<tr><td>Total</td><td>16</td><td>69</td><td>85</td></tr>
</table>
Sensitivity 43.75% (95% CI 19.75-70.12%*)

Specificity 95.65% (95% CI 87.82-99.09%*)

Positive likelihood ratio* 10 (95% CI 2.92-34.72*)

Negative likelihood ratio* 0.59 (95% CI 0.38-0.91*)

Prevalence of hyperplasia 18.82%

b) Polyp</td>
<td>studies:

Patient Selection

A. Risk of Bias

Was a consecutive or random sample of patients enrolled? Unclear (not reported)

Was a case-control design avoided? Yes

Did the study avoid inappropriate exclusions? Unclear. Patients with varicose veins were excluded, no explanation given.

Could the selection of patients have introduced bias? Unclear Risk

B. Concerns regarding applicability:</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>the Indian Medical Association, 105, 2007

Ref Id

511700

Country/ies where the study was carried out

India

Study type

Prospective cohort study

Aim of the study

To evaluate</td>
<td>adenomyosis (3.53%)

Histopathological report showed most of the women had proliferative endometrium (47.06%), followed by secretory endometrium (23.53%) and hyperplastic endometrium (11.76%)

Inclusion Criteria

AUB between ages 40-55 years

Exclusion Criteria

Patients with active bleeding</td>
<td></td>
<td>Endometrial biopsy was taken from apparently unhealthy area under direct vision by hysteroscope. Some cases where localised lesions could not be detected by hysteroscopy, fractional currettage and thorough endometrial currettage were performed. Specimen was preserved in formalin solution and sent for histopathological examination.</td>
<td>
<table>
<tr><td></td><td>Confirmed polyp</td><td>No polyp</td><td>Total</td></tr>
<tr><td>Polyp in index test</td><td>1</td><td>9</td><td>10</td></tr>
<tr><td>No polyp in index test</td><td>1</td><td>74</td><td>75</td></tr>
<tr><td>Total</td><td>2</td><td>83</td><td>85</td></tr>
</table>
Sensitivity 50% (95% CI 1.26%-98.74%*)

Specificity 89.16% (95% CI 80.41%-94.92%*)

Positive likelihood ratio* 4.61 (95% CI 1.01-21.02*)

Negative likelihood ratio* 0.56 (95% CI 0.29-8.24*)

Prevalence of polyps 2.35%

2) Hysteroscopy versus histopathology (hysteroscopy with D&C)
</td>
<td>The proportion of included patients with HMB is unclear. All included women had abnormal uterine bleeding but not specified further.

Are there concerns that the included patients and setting do not match the review question? High concern

Index Test

A. Risk of Bias

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? No (not</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>the causes of abnormal uterine bleeding in perimenopausal women and to achieve the greatest diagnostic accuracy with the least risk for patients

Study dates

January 2005- May 2006

Source of funding

Not reported</td>
<td>per vagina, atrophic vaginitis, carcinoma cervix, cervical polyp, bleeding following trauma, varicoise vein who did not give consent for the study were excluded.</td>
<td></td>
<td></td>
<td>a) Hyperplasia
<table><tr><td></td><td>Confirmed hyperplastia</td><td>No hyperplasia</td><td>Total</td></tr><tr><td>Hyperplasia in index test</td><td>7</td><td>3</td><td>10</td></tr><tr><td>No hyperplasia in index test</td><td>7</td><td>68</td><td>75</td></tr><tr><td>Total</td><td>14</td><td>71</td><td>85</td></tr></table>Sensitivity 50% (95% CI 23.04-76.96*)

Specificity 95.78% (95% CI 88.14-99.12%*)

Positive likelihood ratio* 11.8 (95% CI 3.48-40.29*)

Negative likelihood ratio* 0.52 (95% CI 0.31-0.88 *)

Prevalence of hyperplasia 16.47%

b) Polyp
<table><tr><td></td><td>Confirmed</td><td>No</td><td>Total</td></tr></table></td>
<td>reported)

Could the conduct or interpretation of the index test have introduced bias? High Risk

B. Concerns regarding applicability:

The paper did not report who interpreted the index test or what was the level of experience of the person(s)

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Unclear concern

Reference Standard

A. Risk of Bias</td>
</tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
				<table><tr><td></td><td>polyp</td><td>polyp</td><td></td></tr><tr><td>Polyp in index test</td><td>10</td><td>0</td><td>10</td></tr><tr><td>No polyp in index test</td><td>4</td><td>71</td><td>75</td></tr><tr><td>Total</td><td>14</td><td>71</td><td>85</td></tr></table> Sensitivity 71.43% (95% CI 41.90-91.61%*) Specificity 100% (95% CI 94.94-100%*) Positive likelihood ratio* Negative likelihood ratio* 0.29 (95% CI 0.12-0.65*) Prevalence of polyps 16.47% *Calculated by the NGA technical team	Is the reference standards likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear (not reported) Could the reference standard, its conduct, or its interpretation have introduced bias? Unclear risk B. Concerns regarding applicability Are there concerns that the target condition as defined by the reference standard does not match the question? Low concern

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					Flow and Timing A. Risk of Bias Was there an appropriate interval between index test and reference standard? Yes Did all patients receive the same reference standard? Yes Were all patients included in the analysis? Yes Could the patient flow have introduced bias? Low risk **Other information**
Full citation	**Sample size** n=141	**Tests** Index	**Methods** Ultrasound	**Results** 2D-TVUS versus histopathology (D&C)	**Limitations** **QUADAS-2** a quality

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>Najeeb, R., Awan, A. S., Bakhtiar, U., Akhter, S., Role of transvaginal sonography in assessment of abnormal uterine bleeding in perimenopausal age group, Journal of Ayub Medical College, Abbottabad : JAMC, 22, 2010

Ref Id

511707</td>
<td>Characteristics

The mean age was 44 years (range 40-47 years).

Inclusion Criteria

Women of perimenopausal age group presenting with abnormal uterine bleeding

Exclusion Criteria

Women on any form of hormonal treatment, known gynaecological malignancy or endocrinological disorders were</td>
<td>test

2D transvaginal ultrasouns scan (2D-TVUS)

Reference standard

Histopathology of endometrial currettings from D&C (dilatation and curettage)</td>
<td>TVUS was performed using vaginal transducer of 6.5 MHz frequency on Logic Pro 100-GE USA. Endometrial thickness was measured in postmenstrual period (7-10 days) at the thickest part of the endometrium 1 cm from the endometrial-myometrial interface at the fundus in the longitudial plane as described.

Detection of a hyperechoic area within the endometrial layers was taken as suggestive of endometrial pathology. Endometrial malignancy was suspected when echos were clearly dishomogenous and the endometriomyometrial interface was irregular.

Histopathology

The thickness measured</td>
<td>a) Polyps
<table><tr><td></td><td>Confirmed polyp</td><td>No polyp</td><td>Total</td></tr><tr><td>Polyp in index test</td><td>33</td><td>5</td><td>38</td></tr><tr><td>No polyp in index test</td><td>0</td><td>103</td><td>103</td></tr><tr><td>Total</td><td>33</td><td>108</td><td>141</td></tr></table>Sensitivity* 100% (95% CI 89%-100%*)

Specificity* 95.4% (95% CI 90%-98%*)

Positive likelihood ratio* 21.7 (95% CI 0.72-0.96*)

Negative likelihood ratio* 0.0

Prevalence of polyps 23.4%

b) Myomas
<table><tr><td></td><td>Confirmed</td><td>No</td><td>Total</td></tr></table></td>
<td>assessment tool for diagnostic accuracy studies:

Patient Selection

A. Risk of Bias

Was a consecutive or random sample of patients enrolled? Unclear (not reported)

Was a case-control design avoided? Yes

Did the study avoid inappropriate exclusions? Yes

Could the selection of patients have introduced bias? Unclear risk

B. Concerns regarding applicability:

All women were</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>Country/ies where the study was carried out

Pakistan

Study type

Descriptive

Aim of the study

Establish the role of transvaginal sonography in the diagnosis of abnormal uterine bleeding in perimenap</td>
<td>excluded.</td>
<td></td>
<td>included both the endometrial layers and a cut off value of 8mm was taken, followed by an inpatient D&C.

Histopathology of endometrial currettings was correlated with the sonographic features.</td>
<td>
<table>
<tr><td></td><td>myoma</td><td>myoma</td><td></td></tr>
<tr><td>Myoma in index test</td><td>6</td><td>15</td><td>21</td></tr>
<tr><td>No myoma in index test</td><td>0</td><td>120</td><td>120</td></tr>
<tr><td>Total</td><td>6</td><td>135</td><td>141</td></tr>
</table>
Sensitivity 100% (95% CI 54%-100%*)

Specificity 88.9% (95% CI 82%-94%*)

Positive likelihood ratio* 9.0 (95% CI 5.59-14.50*)

Negative likelihood ratio* 0.0

Prevalence of myomas 4.3%

In addition, hyperplasia results reported in the 2x2 table in the paper but a "false positive" result of -6. This result seems to be an anomaly and the text doesn't provide further information to clarify other than "shows that TVS has to be interpreted with</td>
<td>premenopausal and all had abnormal uterine bleeding, however, the proportion of patients with HMB is not specified.

Are there concerns that the included patients and setting do not match the review question? High concern

Index Test

A. Risk of Bias

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? Unclear. Not clearly defined for</td>
</tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
ausal women **Study dates** January 2006-April 2007 **Source of funding** None reported				caution as 6 cases were missed". No specificity of sensitivity results reported to calculate values in excel. *Calculated by the NGA technical team.	all the conditions, specified for endometrial malignancy and classified all other endometrial pathologies together rather than separating for polyps and myomas. Could the conduct or interpretation of the index test have introduced bias? Unclear risk B. Concerns regarding applicability: The paper did not report who interpreted the index test or what was the level of experience of the person(s) Are there concerns that the index test, its conduct, or

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					interpretation differ from the review question? Unclear concern Reference Standard A. Risk of Bias Is the reference standards likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index tests? Yes Could the reference standard, its conduct, or its interpretation have introduced bias? Low risk B. Concerns regarding applicability Are there concerns

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					that the target condition as defined by the reference standard does not match the question? Low concern Flow and Timing A. Risk of Bias Was there an appropriate interval between index test and reference standard? Yes Did all patients receive the same reference standard? Yes Were all patients included in the analysis? Yes. Could the patient flow have introduced bias? Low risk **Other information**

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					Inclusion criteria were not reported clearly. Characteristics of included patients except for age were not reported. In the results section, the findings regarding hyperplasia were not clear, a FP of -6 was reported. The text did not provide further guidance, other than stating that 6 cases were missed in the TVUS. Unable to calculate the results as reporting is unclear and no sensitivity results were reported.
Full citation Soguktas,	**Sample size** n=93	**Tests** Index test	**Methods** TVUS, SIS, hysteroscopy were	**Results** 1) 2D-TVUS versus histopathology (D&C)	**Limitations** **QUADAS-2** a quality assessment tool for

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>S., Cogendez, E., Kayatas, S. E., Asoglu, M. R., Selcuk, S., Ertekin, A., Comparison of saline infusion sonohysterography and hysteroscopy in diagnosis of premenopausal women with abnormal uterine bleeding, European Journal of Obstetrics,</td>
<td>(4 subjects with inadequate evaluation in any proceedure were removed from the study, and the remaining 89 patients underwent all procedures)

Characteristics

Mean age = 43.1 + 2.9 years (range 36-48)

When endometrial biopsy was considered as the gold standard, no abnormal pathology (47.2%), polypoid lesion (38.2%),</td>
<td>2D transvaginal ultrasound scan (2D-TVUS); hysteroscopy (under general anaesthesia)

Reference standard

Histopathology (D&C)</td>
<td>performed on all participants by different physicians blindly. All women were examined by TVUS, using a 6.5 MHz vaginal probe (General Electric Logic 200) to visualize uterus in the sagittal and coronal planes. If endometrial thickness (double layer) measured less than 15 mm and seemed regular by TVUS, it was considered a normal finding. A centrally placed echo-dense line within the uterus and a homogeneous endometrial lining with distinct margins to the myometrium were also considered normal. Otherwise, if the measured endometrial thickness was thicker than 15 mm, it was considered as endometrial hyperplasia. Irregular focal</td>
<td>a) Any endometrial abnormality
<table>
<tr><th></th><th>Confirmed abnormality</th><th>No abnormality</th><th>Total</th></tr>
<tr><td>Any abnormality in index test</td><td>42*</td><td>12*</td><td>54</td></tr>
<tr><td>No abnormality in index test</td><td>5*</td><td>30*</td><td>35</td></tr>
<tr><td>Total</td><td>47</td><td>42</td><td>89</td></tr>
</table>
Sensitivity 89.4% (95% CI 76.9%-96.5%)

Specificity 71.4% (95% CI 55.4%-84.3%)

Positive likelihood ratio 3.13 (95% CI 2.5-3.9)

Negative likelihood ratio 0.15 (95% CI 0.06-0.4)

Prevalence of any endometrial abnormality 52.8%

b) Polyp
<table>
<tr><th></th><th>Confirmed</th><th>No</th><th>Total</th></tr>
</table>
</td>
<td>diagnostic accuracy studies:

Patient Selection

A. Risk of Bias

Was a consecutive or random sample of patients enrolled? Unclear (not reported)

Was a case-control design avoided? Yes

Did the study avoid inappropriate exclusions? Yes

Could the selection of patients have introduced bias? Unclear risk

B. Concerns regarding applicability: All were premenapausal women with abnormal uterine bleeding,</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>Gynecology, & Reproductive BiologyEur J Obstet Gynecol Reprod Biol, 161, 2012

Ref Id

511952

Country/ies where the study was carried out

Turkey

Study type

Prospective cohort study</td>
<td>endometrial hyperplasia (7.9%), submucosal myoma (4.5%), endometrium carcinoma (2.2%) were found among the study population.

Inclusion Criteria

Premenapausal women with abnormal uterine bleeding such as menorrhagia, metrorrhagia, menometrorrhagia and polymenorrhea related to intracavitary pathology.</td>
<td></td>
<td>endometrial thickenings were considered as endometrium carcinoma. In addition, deformations in the endometrial lining and absence of central echo dense line were also considered abnormal findings.

SIS was performed shortly after TVUS. A 10 or 12 F catheter was inserted into the uterus following direct inspection and then a vaginal probe was reintroduced in the posterior fornix of the vagina behind the catheter. About 10–30 ml sterile saline were injected into the catheter to expand the uterine cavity and the distended uterine cavity was viewed in transverse and longitudinal planes by TVUS. Entire hyperechogenic lesions</td>
<td>
<table>
<tr><td></td><td>polyp</td><td>polyp</td><td></td></tr>
<tr><td>Polyp in index test</td><td>22*</td><td>5*</td><td>27</td></tr>
<tr><td>No polyp in index test</td><td>12*</td><td>50*</td><td>62</td></tr>
<tr><td>Total</td><td>34</td><td>55</td><td>89</td></tr>
</table>
Sensitivity 64.7% (95% CI 46.5%-80.3%)

Specificity 90.9% (95% CI 80.0%-97.0%)

Positive likelihood ratio 7.1 (95% CI 5.5-9.2)

Negative likelihood ratio 0.4 (95% CI 0.1-1.0)

Prevalence of polyps 38.2%

c) Myoma
<table>
<tr><td></td><td>Confirmed myoma</td><td>No myoma</td><td>Total</td></tr>
<tr><td>Myoma in</td><td>3*</td><td>0*</td><td>3</td></tr>
</table>
</td>
<td>however, proportion of women with HMB not reported.

Are there concerns that the included patients and setting do not match the review question? High concern

Index Test

A. Risk of Bias

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? Yes (detailed diagnostic criteria included in the methods)

Could the conduct or</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>Aim of the study

The aim of the study was to compare the diagnostic effectiveness of transvaginal sonography, saline infusion sonohysterography (SIS), and diagnostic hysteroscopy, with the pathologic specimen as a gold standard diagnostic</td>
<td>(no % breakdown recorded of different conditions)

Exclusion Criteria

Pelvic infection, pregnancy and patients with who had abnormal bleeding without intracavitary pathology.</td>
<td></td>
<td>within the uterine cavity were considered as endometrial polyp. Whereas, when compared with myometrium, isoechogenic or hypoechogenic lesions having relation with myometrium and reaching the uterine cavity by pushing the endometrium were considered as submucosal myoma. Regular diffuse endometrial thickness was considered as endometrial hyperplasia. Irregular asymmetric focal endometrial thickness was considered as endometrial cancer. Findings at SIS were defined according to criteria published by Parsons and Lense.

Next day, diagnostic hysteroscopy was performed under general anesthesia by a third</td>
<td>
<table>
<tr><td>index test</td><td></td><td></td><td></td></tr>
<tr><td>No myoma in index test</td><td>1*</td><td>85*</td><td>86</td></tr>
<tr><td>Total</td><td>4</td><td>85</td><td>89</td></tr>
</table>
Sensitivity 75.0% (95% CI 19.4%-99.4%)

Specificity 100% (95% CI 95.8%-100%)

Positive likelihood ratio -

Negative likelihood ratio 0.25 (95% CI 0.05-1.36*)

Prevalence of myoma 4.5%

d) Endometrial hyperplasia
<table>
<tr><td></td><td>Confirmed endometrial hyperplasia</td><td>No endometrial hyperplasia</td><td>Total</td></tr>
<tr><td>Endometrial</td><td>5*</td><td>12*</td><td>17</td></tr>
</table>
</td>
<td>interpretation of the index test have introduced bias? Low risk

B. Concerns regarding applicability: The paper does not report who interpreted the index test or the level of experience of the person(s).

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Unclear concern

Reference Standard

A. Risk of Bias

Is the reference standards likely to correctly classify the target condition? Yes</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>method, in detecting endometrial pathology in premenapausal women with abnormal uterine bleeding.

Study dates

Not Reported

Source of funding

None declared</td>
<td></td>
<td></td>
<td>examiner ussing a rigid 30° hysteroscope with a diagnostic sheath diameter of 5 mm. A rigid resectoscope was inserted through the cervix under direct visualization and the uterine cavity was distended with isotonic solution. If the cavity was flat and pale with small petechial hemorrhages, diagnosis was considered as atrophic endometrium. Pedunculated lesions covered by endometrium were diagnosed as endometrial polyps, and were generally sessile, shiny lesions and sometimes vascularized. Pedunculated lesions not covered by endometrium were diagnosed as submucosal myomas. If a sulcus was found after pressure application to flat endometrium that had polypoid thickness,</td>
<td>
<table>
<tr><td>hyperplasia in index test</td><td></td><td></td><td></td></tr>
<tr><td>No endometrial hyperplasia in index test</td><td>2*</td><td>70*</td><td>72</td></tr>
<tr><td>Total</td><td>7</td><td>82</td><td>89</td></tr>
</table>
Sensitivity 71.4% (95% CI 29.0%-96.3%)

Specificity 85.4% (95% CI 75.8%-92.2%)

Positive likelihood ratio 4.9 (95% CI 3.0-7.9)

Negative likelihood ratio 0.3 (95% CI 0.09-1.2)

Prevalence of endometrial hyperplasia 7.9%

e) Endometrium carcinoma
<table>
<tr><td></td><td>Confirmed endometrium carcinoma</td><td>No endometrium carcinoma</td><td>Total</td></tr>
</table>
</td>
<td>Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Could the reference standard, its conduct, or its interpretation have introduced bias? Low risk

B. Concerns regarding applicability

Are there concerns that the target condition as defined by the reference standard does not match the question? Low concern

Flow and Timing

A. Risk of Bias

Was there an appropriate interval</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>diagnosis was considered as endometrial hyperplasia. If there was irregularity, necrosis, and glandular and vascular disorganization in the endometrial surface, endometrial cancer was considered probable diagnosis.

Operative hysteroscopy was performed in women with endometrial polyp and submucosal myoma following diagnostic HS in same session. A dilatation and curettage was performed after diagnostic hysteroscopy under general anesthesia in the patients who had no intracavitary mass. Histopathological specimens were evaluated by the pathology department. Proliferative, secretory and atrophic endometria</td>
<td>
<table>
<tr><td>Endometrium carcinoma in index test</td><td>1*</td><td>6*</td><td>7</td></tr>
<tr><td>No endometrium carcinoma in index test</td><td>1*</td><td>81*</td><td>82</td></tr>
<tr><td>Total</td><td>2</td><td>87</td><td>89</td></tr>
</table>
Sensitivity 50% (95% CI 1.3%-98.7%)

Specificity 93.1% (95% CI 85.6%-97.4%)

Positive likelihood ratio 7.25 (95% CI 1.8-29)

Negative likelihood ratio 0.54 (95% CI 0.1-2.6)

Prevalence of endometrium carcinoma 2.2%

2) Hysteroscopy (under GA) versus histopathology (D&C)

a) Any endometrial abnormality
</td>
<td>between index test and reference standard? Yes

Did all patients receive the same reference standard? Yes

Were all patients included in the analysis? No (4 patients were excluded due to inadequate evaluation in any procedure)

Could the patient flow have introduced bias? Low (index and reference tests took place on different days, however give the chronic nature of the disease it is unlikely to be detrimental)

Other information</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td>were classified as other or normal findings. Polypoid lesion, submucosal myoma, endometrial hyperplasia and endometrial carcinoma were classified as abnormal pathological findings.</td><td>
<table>
<tr><td></td><td>Confirmed endometrial abnormality</td><td>No endometrial abnormality</td><td>Total</td></tr>
<tr><td>Endometrial abnormality in index test</td><td>46*</td><td>3*</td><td>49</td></tr>
<tr><td>No endometrial abnormality in index test</td><td>1*</td><td>39*</td><td>40</td></tr>
<tr><td>Total</td><td>47</td><td>42</td><td>89</td></tr>
</table>
Sensitivity 97.9% (95% CI 88.7%-99.9%)
Specificity 92.9% (95% CI 80.5%-98.5%)
Positive likelihood ratio 13.7 (95% CI 12.5-15.1)
Negative likelihood ratio 0.02 (95% CI 0.002-0.2)

Prevalence of any endometrial abnormality 52.8%

b) Polyp
</td><td></td></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td>
<table>
<tr><td></td><td>Confirmed polyp</td><td>No polyp</td><td>Total</td></tr>
<tr><td>Polyp in index test</td><td>31*</td><td>1*</td><td>32</td></tr>
<tr><td>No polyp in index test</td><td>3*</td><td>54*</td><td>57</td></tr>
<tr><td>Total</td><td>34</td><td>55</td><td>89</td></tr>
</table>
Sensitivity 91.1 (95% CI 76.3%-98.1%)
Specificity 98.2 (95% CI 90.3%-100%)
Positive likelihood ratio 50.2 (95% CI 44.9-56)
Negative likelihood ratio 0.09 (95% CI 0.01-0.8)

Prevalence of polyps 38.2%

c) Myoma
<table>
<tr><td></td><td>Confirmed myoma</td><td>No myoma</td><td>Total</td></tr>
</table>
</td><td></td></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td>
<table>
<tr><td>Myoma in index test</td><td>4*</td><td>0*</td><td>4</td></tr>
<tr><td>No myoma in index test</td><td>0*</td><td>85*</td><td>85</td></tr>
<tr><td>Total</td><td>4</td><td>85</td><td>89</td></tr>
</table>
Sensitivity 100% (95% CI 39.8%-100%)
Specificity 100% (95% CI 95.8%-100%)
Positive likelihood ratio -
Negative likelihood ratio 0.0

Prevalence of myoma 4.5%

d) Endometrial hyperplasia
<table>
<tr><td></td><td>Confirmed endometrial hyperplasia</td><td>No endometrial hyperplasia</td><td>Total</td></tr>
<tr><td>Endometrial hyperplasia in</td><td>6*</td><td>2*</td><td>8</td></tr>
</table>
</td><td></td></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td>
<table>
<tr><td>index test</td><td></td><td></td><td></td></tr>
<tr><td>No endometrial hyperplasia in index test</td><td>1*</td><td>80*</td><td>81</td></tr>
<tr><td>Total</td><td>7</td><td>82</td><td>89</td></tr>
</table>
Sensitivity 85.7% (95% CI 42.1%-99.6%)
Specificity 97.6% (95% CI 91.5%-99.7%)
Positive likelihood ratio 35.1 (95% CI 25.9-47.6)
Negative likelihood ratio 0.15 (95% CI 0.02-1.4)

Prevalence of endometrial hyperplasia 7.9%

e) Endometrium carcinoma
<table>
<tr><td></td><td>Confirmed endometrium carcinoma</td><td>No endometrium carcinoma</td><td>Total</td></tr>
<tr><td>Endometrium</td><td>2*</td><td>3*</td><td>5</td></tr>
</table>
</td><td></td></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td>
<table>
<tr><td>carcinoma in index test</td><td></td><td></td><td></td></tr>
<tr><td>No endometrium carcinoma in index test</td><td>0*</td><td>84*</td><td>84</td></tr>
<tr><td>Total</td><td>2</td><td>87</td><td>89</td></tr>
</table>
Sensitivity 100% (95% CI 15.8%-100%)
Specificity 96.4% (95% CI 90.3%-99.3%)
Positive likelihood ratio 29.0 (95% CI 27.9-30.2)
Negative likelihood ratio 0.00

Prevalence of endometrium carcinoma 2.2%

*Calculated by the NGA technical team</td><td></td></tr>
<tr><td>Full citation</td><td>Sample size
n=86</td><td>Tests
Index</td><td>Methods
Initially all cases were</td><td>Results
Hysteroscopy (under GA, local anaesthesia or no</td><td>Limitations
QUADAS-2 a quality</td></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>Yildiz, A., Koksal, A., Ates, P. F., Ivit, H., Keklik, A., Cukurova, K., Hysteroscopy in the evaluation of intrauterine cavity. Is it more valuable than dilatation and curettage? , Turkiye Klinikleri Journal of Medical Sciences, 29, 2009

Ref Id

512149</td>
<td>Characteristics

72 (89%) patients were in premenopausal period and 14 were in the postmenopausal period.

Duration of AUB in premenopausal and postmenopausal women were 22.8 (min. 2 months, max. 10 years) and 7.7 (min. 1 month-max. 2 years) months.

The bleeding pattern was menometrorrhagia in 65.1%, metrorrhagia in 18.6% and</td>
<td>Test

Hysteroscopy (under general anaesthesia, spinal/cergical local anaesthesia, no anaesthesia)

Reference Standard

Histopathology (D&C)</td>
<td>evaluated with pelvic examination and transvaginal ultrasonography (General Electric Logic 200 6.5 mHz). Then, D&C was performed in all cases. After a mean duration of 6.3 weeks (min. 3 weeks-max. 7 weeks) following D&C office hysteroscopy was performed. All procedures were done by the same investigators. Meanwhile preoperative preparations of patients with operation indication were carried out. All collected data were recorded on standardized forms. Hysteroscopies (diameter 2 mm, length 26 cm, Forward Oblique Telescope 30o , Bettochi Continuous-Flow Operating Sheath 4.2 mm, semirigid, 5 Fr., length 34 cm instruments, Storz, Germany) we re</td>
<td>anaesthesia) versus histopathology (D&C)

a) Any endometrial abnormality
<table>
<tr><th></th><th>Confirmed endometrial abnormality</th><th>No endometrial abnormality</th><th>Total</th></tr>
<tr><td>Any endometrial abnormality in index test</td><td>66</td><td>0</td><td>66</td></tr>
<tr><td>No endometrial abnormality in index test</td><td>4</td><td>16</td><td>20</td></tr>
<tr><td>Total</td><td>70</td><td>16</td><td>86</td></tr>
</table>
Sensitivity 94% (95% CI 86.0%-98.4%*)

Specificity 100% (95% CI 79.4%-100%*)

Positive likelihood ratio Inf

Negative likelihood ratio 0.06 (95% CI 0.02-0.15)</td>
<td>assessment tool for diagnostic accuracy studies:

Patient Selection

A. Risk of Bias

Was a consecutive or random sample of patients enrolled? Unclear (not reported)

Was a case-control design avoided? Yes

Did the study avoid inappropriate exclusions? Yes

Could the selection of patients have introduced bias? Unclear risk

B. Concerns regarding applicability:

89% of patients were</td>
</tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
Country/ies where the study was carried out Turkey **Study type** Retrospective cohort study **Aim of the study** Compare D&C with office hysteroscopy in the diagnosis of uterine pathologies in women	postmenopausal bleeding in 16.3% 18.6% Normal 25.6% Myoma 18.6% Polyp 14.7% Adenomyosis 9.3% Polyp and Myoma 2.3% Hyperplasia 2.3% Otolytic endometrium 2.3% Inactive endometrium and chromic cervicitis **Inclusion Criteria** Abnormal uterine bleeding		performed in the operation room with intravenous or intratechal general anesthesia or spinal/cervical local anesthesia or without any anesthesia. Uterine cavity was distended with 0.9% NaCl solution. In case of electrocautery, 5% mannitol solution was used. Speculum or tenaculum was not used during the hysteroscopy process. During hysteroscopy vagina was entered with direct vision through the introitus, portio uteri was found and uterine cavity was entered along the endocervical canal. Endocervical canal, fundus, ostia, anterior and posterior walls were observed. Hysterescopies with total inspection of the endometrial cavity and endocervical canal were considered adequate.	Prevalence of any endometrial abnormality 81.4% *Calculated by the NGA technical team	premenopausal. 65% with menometrorrhagia. Inclusion criteria not clearly defined. Are there concerns that the included patients and setting do not match the review question? High concern. Index Test A. Risk of Bias Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified? No. Not clearly defined for all the conditions.

Study details	Participants	Tests	Methods	Outcomes and results	Comments
with abnormal uterine bleeding and to evaluate diagnostic and therapeutic advantages of office hysteroscopy **Study dates** June 2005-March 2006 **Source of funding** Not reported	**Exclusion Criteria** Genital malignancy or pregnancy		Hysterescopies in which no anatomical or endocervical pathology could be observed, were considered normal. Presence of adhesion, polyp, submucosal myoma, pressure effect or any other abnormality in the uterine cavity was considered abnormal hysteroscopy. Irregular shedding, proliferation, menstruation and secretion phase of endometrium were considered normal histopathologic findings in endometrial sampling performed by D&C. Presence of endometrial hyperplasia, myoma uteri and polyps were considered abnormal findings of D&C. Endoscopic biopsies were taken from all cases except myomas and polyps. Fifty-two cases		Could the conduct or interpretation of the index test have introduced bias? High risk B. Concerns regarding applicability: The paper did not report who interpreted the index test or what was the level of experience of the person(s), only that all investigations were carried out by the same investigator. Are there concerns that the index test, its conduct, or interpretation differ from the review question? Unclear concern Reference Standard

Study details	Participants	Tests	Methods	Outcomes and results	Comments
			underwent total abdominal hysterectomy after hysteroscopy. Their indications were menometrorrhagia resistant to medical therapy, myoma uteri and postmenopausal bleeding with adnexial cyst or polyp. Diagnostic values of D&C and office hysteroscopy were compared by calculation of sensitivity, specificity, positive predictive value and negative predictive value (PPV and NPV) setting the tables separately. Statistical analysis was done with SPSS version 13.0. A p value less than 0.05 was considered significant.		A. Risk of Bias Is the reference standards likely to correctly classify the target condition? Yes. Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear Could the reference standard, its conduct, or its interpretation have introduced bias? Unclear risk B. Concerns regarding applicability Are there concerns that the target condition as defined by the reference standard does not

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					match the question? Low concern Flow and Timing A. Risk of Bias Was there an appropriate interval between index test and reference standard? Yes Did all patients receive the same reference standard? Yes Were all patients included in the analysis? Yes. Could the patient flow have introduced bias? Low risk **Other information** Inclusion criteria not clearly defined

Study details	Participants	Tests	Methods	Outcomes and results	Comments
Full citation Critchley, H. O. D., Warner, P., Lee, A. J., Brechin, S., Guise, J., Graham, B., Evaluation of abnormal uterine bleeding: Comparison of three outpatient procedures within cohorts defined by age and	**Sample size** N=683 women in total in three groups according to risk of endometrial cancer: high risk: n=200 postmenopausal women (not considered in this review); moderate risk: n=326 premenopausal women either aged >=40 years, or aged <40 years but with specific risk factors for endometrial cancer (polycystic	**Tests** Transvaginal ultrasound usually in conjunction with abdominal ultrasound or sometimes substituted by abdnominal ultrasound; Hysteroscopy with	**Methods** Interventions Women in the moderate risk group were equally randomised to receive either 1) hysteroscopy + biopsy, 2) blind endometrial biopsy, 3) hysteroscopy + biopsy + ultrasound, 4) biopsy + ultrasound. All the biopsies included both Pipelle sampler and Tao brush in a random order (50% were allocated to receive Pipelle sampler first, the other 50% was allocated to have Tao brush first). All three interventions were outpatient investigations. It was considered important that the comparison of evaluation	**Results** Finding investigation 'markedly unpleasant' Proportion of women in the moderate risk group that found the investigation 'markedly unpleasant' (numerator is the number of women who answered the investigation to be markedly unpleasant and the denominator is the number of women who answered the question): Hysteroscopy + biopsy: 23/149=15% Ultrasound: 1/147=<1% Blind endometrial biopsy: 54/296=18% Intention to treat analysis (those who did not have investigation or who did not answer the question are imputed to have found the investigation unpleasant. Numerator is the women answered the investigation to be unpleasant and thre women who did not have the investigation and the women who did not answer the question, and the denominator is the women randomised to receive the investigation): Hysteroscopy + biopsy: 40/166=24%	**Limitations** **Cochrane risk of bias tool** Selection bias Random sequence generation: Low risk of bias Allocation concealment: Low risk of bias Performance bias Blinding of participants and personnel: High risk of bias (Due to the nature of the study, blinding was not possible in terms of the investigation for the investigator and the participants.)

Study details	Participants	Tests	Methods	Outcomes and results	Comments
menopausal status, Health Technology Assessment, 8, iii-77, 2004 **Ref Id** 548454 **Country/ies where the study was carried out** UK **Study type** Randomised controlled study **Aim of the**	ovarian syndrome, prior use of unopposed aestrogens or tamoxifen, obesity, diabetes or family history of endometrial cancer); low risk: n=157 premenopausal women aged <40 years without specific risk factor (not considered in this review because <2/3 have HMB) **Characteristics** Women in moderate risk group (considered in this review):	biopsy the Pipelle sampler and/or Tao brush; Blind endometrial biopsy using the Pipelle sampler and/or Tao brush (not of interest in this review).	methods was undertaken in a setting as close as possible to normal clinic operation. For this reason, and to maximise clinician compliance with the study, a pragmatic design was used. After execution of the randomly assigned investigations the clinician could continue management of the patient unconstrained by the study, so that if further outpatient or inpatient investigations were indicated they could be offered in the normal way. For assigned ultrasound investigations the transvaginal method would be used wherever possible, but the investigation would be limited to abdominal if that was preferable for a particular woman. The recruiting research	Ultrasound: 16/162=10% Blind endometrial biopsy: 84/326=26% p=0.001 Abdominal discomfort after the investigation Proportion of women in the moderate risk group (all underwent a biopsy, N=280 answered the questionnaire) that reported experiencing abdominal discomfort at home after the investigation: Hysteroscopy: 31.5% No hysteroscopy: 26.3% Ultrasound: 31.6% No ultrasound: 26.6% Hysteroscopy versus no hysteroscopy p=0.418 Ultrasound versus no ultrasound p=0.434 Bleeding after the investigation Proportion of women in the moderate risk group (all	Detection bias Blinding of outcome assessment: High risk of bias (Outcomes of interest for this review were the participants' self-report of experiences etc. after the investigation, therefore, it was not possible to do blinding.) Attrition bias Incomplete outcome data: High risk of bias (69.5% of the eligible participants were recruited. Follow-up rate for questionnaire immediately after investigation was 100%; follow-up rate for questionnaire one day after investigation was 91.4% [298/326];

Study details	Participants	Tests	Methods	Outcomes and results	Comments
study To compare three outpatient methods of endometrial evaluation in terms of performance, patient acceptability and cost-effectiveness. **Study dates** January 1999 and May 2001 **Source of funding** HTA	Mean age: 45.2 (SD 0.26) years Age: 19-29y: 1% 30-34y: 2% 35-39y: 3% 40-44y: 36% 45-49y: 40% 50-54y: 17% 55-59y: 1% On oral contraception: 3% Sterilised: 38% On hormone replacement therapy: 9% Presenting complaint:		assistants spoke with the women before they were seen by their clinicians. If a woman consented to take part in the study, the next available randomisation envelope for the relevant stratification group (determined by age and menopausal status only) was attached to her recruitment forms. Before the woman was seen by the doctor, the recruiting research assistant described the study to the doctor, gave him or her an information sheet, explained that the woman had agreed to take part in the study, and gave the doctor an eligibility/recruitment form. This was to be completed by the doctor after he or she had spoken to the woman. This form was used to obtain the	underwent a biopsy, N=280 completed the questionnaire) reporting experiencing abdominal discomfort at home after the investigation: Hysteroscopy: 21.5% No hysteroscopy: 10.8% Ultrasound: 14.3% No ultrasound: 18.4% Hysteroscopy versus no hysteroscopy p=0.025 Ultrasound versus no ultrasound p=0.445 Feelings about the clinic visit Proportion of women in the moderate risk group (all underwent a biopsy, N=280 completed the questionnaire) expressing agreement with the statements about their feelings about the clinic visit(s): 1) I am more worried than before the clinic attendance Hysteroscopy: 12.9% No hysteroscopy: 12.8%	follow-up rate for questionnaire 10 months after investigation was 80.1% [261/326]; follow-up rate for questionnaire 24 months after investigation was 55.8% [182/326].) Reporting bias Selective reporting: Unclear risk of bias (The paper does not report statistical analyses on most of the outcomes of interest. The paper also reports outcomes for different subgroup stratification depending on the outcome.) Other bias Other sources of

Study details	Participants	Tests	Methods	Outcomes and results	Comments
Programme	Postmenopausal bleeding: 1% Heavy periods: 68% Postcoital bleeding: 8% Intermenstrual bleeding: 22% Irregular periods: 47% Bleeding on tamoxifen: 0% Pain: 3% Long periods: 2% Frequent periods: 1% Other: 2% **Inclusion Criteria**		clinician's consent and, since for premenopausal women under 40 years of age their group could be low or moderate risk, depending on specific clinical risk factors, to confirm the stratification/risk group. Randomisation Randomisation was undertaken to industry standard via a customised computer program. Allocation concealment Sealed "payslip style" envelopes were used containing the randomisation codes, shading in the inside of the slip ensured that the code could not be seen through with strong light. The slip was opened only if and when a clinician confirmed that the woman	Ultrasound: 9.8% No ultrasound: 15.6% 2) I do not really understand what the doctor told me about my bleeding Hysteroscopy: 15.1% No hysteroscopy: 13.7% Ultrasound: 15.7% No ultrasound: 13.3% 3) I wish I had not bothered Hysteroscopy: 3.6% No hysteroscopy: 5.2% Ultrasound: 6.8% No ultrasound: 2.1% 4) I would have liked more investigations of my bleeding problem Hysteroscopy: 18.3% No hysteroscopy: 25.6%	bias: Low risk of bias **Other information** No p-values or other statistical measures were reported comparing different tests for most of the outcomes of interest for this review. All women underwent biopsy.

Study details	Participants	Tests	Methods	Outcomes and results	Comments
	All women referred to the gynaecology outpatient clinic at the Royal Infirmary Edinburgh, Scotland, for abnormal uterine bleeding, but only if the managing clinician consented to the woman being approached about the study and the referral complaint of abnormal bleeding had been verified by that clinician. **Exclusion Criteria**		was eligible for the study (and the woman had consented). Blinding The nature of the interventions (their being procedures undertaken by the clinician and undergone by the woman) meant that blinding was not possible. Outcomes Women's experiences of endometrial evaluation were assessed prospectively by means of report forms completed immediately after the appointment. For each randomised investigation undergone, which may have been on that day or later, a separate report was completed immediately afterwards, covering explanation	Ultrasound: 21.7% No ultrasound: 22.0% 5) I feel reassured by the visit Hysteroscopy: 84.4% No hysteroscopy: 90.4% Ultrasound: 90.0% No ultrasound: 85.2% 6) I am glad I had the investigation Hysteroscopy: 90.6% No hysteroscopy: 98.5% Ultrasound: 94.0% No ultrasound: 95.0% How worthwhile women considered the visit Proportion of women in the moderate risk group (intention to treat) Hysteroscopy + biopsy: 67%	

Study details	Participants	Tests	Methods	Outcomes and results	Comments
	Pregnancy; difficulty reading or writing English.		received, time taken and reaction to that investigation. At the end of the initial (recruitment) appointment the woman completed a questionnaire report on her experience of the clinic visit. This included rationale for consultation with the doctor, information received before clinic attendance, prior investigations for abnormal bleeding and time issues. Acceptability in the short term was assessed by means of: 1) rating the unpleasantness (or not) of the investigation 2) reporting postinvestigation on the after-effects, abdominal discomfort and bleeding 3) reporting their feelings	Ultrasound + biopsy: 64% Blind endometrial biopsy: 61% Hysteroscopy + ultrasound + biopsy: 62% Women's self-report of outcome and health at 10 months postevaluation Proportion of women in the moderate risk group (all underwent biopsy, N=261 completed the questionnaire) reporting on the following: 1) Symptoms much improved Hysteroscopy: 42% No hysteroscopy: 38% Ultrasound: 38% No ultrasound: 42% 2) Satisfied with care (very true) Hysteroscopy: 65% No hysteroscopy: 50% Ultrasound: 62%	

Study details	Participants	Tests	Methods	Outcomes and results	Comments
			about the clinic visit (whether they are glad to have had the investigation, how reassured they are, and whether they would have liked more investigation) 4) ascertaining each woman's subjective judgement as to how worthwhile the clinic visit has been. In the clinic review questionnaire completed at home on the day after the last investigation, women were asked whether they had suffered from cramps, bleeding or discomfort at home after their clinic visit(s). The questionnaire asked for an answer overall for the clinic investigations, as where there had been multiple investigations (e.g. TVUS and	No ultrasound: 54% 3) Reassured by clinic attendance (very true) Hysteroscopy: 64% No hysteroscopy: 52% Ultrasound: 61% No ultrasound: 55% 4) Glad attended clinic (very true) Hysteroscopy: 71% No hysteroscopy: 65% Ultrasound: 70% No ultrasound: 67% 5) Worthwhile attending ("very" or "extremely") Hysteroscopy: 75% No hysteroscopy: 62% Ultrasound: 73% No ultrasound: 65% 6) Symptoms persisting (yes)	

Study details	Participants	Tests	Methods	Outcomes and results	Comments
			hysteroscopy plus biopsy) it would be impossible to attribute any after-effects to one or other investigation. A single abdominal discomfort variable has been created from the two after-effects of cramps and discomfort, being for each woman the more severe of the two ratings given. The response choice was not at all, hardly any, some, a lot or severe. The latter two response categories were combined and are reported here as a binary outcome. Feelings about the clinic visit were ascertained on the day after the last randomised investigation by agreeing or disagreeing with the following six statements: -I am more worried than	Hysteroscopy: 49% No hysteroscopy: 53% Ultrasound: 53% No ultrasound: 49% 7) Attendance failed to cure the problem (very true) Hysteroscopy: 27% No hysteroscopy: 26% Ultrasound: 27% No ultrasound: 26% 8) Would have liked more investigation (fairly/very true) Hysteroscopy: 20% No hysteroscopy: 35% Ultrasound: 22% No ultrasound: 32% Biopsy only*: 42%	

Study details	Participants	Tests	Methods	Outcomes and results	Comments
			before the clinic attendance -I do not really understand what the doctor told me about my bleeding -I wish I had not bothered -I would have liked more investigation of my bleeding problem -I feel reassured by the visit -I am glad I had the investigation The women were also asked to complete follow-up questionnaires, sent by mail, at 10 and 24 months. In these they were asked to report whether they still had symptoms, whether, since their initial appointment, they had visited their GP or been a hospital day case or	*Only reported on this outcome. Women's self-report of outcome and health at 24 months post-evaluation Proportion of women in the moderate risk group (all underwent biopsy, N=182 completed the questionnaire) reporting on the following: 1) Symptoms much improved Hysteroscopy: 60% No hysteroscopy: 55% Ultrasound: 61% No ultrasound: 53% 2) Satisfied with care (very true) Hysteroscopy: 73% No hysteroscopy: 53% Ultrasound: 67% No ultrasound: 60% 3) Reassured by clinic attendance (very true)	

Study details	Participants	Tests	Methods	Outcomes and results	Comments
			inpatient for the bleeding problem, whether they had attended any hospital gynaecology clinic, how they felt about their care at the time of recruitment, and how they would feel if they required further investigations in the future.	Hysteroscopy: 57% No hysteroscopy: 49% Ultrasound: 61% No ultrasound: 46% 4) Glad attended clinic (very true) Hysteroscopy: 73% No hysteroscopy: 61% Ultrasound: 74% No ultrasound: 61% 5) Worthwhile attending ("very" or "extremely") Hysteroscopy: 71% No hysteroscopy: 62% Ultrasound: 68% No ultrasound: 65% 6) Symptoms persisting (yes) Hysteroscopy: 42% No hysteroscopy: 48%	

Study details	Participants	Tests	Methods	Outcomes and results	Comments
				Ultrasound: 44% No ultrasound: 46% 7) Attendance failed to cure the problem (very true) Hysteroscopy: 27% No hysteroscopy: 28% Ultrasound: 29% No ultrasound: 26% 8) Would have liked more investigation (fairly/very true) Hysteroscopy: 16% No hysteroscopy: 31% Ultrasound: 17% No ultrasound: 29% Biopsy only*: 38% *Only reported on this outcome.	

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr>
<td>Full citation

Taylor, S., Jones, S., Dixon, A. M., O'Donovan, P., Evaluation of ultrasound in an outpatient hysteroscopy clinic: Does it alter management in premenopausal women?, Gynaecological Endoscopy</td>
<td>Sample size

n = 219

(n=196 analysed, 23 excluded:

8 women did not have a scan before the hysteroscopy

15 women did have a scan, but did not have hysteroscopy for the following reasons - 5 inappropriate referrals, 2 sx improved, 3 needed a laparotomy, 5 hysteroscopies unsuccessful owing to</td>
<td>Tests

Index Test

2D transvaginal ultrasound scan

Reference Standard

Hysteroscopy</td>
<td>Methods

Patients were seen at a "one-stop" clinic where, immediately before the hysteroscopy, they were scanned by an ultrasonographer. This involved a transabdominal scan, with a full bladder, followed by a transvaginal scan, enabling a detailed assessment of i) the outline of the the uterine cavity; ii) endometrial thickness; iii)abnormal endometrial morphology; iv) myometrial pathology, such as fibroids >2cm diameter or possible adenomyosis, and v) adnexal abnormalities

The ultrasound report was taken by the patient to the hysteroscopy suite where</td>
<td>Results

2D-TVUS versus hysteroscopy

a) Polyps
<table>
<tr><th></th><th>Confirmed polyps</th><th>No polyps</th><th>Total</th></tr>
<tr><td>Polyps in index test</td><td>11</td><td>8</td><td>19</td></tr>
<tr><td>No polyps in index test</td><td>23</td><td>154</td><td>177</td></tr>
<tr><td>Total</td><td>34</td><td>162</td><td>196</td></tr>
</table>
Sensitivity 32.35%* (95% CI 17.4%-50.5%)

Specificity 95.06%* (95% CI 90.5%-97.8%)

Positive likelihood ratio 6.55* (95% CI 2.85-15.06)

Negative likelihood ratio 0.71* (95% CI 0.56-0.90)

Prevalence of polyps 17%.</td>
<td>Limitations

QUADAS-2 a quality assessment tool for diagnostic accuracy studies:

Patient Selection

A. Risk of Bias

Was a consecutive or random sample of patients enrolled? Unclear (not reported)

Was a case-control design avoided? Yes

Did the study avoid inappropriate exclusions? Unclear (lack of information on exclusion criteria)

Could the selection of patients have</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>, 10, 173-178, 2001

Ref Id

548456

Country/ies where the study was carried out

UK

Study type

Retrospective cohort study

Aim of the study

To asses the role of ultrasound with respect to</td>
<td>cervical stenosis)

Characteristics

No details provided

Inclusion Criteria

Premenopausal women
with abnormal uterine bleeding

Exclusion Criteria

None specified</td>
<td></td>
<td>it was seen by the doctor before the hysteroscopy was started. In each case, the procedure was performed using a 2.5mm semirigid Storz fibreoptic scope with saline distention. The operator was either a consultant or a specialist registrar working under supervision.

Local anaesthetic was applied to the anterior lip of the cervix only, in order to enable the use of a tenaculum. In cases where an endometrial biopsy was taken, a pipelle sampling device was used. After the hysteroscopy, both hysteroscopy and ultrasound findings were discussed with the patient, and a management plan recorded.</td>
<td>b) Suspicious focal thickening
<table>
<tr><td></td><td>Suspicious in reference standard test</td><td>Not suspicious</td><td>Total</td></tr>
<tr><td>Suspicious in index test</td><td>0</td><td>12</td><td>12</td></tr>
<tr><td>Not suspicious in index test</td><td>6</td><td>178</td><td>184</td></tr>
<tr><td>Total</td><td>6</td><td>190</td><td>196</td></tr>
</table>
Sensitivity 0%* (95% CI 0%-45.9%)

Specificity 93.68%* (95% CI 89.2%-96.7%)

Positive likelihood ratio 0.00

Negative likelihood ratio 1.07* (95% CI 1.03-1.11)

Prevalence of suspicious focal thickening 3.1%.</td>
<td>introduced bias? Unclear risk

B. Concerns regarding applicability: All were premenopausal women with abnormal uterine bleeding, however, the proportion of women with HMB not reported.

Are there concerns that the included patients and setting do not match the review question? High concern

Index Test

A. Risk of Bias

Were the index test results interpreted without knowledge of the results of the reference standard?</td>
</tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
management decisions in premenopausal women with abnormal uterine bleeding attending an outpatient hysteroscopy clinic. **Study dates** September 1996-October 1997 **Source of funding** Not stated				*Calculated by the NGA technical team	Yes If a threshold was used, was it pre-specified? No. Not clearly defined. Could the conduct or interpretation of the index test have introduced bias? High risk B. Concerns regarding applicability: Are there concerns that the index test, its conduct, or interpretation differ from the review question? Low concern Reference Standard A. Risk of Bias Is the reference standards likely to

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index tests? No Could the reference standard, its conduct, or its interpretation have introduced bias? High risk B. Concerns regarding applicability Are there concerns that the target condition as defined by the reference standard does not match the question? Low concern Flow and Timing A. Risk of Bias

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					Was there an appropriate interval between index test and reference standard? Yes Did all patients receive the same reference standard? Yes Were all patients included in the analysis? No, 23/219 dropped out, but explanations for all the dropouts were given. Could the patient flow have introduced bias? Unclear risk **Other information**
Full	**Sample size**	**Tests**	**Methods**	**Results**	**Limitations**

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>citation

Vercellini, P., Cortesi, I., Oldani, S., Moschetta, M., De Giorgi, O., Crosignani, P. G., The role of transvaginal ultrasonography and outpatient diagnostic hysteroscopy in the evaluation of patients with menorrhagia, Human Reproduction, 12, 1768-1771,</td>
<td>n=793

(n=770 analysed, 13 cases hysteroscopy not completed as not tolerated, 10 complete visualisation of cavity prevented by interuterine bleeding, 15 cases biopsy refused, 17 cases quantity of mucosa insufficient for pathologist to make diagnosis)

Characteristics

Mean age: 41.5 + 7.8

Nullipara: 148 (18.7%)</td>
<td>Index Test

2D transvaginal ultrasound scan (2D-TVUS)

Reference Standard

Diagnostic hysteroscopy (with histopathology)</td>
<td>Ultrasonography was performed by gynaecologists independently of the phase of the cycle using Ansaldo AU 440 (Ansaldo, Genoa, Italy)or AU 580 synchronous (Hitachi, Tokyo, Japan) equipment and a transvaginal transducer of 6.5MHz. The endometrial cavity outline was studied from the internal os to the uterine fundus in sagittal and coronal sections. The ultrasound finding was considered abnormal when the ultrasonographer visualised a lesion inside the cavity or when the maximum endometrial thickness measured in the sagittal plane according to the technique of Fleischer et al was >14 mm. Doubtful sonograms with</td>
<td>2D-TVUS versus hysteroscopy

a) Any abnormality
<table>
<tr><th></th><th>Confirmed uterine abnormality</th><th>No uterine abnormality</th><th>Total</th></tr>
<tr><td>Any abnormality in index test</td><td>426</td><td>44</td><td>470</td></tr>
<tr><td>No abnormality in index test</td><td>19</td><td>281</td><td>300</td></tr>
<tr><td>Total</td><td>445</td><td>325</td><td>770</td></tr>
</table>
Sensitivity 96% (95% CI 93.4%-97.4%*)

Specificity 86% (95% CI 82.3%-90.0%*)

Positive likelihood ratio 7.07* (95% CI 5.37-9.31)

Negative likelihood ratio 0.05* (95% CI 0.03-0.08)

Prevalence of abnormality 58%.</td>
<td>QUADAS-2 a quality assessment tool for diagnostic accuracy studies:

Patient Selection

A. Risk of Bias

Was a consecutive or random sample of patients enrolled? Unclear (not reported)

Was a case-control design avoided? Yes

Did the study avoid inappropriate exclusions? No, excluded patients with IUD or hormone use, less generalisable

Could the selection of patients have introduced bias? High risk</td>
</tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
1997 **Ref Id** 548488 **Country/ies where the study was carried out** Italy **Study type** Prospective cohort study **Aim of the study** To verify the reliability of transvaginal	**Inclusion Criteria** Premenopausal women (FSH <30 mIU/ml) referred for abnormal bleeding. All the women with uterine volume less than 12-week pregnancy, iron deficiency anaemia, and menstrual score >100 and who underwent a complete physical examination, transvaginal ultrasonograpgy		findings neither definitively negative nor positive due to poor visualisation and/or difficult interpretation were considered abnormal. Submucosal myoma was diagnosed at ultrasonography in the presence of a nodular formation with well defined margins, heterogenous structure and varying echogeneity, which displaced the endometrial lining. Hysteroscopy was performed in the same or subsequent menstrual cycle, preferably in the proliferative phase, wit ha rigid 30 degree hysteroscope and diagnostic sheeth of 5mm diameter. Thirty minutes before the proceedure, 0.5mg atropine was injected i.m. Hysteroscopy was always carried out in sterile conditions after	*Calculated by the NGA technical team. Sensitivity and specificity without 95% CI reported by the paper for submucosal fibroids, polyps, and endometrial hyperplasia, however, not enough data to form 2x2 table and calculate LR+ and LR-.	B. Concerns regarding applicability: Are there concerns that the included patients and setting do not match the review question? Low concern. Index Test A. Risk of Bias Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified? Yes Could the conduct or interpretation of the index test have introduced bias? Low

Study details	Participants	Tests	Methods	Outcomes and results	Comments
ultrasonography in diagnosis of intrauterine diseasean d in evaluation of the operability of submucosal myomas, and to determine the feasibility, acceptability and validity of hysteroscopy in menorrhagic women **Study dates**	, and outpatient hysteroscopy with endometrial biopsy, were included in the study. **Exclusion Criteria** Patients with an IUD, who had received hormonal treatment in the last 3 months (6 months for GnRh), or who have already undergone D&C or diagnostic or operative hysteroscopy were excluded from this analysis.		careful cleansing of external genitalia, vagina, and cervix iwth a povidone-iodine antiseptic solution. The investigation was postponed if an acute cervico-vaginal infection was present. Only in women with a history of previous pelvic inflammatory disease was a single prophylactic 2g dose of cefoxitin injected before hysteroscopy. Normal saline or a urological solution of 2.7% sorbitol and 0.54% mannitol was used to dilate the uterine cavity, infused by a pneumatic cuff under manometric control at a pressure of 100-120 mmHg. For illumination, a cold light source of high intensity and fibre optic cable was used. All the procedures were monitored using an endoscopic single-chip		risk B. Concerns regarding applicability Are there concerns that the index test, its conduct, or interpretation differ from the review question? Low concern Reference Standard A. Risk of Bias Is the reference standards likely to correctly classify the target condition? Yes. Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear Could the reference

Study details	Participants	Tests	Methods	Outcomes and results	Comments
July 1991-July 1996 **Source of funding** Not stated			video camera and the images were projected onto a monitor visible to both gynaecologist and patient. Paracervical anaesthesia was administered only for comparative clinical studies or at the specific request of the patient. During hysteroscopy the patients were constantly attended and encouraged by a nurse and the gynaecologist explained every manouvre performed and described the progress of the investigation, commenting on the images projected on the monitor. Hysteroscopic diagnosis of myoma was made from the presence of a firm intracavitary formation with thin or no endometrial covering and superficial large blood vessels. The intramural extension of		standard, its conduct, or its interpretation have introduced bias? Unclear risk B. Concerns regarding applicability Are there concerns that the target condition as defined by the reference standard does not match the question? Low concern Flow and Timing A. Risk of Bias Was there an appropriate interval between index test and reference standard? Yes Did all patients receive the same reference standard? Yes

Study details	Participants	Tests	Methods	Outcomes and results	Comments
			sessile tumours was determined by hysteroscopically by observing the angle of the fibroid with the myometrium at the uterine wall attachment. An endometrial polyp was diagnosed when a soft intracavitrary formation was observed that was easily mobilised and covered by a mucosa with endometrial glands and no distended vascular network. Endometrial hyperplasia was defined as a thick, hypervascular, friable mucosa that was mamillated or polypoid. At the end of the proceedure an intrauterine biospy was obtained with a small cutting curette. Expert operators performed all the ultrasonographic and hysteroscopic procedures and reported the findings in detail on pre-printed		Were all patients included in the analysis? No, 2.9% (23/793) dropped out, but explanations for all the dropouts were provided. Could the patient flow have introduced bias? Low risk **Other information**

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td>forms. Submucosal myomas were subdivided independently at ultrasonography and hysteroscopy into tumors with intramural extension <50% (operable endoscopically) or >50% (no operable endoscopically).</td><td></td><td></td></tr>
<tr><td>Full citation

Nanda, S., Chadha, N., Sen, J., Sangwan, K., Transvaginal sonography and saline infusion sonohysterography in</td><td>Sample size

n = 50

Characteristics

Aged 30-50, hospitalised for hysterectomy for benign gynaecological indications

Inclusion Criteria

Abnormal</td><td>Tests

Index test

2D transvaginal ultrasound scan (2D-TVUS)

Reference standard</td><td>Methods

All patients had undergone diagnostic endometrial curettage before admission. The indications for surgery were dysfunctional uterine bleeding (23 Patients) and fibroid uterus (27 patients). TVUS was performed using a broad-band endovaginal probe of 7.5MHz.

Each patient underwent</td><td>Results

2D-TVUS versus histopathology (hysterectomy)

a) Endometrial polyp
<table><tr><td></td><td>Confirmed polyp</td><td>No polyp</td><td>Total</td></tr><tr><td>Polyp in index test</td><td>2</td><td>0</td><td>2</td></tr><tr><td>No polyp in index test</td><td>1</td><td>47*</td><td>48</td></tr><tr><td>Total</td><td>3</td><td>47</td><td>50</td></tr></table></td><td>Limitations

QUADAS-2 a quality assessment tool for diagnostic accuracy studies:

Patient Selection

A. Risk of Bias

Was a consecutive or random sample of patients enrolled? Unclear (not reported)</td></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>the evaluation of abnormal uterine bleeding, Australian and New Zealand Journal of Obstetrics and Gynaecology, 42, 530-534, 2002

Ref Id

548500

Country/ies where the study was carried out

India</td>
<td>uterine bleeding

Exclusion Criteria

Not specified</td>
<td>Histopathology (hysterectomy)</td>
<td>hysterectomy within a week of TVUS and SIS. After being removed, the uterus was opened and the left margin and fundus, and any lesions present in the uterine cavity were noted. Specimens were subsequently examined histologically. The pathologist was unaware of the ultrasound results. The findings of the pathologist were compared with those obtained at TVUS and SIS.</td>
<td>Sensitivity 66.7% (95% CI 9.4%-99.2%*)

Specificity 100% (95% CI 92.5%-100%*)

Positive likelihood ratio inf

Negative likelihood ratio 0.3 (95% CI 0.07-1.65*)

Prevalence of polyps 6%

b) Submucosal fibroid
<table>
<tr><th></th><th>Confirmed submucosal fibroid</th><th>No submucosal fibroid</th><th>Total</th></tr>
<tr><td>Submucosal fibroid in index test</td><td>14</td><td>1</td><td>15</td></tr>
<tr><td>No submucosal fibroid in index test</td><td>5</td><td>30*</td><td>35</td></tr>
</table>
</td>
<td>Was a case-control design avoided? Yes

Did the study avoid inappropriate exclusions? Unclear, exclusions not specified in methods

Could the selection of patients have introduced bias? Unclear risk

B. Concerns regarding applicability: All premenopausal women with abnormal uterine bleeding, however, the proportion with HMB not reported.

Are there concerns that the included patients and setting do not match the review</td>
</tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
Study type Prospective cohort study **Aim of the study** To evaluate the accuracy of transvaginal sonography and saline infusion sonohysterography (SIS) in diagnosing submucosal fibroids and endometri				<table><tr><td>Total</td><td>19</td><td>31</td><td>50</td></tr></table> Sensitivity 70% (95% CI 48.8%-90.9%*) Specificity 96.7% (95% CI 83.3%-99.9%*) Positive likelihood ratio 21.2 (95% CI 3.25-160.02*) Negative likelihood ratio 0.3 (95% CI 0.13-0.58*) Prevalence of submucosal fibroids 38%	question? High concern Index Test A. Risk of Bias Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified? No, not clearly defined Could the conduct or interpretation of the index test have introduced bias? High risk B. Concerns regarding applicability: The paper did not report who interpreted the

Study details	Participants	Tests	Methods	Outcomes and results	Comments
al polyps in the patients of AUB **Study dates** Not stated **Source of funding** Not stated					index test or what was the level of experience of the person(s). Are there concerns that the index test, its conduct, or interpretation differ from the review question? Unclear concern Reference Standard A. Risk of Bias Is the reference standards likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index tests? Yes Could the reference

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					standard, its conduct, or its interpretation have introduced bias? Low risk B. Concerns regarding applicability Are there concerns that the target condition as defined by the reference standard does not match the question? Low concern Flow and Timing A. Risk of Bias Was there an appropriate interval between index test and reference standard? Yes Did all patients receive the same reference standard? Yes

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>Were all patients included in the analysis? Yes

Could the patient flow have introduced bias? Low risk

Other information</td></tr>
<tr><td>Full citation

Dueholm, M., Forman, A., Jensen, M. L., Laursen, H., Kracht, P., Transvaginal sonography combined</td><td>Sample size

n = 452 included in whole study

(n = 189 underwent operative follow up and this cohort was used as the reference standard to TVUS)

Characteristics

Mean age 44.2</td><td>Tests

Index Test

2D transvaginal ultrasound scan (2D-TVUS)

Reference Test</td><td>Methods

TVUS

Transvaginal ultrasound scan was performed using a 5-7.5 MHz transvaginal transducer. Measure ment of the endometrium included both endometrial layers (double layer). The contours of the endometrial cavity were studied from the internal os to the fundus in the longitudinal and transverse planes. The</td><td>Results

2D-TVUS versus histopathology (operative hysteroscopy or hysterectomy)

a) Polyp or submucosal myoma
<table><tr><td></td><td>Confirmed polyp/myoma</td><td>No polyp/ myoma</td><td>Total</td></tr><tr><td>Polyp/myoma in index test</td><td>108</td><td>27</td><td>82</td></tr><tr><td>No polyp/myoma in index test</td><td>10</td><td>44</td><td>107</td></tr><tr><td>Total</td><td>118</td><td>71</td><td>189</td></tr></table></td><td>Limitations

QUADAS-2 a quality assessment tool for diagnostic accuracy studies:

Patient Selection

A. Risk of Bias

Was a consecutive or random sample of patients enrolled? Unclear (not reported)

Was a case-control</td></tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
with saline contrast sonohysterography in evaluating the uterine cavity in premenopausal patients with abnormal uterine bleeding, Ultrasound in Obstetrics and Gynecology, 18, 54-61, 2001 **Ref Id** 548501 **Country/ies where the study was**	+ 5.7 (range, 22-55) years **Inclusion Criteria** Abnormal uterine bleeding (menorrhagia, metrorrhagia, and menometrorrhagia), were premenopausal (defined as being within 1 year of arrest of bleeding) and were below the age of 55 years. Patients on HRT and who had an indefinite menopausal status were	Histopathology (via operative hysteroscopy or hysterectomy)	midline echo was considered to be normal when a straight regular endometrial lining, with well-defined margins and without echodense foci, was found. When the midline echo was disturbed, polyps were defined as echogenic masses with a fairly homogenous texture without disruption of the myometrial-endometrial interface, while submucosal myomas had an inhomogeneous texture with possible continuity with the myometrium. Myomas disturbing the midline echo or exceeding a diameter of 15mm in the myometrium were counted. Submucosal myomas were classified according to the European	Sensitivity 92% (95% CI 85%-96%) Specificity 62% (95% CI 50%-73%) Positive likelihood ratio 2.41* (95% CI 1.78-3.26) Negative likelihood ratio 0.14* (95% CI 0.07-0.25) Prevalence of polyp/myoma 62% The paper reports also on "possible abnormality" in index test. In order to calculate diagnostic accuracy, "possible abnormalities" are grouped together with "abnormalities".	design avoided? Yes Did the study avoid inappropriate exclusions? No, participants with a IUD were excluded, less generalisable Could the selection of patients have introduced bias? High risk B. Concerns regarding applicability: All women premenopausal with abnormal uterine bleeding, however, the proportion of women with HMB not reported. Are there concerns that the included patients and setting do not match the review

Study details	Participants	Tests	Methods	Outcomes and results	Comments
carried out Denmark **Study type** Prospectiv e cohort study **Aim of the study** To evaluate whether saline contrast sonohyster ography (SCSH) adds additional information to that obtained by transvagin	included when the duration of HRT was less than 3 years. **Exclusion Criteria** <35 years of age with a +ve chlamydia test, intrauterine contraceptive device, cardiopulmonar y disease, pregnancy, or infection-related bleeding disorders.		Society of Gynaecologic Endoscopy classificatio: type 0 (pedunculated submucosal myomaswithout intramural extension), type I (sessile and with an intramural part of less than 50%) and type II (with an intramural part of 50% or more). The investigators classified the quality of the examinations as sufficient or insufficient for evaluation of the uterine cavity. Operative hysteroscopy/hysterectom y During operative hysteroscopy or hysterectomy the uterine cavity was described according to a standard form. The number of polyps and myomas was recorded and the mean		question? High concern Index Test A. Risk of Bias Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified? Yes Could the conduct or interpretation of the index test have introduced bias? Low risk B. Concerns regarding applicability: The paper did not report who interpreted the index test or what

Study details	Participants	Tests	Methods	Outcomes and results	Comments
al sonography for prediciting endometrial abnormality in premenapausal patients with abnormal uterine bleeding **Study dates** January 1st 1994-October 1st 1995 (centre 1) March 1st 1995-October 1st 1995 (centre 2)			diameter of the largest measured. Again myoma were classified according to the European Society of Gynaecologic Endoscopy classification. Operative hysteroscopy using a retroscope was performed according to general guidelines. Three experienced hysteroscopists performed these procedures. The resected material was sent for pathological examination and curettage was performed. At hysterectomy the presence and size of abnormalities and the percentage of myomas in the uterine cavity were described. The operative procedures were performed within 3 months of the sonographic examinations (abstract states 4 months -		was the level of experience of the person(s) Are there concerns that the index test, its conduct, or interpretation differ from the review question? Unclear concern Reference Standard A. Risk of Bias Is the reference standards likely to correctly classify the target condition? Yes. Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear, interpreted by a pathologist, however

Study details	Participants	Tests	Methods	Outcomes and results	Comments
Source of funding Not reported			discrepancy). Hysterectomy was performed in 74 patients, while 79 underwent hysteroscopic resection of polyps, myomas or endometrium.		no documentation whether he was aware of the results or not Could the reference standard, its conduct, or its interpretation have introduced bias? Unclear risk B. Concerns regarding applicability Are there concerns that the target condition as defined by the reference standard does not match the question? Low concern Flow and Timing A. Risk of Bias Was there an appropriate interval between index test and reference

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					standard? No. The interval was 4 months between the tests. Did all patients receive the same reference standard? Yes, however method of retrieval was different in patients, hysteroscopy vs. hysterectomy. Were all patients included in the analysis? Yes, all patients who underwent surgical intervention were analysed. Could the patient flow have introduced bias? High risk **Other information** For TVUS vs histopathology, the paper reports a 3 x 3

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>table is used with an added indicator of "possible abnormality". Abnormalities and possible abnormalities combined under same indicator to calculate sensitivity and specificity.</td></tr>
<tr><td>Full citation

Krampl, E., Bourne, T., Hurlen-Solbakken, H., Istre, O., Transvaginal ultrasonography sonohysterography</td><td>Sample size

n = 100

(n = 88 for analysis, as information on 12 participants could not be extracted by one or more of the 2 methods)

Characteristics

P</td><td>Tests

Index test

2D transvaginal ultrasound scan (2D-TVUS; hysteroscopy</td><td>Methods

The assessment of the uterine cavity consisted of 3 steps:

Transvaginal ultrasound scan

Sonohysterography

Operative hysterography

TVUS

Steps 1 and 2 were carried out in the</td><td>Results

1) 2D-TVUS versus histopathology

a) Thickened endometrium
<table><tr><td></td><td>Confirmed thickened endometrium</td><td>No thickened endometrium</td><td>Total</td></tr><tr><td>Thickened endometrium in index test</td><td>3</td><td>9*</td><td>12</td></tr><tr><td>No thickened</td><td>6*</td><td>70*</td><td>76</td></tr></table></td><td>Limitations

QUADAS-2 a quality assessment tool for diagnostic accuracy studies:

Patient Selection

A. Risk of Bias

Was a consecutive or random sample of patients enrolled? Unclear (not reported)</td></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>and operative hysteroscopy for the evaluation of abnormal uterine bleeding, Acta Obstetricia et Gynecologica Scandinavica, 80, 616-622, 2001

Ref Id

548502

Country/ies where the study was carried out</td>
<td>remenopausal (n=89) Postmenopausal (n=11)

Age 43.8y + 5.3 (range 29-54 56.6y + 7.4 (48-73)

Hormonal Tx 30.4%

54.6%

Inclusion Criteria

Abnormal uterine bleeding

Exclusion Criteria

An endometrial biopsy within the past year, large multiple fibroids causing</td>
<td>Reference Standard

Histopathology (via hysteroscopy)</td>
<td>outpatient clinic by the same operators.

For transvaginal ultrasonography a 6 MHz transducer or a 7.5MHz transducer was used. The uterine position was recorded. The anterior/posterior diameter of the uterus, cavity length from the fundus to the isthmus and double layer endometrial thickness were measured in the longitudinal plane as previously described. If polyps and fibroids were present, the largest diameters perpendicular to each other were measured. Sonohysterography was then performed.

Endometrium: normal/abnormal. In premenopausal women, double-layer endometrium</td>
<td>
<table>
<tr><td>endometrium in index test</td><td></td><td></td><td></td></tr>
<tr><td>Total</td><td>9</td><td>79</td><td>88</td></tr>
</table>
Sensitivity 33.3% (95% CI 7.5%-70.1%)

Specificity 88.6% (95% CI 79.5%-94.7%)

Positive likelihood ratio 2.93* (95% CI 0.96-8.88)

Negative likelihood ratio 0.75* (95% CI 0.47-1.20)

Prevalence of thickened endometrium 10%

b) Focal pathology (polyps/fibroids)#
<table>
<tr><td></td><td>Confirmed focal pathology</td><td>No focal pathology</td><td>Total</td></tr>
<tr><td>Focal pathology in index test</td><td>5*</td><td>5*</td><td>10</td></tr>
<tr><td>No focal pathology</td><td>16*</td><td>62*</td><td>78</td></tr>
</table>
</td>
<td>Was a case-control design avoided? Yes

Did the study avoid inappropriate exclusions? Yes

Could the selection of patients have introduced bias? Unclear risk

B. Concerns regarding applicability:

No % breakdown of patients with AUB that have HMB, i.e. is the population >66% is unclear. Additionally, 11% of population postmenopausal.

Are there concerns that the included patients and setting do not match the</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>Norway (collaboration with U.K.)

Study type

Prospective cohort study

Aim of the study

To evaluate the diagnostic accuracy or transvaginal ultrasonography, sonohysterography and hysterosco</td>
<td>discomfort and patients considered medically unfit for general or spinal anaesthesia.</td>
<td></td>
<td>thickness of less than 12mm and single-layer endometrium thickness of less than 6mm were arbitrarily considered to be normal, and thicker endometrium was classified as abnormal. In postmenopausal women 4mm was used as a cut-off level to define normality. Irregularly thickened hyperechogenic endometrium was considered to be suggestive of endometrial carcinoma. If endometrium was not clearly visible, the patient was excluded from analysis.

Focal pathology: present/not present. Focal lesions of variable shape with an echo pattern similar to the endometrium were classified as polyps. Well defined round</td>
<td>
<table>
<tr><td>in index test</td><td></td><td></td><td></td></tr>
<tr><td>Total</td><td>21</td><td>67</td><td>88</td></tr>
</table>
Sensitivity 23.5% (95% CI 6.8%-49.9%)

Specificity 93.0% (95% CI 78.0%-97.7%)

Positive likelihood ratio 3.19* (95% CI 1.02-9.96)

Negative likelihood ratio 0.82* (95% CI 0.64-1.06)

Prevalence of focal pathology 24%

2) Hysteroscopy versus histopathology

a) Thickened endometrium
<table>
<tr><td></td><td>Confirmed thickened endometrium</td><td>No thickened endometrium</td><td>Total</td></tr>
<tr><td>Thickened endometrium in index test</td><td>2</td><td>10*</td><td>12</td></tr>
<tr><td>No thickened</td><td>7*</td><td>69*</td><td>76</td></tr>
</table>
</td>
<td>review question? High concern

Index Test

A. Risk of Bias

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was used, was it pre-specified? Yes

Could the conduct or interpretation of the index test have introduced bias? Low risk

B. Concerns regarding applicability: The test was conducted and interpreted by 2 of the</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>py in patients presenting with abnormal uterine bleeding.

Study dates

Not reported

Source of funding

Not reported</td>
<td></td>
<td></td>
<td>structures were classified as fibroids. The fibroid position were recorded.

Hysteroscopy

Operative hysteroscopy was performed within 7 days in all cases. It was either performed or supervised by an experienced hysteroscopic surgeon, who had no knowledge of the ultrasonography result. A 10mm restroscope was used. The cavity was first evaluated visually. Focal lesions were completely removed and measured. Two large endometrial biopsies (depth 4mm) were taken by retroscope, one from the anterior wall and one from the posterior wall. Specimens obtained were immediately embedded in</td>
<td>
<table>
<tr><td>endometrium in index test</td><td></td><td></td><td></td></tr>
<tr><td>Total</td><td>9</td><td>79</td><td>88</td></tr>
</table>
Sensitivity 22.2% (95% CI 2.8%-60.6%)

Specificity 87.3% (95% CI 78.0%-93.8%)

Positive likelihood ratio 1.76* (95% CI 0.45-6.79)

Negative likelihood ratio 0.89* (95% CI 0.062-1.28)

Prevalence of abnormal endometrium 10%

b) Focal pathology (polyps/fibroids)#
<table>
<tr><td></td><td>Confirmed focal pathology</td><td>No focal pathology</td><td>Total</td></tr>
<tr><td>Focal pathology in index test</td><td>21*</td><td>9*</td><td>30</td></tr>
<tr><td>No focal pathology</td><td>0*</td><td>58*</td><td>58</td></tr>
</table>
</td>
<td>authors in the paper, it is not clear the experience of the physicians at the time of publishing the paper in 2001.

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Unknown concern

Reference Standard

A. Risk of Bias

Is the reference standards likely to correctly classify the target condition? Yes.

Were the reference standard results interpreted without knowledge of the results of the index</td>
</tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
			formaldehyde and sent for histological examination at the department of gynaecological pathology. Endometrium: the endometrium was considered abnormal if one or more of the following criteria were present: focal or diffuse increase of the endometrial thickness, irregularity of the endometrial surface, button-like proliferations, dilated glandular opening of yellowish colouror large superficial vessels. Friable necrotic areas and an irregular surface with irregular vascularisation were classified as endometrial carcinoma. Focal pathology: focal lesions, which were firm and round, were classified fibroids. Any pedunculated	<table><tr><td>in index test</td><td></td><td></td><td></td></tr><tr><td>Total</td><td>21</td><td>57</td><td>88</td></tr></table> Sensitivity 100% (95% CI 80.5%-100%) Specificity 87.3% (95% CI 77.3%-94.0%) Positive likelihood ratio 7.44* (95% CI 4.05-13.67) Negative likelihood ratio 0.00* Prevalence of focal pathology 24% #For focal pathology, the results are not clear. The data that the paper reports is limited: total numbers of focal pathology in index tests and in reference standard was reported, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were reported. The total numbers and sensitivity and specificity were used to calculate the 2x2 table from which LR+ and LR- with 95% CI could be calculated. However, there is a discrepancy between the reporting of PPV and NPV compared to the calculations done by the NGA technical team. Therefore, there is some doubt in the reporting of the results.	tests? Unclear, interpreted by a pathologist, however no documentation whether he was aware of the results or not Could the reference standard, its conduct, or its interpretation have introduced bias? Unclear risk B. Concerns regarding applicability Are there concerns that the target condition as defined by the reference standard does not match the question? Low concern Flow and Timing A. Risk of Bias Was there an

Study details	Participants	Tests	Methods	Outcomes and results	Comments
			lesion protruding into the uterine cavity, whihc did not fulfil these criteria, was classified as endometrial polyp	*Calculated by NGA technical team	appropriate interval between index test and reference standard? Yes Did all patients receive the same reference standard? Yes Were all patients included in the analysis? No, 12/100 patients were unable to be analysed, however text fully explains reasons for not being able to analyse. Could the patient flow have introduced bias? Unclear risk **Other information** For focal pathology, the results are not clear. The data that the paper reports is

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					limited: total numbers of focal pathology in index tests and in reference standard was reported, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were reported. The total numbers and sensitivity and specificity were used to calculate the 2x2 table from which LR+ and LR- with 95% CI could be calculated. However, there is a discrepancy between the reporting of PPV and NPV compared to the calculations done by the NGA technical team. Therefore, there is some doubt in the reporting of the results.

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr>
<td>Full citation

Cicinelli, E., Romano, F., Anastasio, P. S., Blasi, N., Parisi, C., Galantino, P., Transabdominal sonohysterography, transvaginal sonography, and hysteroscopy in the evaluation of submucos</td>
<td>Sample size

n=52

Characteristics

40-51 years old

Premenopausal

32 patients (67%) with Menometrorrhagia

No patients had pelvic inflammatory disease or Pap smear abnormalities

Inclusion Criteria

Premenopausal women hospitalised for</td>
<td>Tests

Index test

2D transvaginal ultrasound scan (2D-TVUS); hysteroscopy (outpatient)

Reference Standard

Histopathology (via hysterectomy)</td>
<td>Methods

Before surgery, all of the patients underwent diagnostic hysteroscopy, conventional transvaginal ultrasound, and transabdominal sonohysteroscopy over a period of no more than 4 days. Diagnostic hysteroscopy was performed using a thin, rigid endoscope without any premedication. We obtained uterine distention by insufflating carbon dioxide with the hysteroflator, and the procedure was performed using a 250-W cold light source.

The ultrasound investigations consisted of conventional transvaginal</td>
<td>Results

1) 2D-TVUS versus histopathology (hysterectomy)

a) Myoma
<table>
<tr><td></td><td>Confirmed myoma</td><td>No myoma</td><td>Total</td></tr>
<tr><td>Myoma in index test</td><td>9</td><td>1</td><td>10</td></tr>
<tr><td>No myoma in index test</td><td>1</td><td>41</td><td>42</td></tr>
<tr><td>Total</td><td>10</td><td>42</td><td>52</td></tr>
</table>
Sensitivity 90% (95% CI 55.5%-99.8%*)

Specificity 97.6% (95% CI 87.4%-99.9%*)

Positive likelihood ratio 37.80* (95% CI 5.39-265.03)

Negative likelihood ratio 0.1* (95% CI 0.02-0.66)

Prevalence of myoma 19.23%</td>
<td>Limitations

QUADAS-2 a quality assessment tool for diagnostic accuracy studies:

Patient Selection

A. Risk of Bias

Was a consecutive or random sample of patients enrolled? Unclear (not reported)

Was a case-control design avoided? Yes

Did the study avoid inappropriate exclusions? Unclear, no exclusions reported, inclusion criteria not well defined.</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>al myomas, Obstet GynecolObstetrics and gynecology, 85, 42-7, 1995

Ref Id

557723

Country/ies where the study was carried out

Italy

Study type

Prospective cohort study

Aim of the</td>
<td>hysterectomy for benign gynecologic indications.

Exclusion Criteria

None specified</td>
<td></td>
<td>scanning followed by transabdominal sonohysterography, using an Aloka680 echograph equipped with a 3.5-MHz transabdominal convex probe and a 7.5-MHz transvaginal probe.

All of the investigations were performed by personnel unaware of the findings of the other examinations. The hysteroscopic examinations used appropriate video equipment, and both the hysteroscopic and echographic images were recorded on video. All of the hysteroscopy and sonohysterography examinations were performed without holding the cervix uteri with a tenaculum.

Each patients underwent</td>
<td>b) Polyp
<table><tr><th></th><th>Confirmed polyp</th><th>No polyp</th><th>Total</th></tr><tr><td>Polyp in index test</td><td>0</td><td>0</td><td>0</td></tr><tr><td>No polyp in index test</td><td>1</td><td>51</td><td>52</td></tr><tr><td>Total</td><td>1</td><td>51</td><td>52</td></tr></table>Sensitivity 0.00%* (95% CI 0%-97.5%)

Specificity 100%* (95% CI 93.0%-100%)

Positive likelihood ratio n/a

Negative likelihood ratio 1.00 (95% CI 1.00-1.00)

Prevalence of polyp 1.92%

2) Hysteroscopy (outpatient) versus histopathology</td>
<td>Could the selection of patients have introduced bias? Unclear risk

B. Concerns regarding applicability: Only 67% of the sample had HMB.

Are there concerns that the included patients and setting do not match the review question? High concern

Index Test

A. Risk of Bias

Were the index test results interpreted without knowledge of the results of the reference standard? Yes

If a threshold was</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>study

To assess the usefulness of transabdominal sonohysterography in the diagnosis and evaluation of submucosal myomas.

Study dates

August 1993-April 1994

Source of funding

Not</td>
<td></td>
<td></td>
<td>hysterectomy within 7 days of her last examination. None received steroids or underwent dilation and curettage before hysterectomy. After surgical removal, the uterus was cut in a frontal plane passing through the uterine cavity, and any lesions were described carefully by a pathologist who was unaware of the clinical results. The pathologist was asked to measure the largest diameter of the myomas, define their location, and calculate the percent of tumor intracavity growth. The specimens were then placed in a 10% formol saline solution for subsequent histologic confirmation of the diagnosis of myoma.

At hysteroscopy,</td>
<td>(hysterectomy)

a) Myoma
<table><tr><td></td><td>Confirmed myoma</td><td>No myoma</td><td>Total</td></tr><tr><td>Myoma in index test</td><td>10</td><td>0</td><td>10</td></tr><tr><td>No myoma in index test</td><td>0</td><td>42</td><td>42</td></tr><tr><td>Total</td><td>10</td><td>42</td><td>52</td></tr></table>Sensitivity 100% (95% CI 69.2%-100%)

Specificity 100% (95% CI 91.6%-100%)

Positive likelihood ratio inf

Negative likelihood ratio 0.00

Prevalence of myoma 19.23%

b) Polyp</td>
<td>used, was it pre-specified? Yes

Could the conduct or interpretation of the index test have introduced bias? Low risk

B. Concerns regarding applicability: The paper did not report who interpreted the index test or what was the level of experience of the person(s)

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Unclear concern

Reference Standard

A. Risk of Bias</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>reported</td>
<td></td>
<td></td>
<td>submucosal myomas and other endouterine abnormalities were distinguished according to the criteria published by Hamou et al. At sonohysterography, myomas were distinguished from polyps based on the complete endoluminal location of the polyp and its motility during fluid injection, the less-echogenic nature of myomas in comparison with polyps or endometrium, and the possibility of recognizing a continuity between a myoma and the myometrium. These last criteria were also used for conventional transvaginal sonography.

The site of submucosal myoma was defined on the basis of its level in relation to the uterine</td>
<td>
<table>
<tr><td></td><td>Confirmed polyp</td><td>No polyp</td><td>Total</td></tr>
<tr><td>Polyp in index test</td><td>1</td><td>0</td><td>1</td></tr>
<tr><td>No polyp in index test</td><td>0</td><td>51</td><td>51</td></tr>
<tr><td>Total</td><td>1</td><td>51</td><td>52</td></tr>
</table>
Sensitivity 100% (95% CI 2.5%-100%)

Specificity 100% (95% CI 93.0%-100%)

Positive likelihood ratio inf

Negative likelihood ratio 0.00

Prevalence of polyp 1.92%

*Calculated by the NGA technical team.
</td>
<td>Is the reference standards likely to correctly classify the target condition? Yes

Were the reference standard results interpreted without knowledge of the results of the index tests? Yes

Could the reference standard, its conduct, or its interpretation have introduced bias? Low risk

B. Concerns regarding applicability

Are there concerns that the target condition as defined by the reference standard does not match the question? Low concern</td>
</tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
			cavity, the wall (anterior or posterior) and the side of implantation (right or left). The levels of the tumor sites were classified as follows: I, the lower half of the cervical canal; II, the upper half of the cervical canal; III, the supristhmic zone; IV, the corporal zone; and V, the fundal zone. The border between the corporal and fundal zones was used as an imaginary line passing through the tubal ostia. Care was taken to define the ingrowth of the myomas in the cavity, expressed as a percentage of the estimated size of the whole tumor.		Flow and Timing A. Risk of Bias Was there an appropriate interval between index test and reference standard? Yes Did all patients receive the same reference standard? Yes Were all patients included in the analysis? Yes. Could the patient flow have introduced bias? Low risk **Other information**
Full	**Sample size**	**Tests**	**Methods**	**Results**	**Limitations**

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>citation

Williams, C. D., Marshburn, P. B., A prospective study of transvaginal hydrosonography in the evaluation of abnormal uterine bleeding, Am J Obstet GynecolAmerican journal of obstetrics and gynecology, 179, 292-8, 1998</td>
<td>n=47

(n = 39 in analysis, 8 women didn't complete study, 4 were lost to follow up, 2 patients were scheduled for total abdominal hysterectomy after the closing date of the study, 1 uterus was morcellated during a total vaginal hysterectomy, and 1 patient refused hysteroscopy)

Characteristics

Mean age 38.5 years

92%</td>
<td>Index Test

2D transvaginal ultrasound scan (2D-TVUS)

Reference Standard

Histopathology (via hysteroscopy/hysterectomy)</td>
<td>All patients underwent 3 seperate studies:

1) routine vaginal probe ultrasonography

2) hydrosonography,

3) either hysteroscopy or hysterectomy.

TVUS

The participants first received a routing vaginal probe ultrasonographic examination by a sonographer who was blinded. The uterus was visualised longitudinally and axially and a measurement of myometrial and endometrial thicknessand echogenicity was noted. Gross lesions of the myometrium, endometrium, and adnexa were noted. The</td>
<td>2D-TVUS versus histopathology (hysteroscopy/hysterectomy)

a) Any endometrial abnormality
<table>
<tr><th></th><th>Confirmed abnormality</th><th>No abnormality</th><th>Total</th></tr>
<tr><td>Any abnormality in index test</td><td>8</td><td>2</td><td>10</td></tr>
<tr><td>No abnormality in index test</td><td>4</td><td>25</td><td>29</td></tr>
<tr><td>Total</td><td>12</td><td>27</td><td>39</td></tr>
</table>
Sensitivity 67% (95% CI 34.9%-90.1%*)

Specificity 93% (95% CI 75.7%-99.1%*)

Positive likelihood ratio 9.0* (95% CI 2.24-36.22)

Negative likelihood ratio 0.36* (95% CI 0.16-0.81)

Prevalence of endometrial abnormality 30.8%</td>
<td>QUADAS-2 a quality assessment tool for diagnostic accuracy studies:

Patient Selection

A. Risk of Bias

Was a consecutive or random sample of patients enrolled? Unclear (not reported)

Was a case-control design avoided? Yes

Did the study avoid inappropriate exclusions? Yes

Could the selection of patients have introduced bias? Unclear risk

B. Concerns regarding applicability:</td>
</tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
Ref Id 557724 **Country/ies where the study was carried out** U.S.A **Study type** Prospective cohort study **Aim of the study** To determine whether the intrauterine instillation	premenopausal 8% postmenopausal 72% black, 23% white, and 5% hispanic **Inclusion Criteria** Abnormal uterine bleeding that had not responded to appropriate medical therapy **Exclusion Criteria** Inability to undergo endovaginal ultrasonography, refusal to undergo hysteroscopy,		sonographer then recorded the findings on a datasheet. Next, a physician who was blinded performed the hydrosonography. This was either a 3rd or 4th year obstetrics-gynaecology resident physician who was supervised by an attending physician. After an open-sided vaginal speculum was inserted, the vagina and cervix were cleansed with an antiseptic solution. Hysteroscopy A diagnostic hysteroscopy was then performed during the same visit in the case that no lesions were found during ultrasonographic studies. Diagnostic hysteroscopy was performed with use of of a 5mm hysteroscope	*Calculated by the NGA technical team.	The proportion of patients with HMB is not specified, 92% premenopausal with abnormal uterine bleeding. Are there concerns that the included patients and setting do not match the review question? High concern Index Test A. Risk of Bias Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified? No (not reported)

Study details	Participants	Tests	Methods	Outcomes and results	Comments
of saline solution during transvaginal ultrasonographic imaging (hydrosonography) improves the diagnostic accuracy in detecting intrauterine abnormalities determined by direct visualization of the intrauterine cavity with either hysteroscopy or after	interval pregnancy, suspected current cervical, uterine, or tubal infection, patients suspected as having anovulatory (dysfunctional) bleeding, and active menstrual bleeding.		with carbon dioxide gas insufflation. After preparing the cervix with an antiseptic solution, a paracervical block was placed. A 5mm hysteroscope was then advanced under direct visualisation into the uterus. Any masses found were characterised, measured, and recorded on a seperate data sheet. If masses were detected during the ultrasonographic studies, patients were scheduled for outpatient operative hysteroscopy, allowing confirmation of the diagnosis and removal of the masses at the same time.		Could the conduct or interpretation of the index test have introduced bias? High risk B. Concerns regarding applicability: Sonographer performed the vaginal ultrasound, however experience not mentioned. Are there concerns that the index test, its conduct, or interpretation differ from the review question? Unclear concern Reference Standard A. Risk of Bias Is the reference standards likely to

Study details	Participants	Tests	Methods	Outcomes and results	Comments
hysterectomy. **Study dates** July 1, 1996-September 1, 1997 **Source of funding** Not reported					correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index tests? Unclear Could the reference standard, its conduct, or its interpretation have introduced bias? Unclear risk B. Concerns regarding applicability Are there concerns that the target condition as defined by the reference standard does not match the question? Low concern Flow and Timing A. Risk of Bias

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					Was there an appropriate interval between index test and reference standard? Yes Did all patients receive the same reference standard? No (either hysteroscopy or hysterectomy) Were all patients included in the analysis? No, 8/47 dropped out, but all accounted for in the text. Could the patient flow have introduced bias? Unclear risk **Other information** Diagnostic tests were aimed to be scheduled 2-3 days

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					after menses. Is this a true representation of clinical practice?

What is the most clinically effective imaging strategy for diagnosing adenomyosis in women with heavy menstrual bleeding?

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>Full citation

Dakhly, D. M. R., Abdel Moety, G. A. F., Saber, W., Gad Allah, S. H., Hashem, A. T., Abdel Salam, L. O. E., Accuracy of Hysteroscopic</td>
<td>Sample size

N=404 original sample

N=292 included in analysis

Characteristics

Mean age in adenomyosis</td>
<td>Tests

Index test

2D transvaginal ultrasound scan (2D-TVUS)

Reference standard</td>
<td>Methods

Ultrasound

2D-TVUS was performed for all participants by a single investigator using the 7.5-MHz vaginal transducer of the Medison Sonoace X6 ultrasound machine (Medison Sonoace X6, South Korea). Ultrasound was performed in the postmenstrual period for patients with menorrhagia,</td>
<td>Results

2D-TVUS versus histopathology (hysterectomy)
<table>
<tr><td></td><td>Confirmed adenomyosis</td><td>No adenomyosis</td><td>Total</td></tr>
<tr><td>Adenomyosis in index test</td><td>136*</td><td>52*</td><td>188*</td></tr>
<tr><td>No adenomyosis</td><td>26*</td><td>78*</td><td>104*</td></tr>
</table>
</td>
<td>Limitations

QUADAS-2 a quality assessment tool for diagnostic accuracy studies:

Patient Selection

A. Risk of Bias</td>
</tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
Endomyometrial Biopsy in Diagnosis of Adenomyosis, Journal of Minimally Invasive Gynecology, 23, 364-371, 2016 **Ref Id** 510617 **Country/ies where the study was carried out** Egypt **Study type** Prospective cohort study **Aim of the study** To investigate the diagnostic	group 44.46 years (SD 3.3); in nonadenomyosis group 44.77 years (SD 3.93). Mean BMI in adenomyosis group 29.07 (SD 2.82); in nonadenomyosis group 29.08 (SD 2.76). Mean parity in adenomyosis group 4.35 (SD 1.53); in nonadenomyosis group 4.17 (SD 1.15). Clinical symptoms in adenomyosis group: dysmenorrhea 54.3%,	Histopathological hysterectomy specimen	and when the bleeding was minimal for patients with metrorrhagia. The uterus was scanned systematically. First, it was examined in the longitudinal view. The endometrial thickness was measured at the widest point between the endometrial–myometrial interfaces. The uterine volume was obtained by measuring the uterine dimensions in 3 planes (length, width, and height), and the volume was automatically calculated by the ultrasound machine. Adenomyosis was diagnosed in the presence of ≥2 of the following 5 criteria: heterogeneous myometrial echo-texture; myometrial cysts; subendometrial echogenic linear striations; asymmetry of the anterior and posterior myometrium; and a poorly defined endometrial–myometrial junction. Heterogeneous myometrium	<table><tr><td>in index test</td><td></td><td></td><td></td></tr><tr><td>Total</td><td>162</td><td>130</td><td>292</td></tr></table> Sensitivity 84% (95% CI* 77-89%) Specificity 60% (95% CI* 51-68%) Positive likelihood ratio* 2.10 (95% CI 1.68-2.62) Negative likelihood ratio* 0.27 (95% CI 0.18-0.39) Prevalence of adenomyosis 55.5% *Calculated by the NGA technical team	Was a consecutive or random sample of patients enrolled? Yes. Was a case-control design avoided? Yes. Did the study avoid inappropriate exclusions? Yes. Could the selection of patients have introduced bias? Low risk. B. Concerns regarding applicability: Not all participants had heavy menstrual

Study details	Participants	Tests	Methods	Outcomes and results	Comments
accuracy of endomyometrial biopsy obtained via office hysteroscopy for the diagnosis of adenomyosis. **Study dates** January 2015 to August 2015. **Source of funding** Not reported.	dyspareunia 60.5%, chronic pelvic pain 69.1%, menorrhagia 64.2%, menometrorrhagia 35.8%; in nonadenomyosis group: dysmenorrhea 60.0%, dyspareunia 44.6%, chronic pelvic pain 66.2%, menorrhagia 55.4%, menometrorrhagia 43.1%. **Inclusion Criteria** Premenopausal women with clinical symptoms of adenomyosis, including		was defined by the presence of an indistinctly defined myometrial area with decreased or increased echogenicity. Subendometrial echogenic linear striations were defined by the appearance of echogenic lines fanning out from the endometrial layer. Myometrial cysts were defined by the presence of variable-sized nonvascularized cystic anechoic spaces or lakes in the myometrium. For the diagnosis of myometrial asymmetry, the ratio between the anterior and posterior wall thickness was calculated. A ratio of approximately 1 indicated that the myometrial walls were symmetrical, and a ratio >1or <1 indicated asymmetry. Histopathology For the hysterectomy specimens, 6 to 8 slides per		bleeding, 64.2% had menorrhagia (HMB) and 35.8% had menometrorrhagia. Are there concerns that the included patients and setting do not match the review question? High concern. Index Test A. Risk of Bias Were the index test results interpreted without knowledge of the results of the reference standard? Yes.

Study details	Participants	Tests	Methods	Outcomes and results	Comments
	chronic pelvic pain, heavy menstrual bleeding (menorrhagia), menometrorrhagia, dysmenorrhea, and/or dyspareunia. **Exclusion Criteria** Postmenopausal bleeding, pregnancy, refusal.		area were obtained from the fundus, anterior, posterior, and right and left lateral uterine walls, in addition to samples obtained from macroscopically abnormal areas of the myometrium. Adenomyosis was defined microscopically by the presence of ectopic endometrial glands and/or stroma in the myometrium, located .2.5 mm beyond the endometrial junction. Adenomyosis sometimes presented as a diffuse pattern affecting the whole myometrium or a focal pattern in whicha circumscribed nodular lesion mimicking an intramural myoma was seen. Adenomyosis was either superficial (affecting the inner one-third of the myometrium) or deep (affecting the outer two-thirds of the whole myometrium).		If a threshold was used, was it pre-specified? Yes. (Diagnostic criteria of adenomyosis was defined.) Could the conduct or interpretation of the index test have introduced bias? Low risk. B. Concerns regarding applicability: The paper does not report who interpreted the index test or the level of experience of the person(s). Are there concerns that the index test,

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					its conduct, or interpretation differ from the review question? Unclear concern. Reference Standard A. Risk of Bias Is the reference standards likely to correctly classify the target condition? Yes. Were the reference standard results interpreted without knowledge of the results of the index tests? Yes. Could the

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					reference standard, its conduct, or its interpretation have introduced bias? Low risk. B. Concerns regarding applicability Are there concerns that the target condition as defined by the reference standard does not match the question? Low concern. Flow and Timing A. Risk of Bias Was there an appropriate interval between index

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					test and reference standard? Yes. Did all patients receive the same reference standard? Yes. Were all patients included in the analysis? No. (112 women were excluded: 64 women were given progesterone for dysfunctional uterine bleeding as proved by endometrial biopsy and the absence of other ultrasound abnormalities; 17 women declined

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>hysterectomy; 31 women did not show up.)

Could the patient flow have introduced bias? High risk.

Other information</td></tr>
<tr><td>Full citation

Abdel Hak, A. M., Accuracy of sonographic criteria for diagnosis of adenomyosis in perimenopausal women with menorrhagia, Middle East Fertility Society</td><td>Sample size

N=50

Characteristics

Mean age 44.88 years (SD 2.84).

Mean gravidity 4.94 (SD 2.23).

Mean parity 4.26 (SD 1.51).</td><td>Tests

Index test

2D transvaginal ultrasound scan (2D-TVUS)

Reference standard

Histopathologic specimen (hysterectom</td><td>Methods

Ultrasound

All women underwent 2D transvaginal ultrasound examination using An Acuson XP unit (Mountain View, California). All examinations were videotaped for further review by the same author, and representative images were stored on hard-copy films. During each 2D transvaginal US examination, uterine size, endometrial thickness, and</td><td>Results

2D-TVUS versus histopathology (hysterectomy)
<table><tr><td></td><td>Confirmed adenomyosis</td><td>No adenomyosis</td><td>Total</td></tr><tr><td>Adenomyosis in index test</td><td>10</td><td>2</td><td>12</td></tr><tr><td>No adenomyosis in index</td><td>5</td><td>33</td><td>38</td></tr></table></td><td>Limitations

QUADAS-2 a quality assessment tool for diagnostic accuracy studies:

Patient Selection

A. Risk of Bias

Was a consecutive or random sample</td></tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
Journal, 15, 35-38, 2010 **Ref Id** 369839 **Country/ies where the study was carried out** Egypt **Study type** Prospective cohort study **Aim of the study** To determine the accuracy of transvaginal ultrasound in the diagnosis of uterine adenomyosis in perimenopau	**Inclusion Criteria** Perimenopausal women planned for hysterectomy for heavy menstrual bleeding. **Exclusion Criteria** Women with chronic pelvic pain.	y)	subendometrial halo thickness were measured. The diagnosis of adenomyosis was made when a poorly defined area of abnormal echo texture was noted within the myometrium. Abnormal myometrial echo texture was defined if the myometrium demonstrated heterogeneity, decreased or increased echogenicity, and/or the presence of cysts, presence of linear striation, globular configuration of the uterus. The exact location (ventral, dorsal, ventral and dorsal, or diffuse) of the area suspicious for adenomyosis as well as the maximum depth of involvement (inner, middle, or outer third of the myometrium) were documented for most patients. Histopathology All patients underwent a hysterectomy within of 7 days	<table><tr><td>test</td><td></td><td></td><td></td></tr><tr><td>Total</td><td>15</td><td>35</td><td>50</td></tr></table> Sensitivity* 66.67% (95% CI 38.38-88.18%) Specificity* 94.29% (95% CI 80.84-99.30%) Positive likelihood ratio* 11.67 (95% CI 2.90-46.96) Negative likelihood ratio* 0.35 (95% CI 0.17-0.73) Prevalence of adenomyosis 24.0% *Calculated by the NGA technical team	of patients enrolled? Unclear. (Not reported.) Was a case-control design avoided? Yes. Did the study avoid inappropriate exclusions? Yes. (Although it is not clear whether or not the excluded women with chronic pelvic pain might have also had HMB.) Could the selection of patients have introduced bias? Unclear risk. B. Concerns regarding

Study details	Participants	Tests	Methods	Outcomes and results	Comments
sal menorrhagia. **Study dates** April 2008 to September 2008 **Source of funding** Not reported.			after undergoing endovaginal US. The initial histologic examination was performed by pathologists who were blinded to the findings at endovaginal US. The associated pathologic findings were documented for each patient. Histologic specimens were routinely taken from the anterior and posterior wall of each uterine section. Criteria used for the diagnosis of adenomyosis included the presence of endometrial glands and/or stroma greater than one high-power field deep to the endometrial–myometrial junction.		applicability Are there concerns that the included patients and setting do not match the review question? Low concern. Index Test A. Risk of Bias Were the index test results interpreted without knowledge of the results of the reference standard? Unclear. (Not reported.) If a threshold was used, was it pre-specified? Yes. (Criteria

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					for TVUS diagnosis of adenomyosis was defined.) Could the conduct or interpretation of the index test have introduced bias? Unclear risk. B. Concerns regarding applicability: The paper did not report who interpreted the index test or the level of experience of the person(s). Are there concerns that the index test, its conduct, or interpretation differ from the

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					review question? Unclear concern. Reference Standard A. Risk of Bias Is the reference standards likely to correctly classify the target condition? Yes. Were the reference standard results interpreted without knowledge of the results of the index tests? Yes. Could the reference standard, its conduct, or its

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					interpretation have introduced bias? Low risk. B. Concerns regarding applicability Are there concerns that the target condition as defined by the reference standard does not match the question? Low concern. Flow and Timing A. Risk of Bias Was there an appropriate interval between index test and reference standard? Yes.

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					Did all patients receive the same reference standard? Yes. Were all patients included in the analysis? Yes. Could the patient flow have introduced bias? Low risk. **Other information** Sensitivity and specificity were incorrectly reported in the paper. The correct sensitivity and specificity were reported as positive and negative predictive

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>values while the correct positive and negative predictive values were reported as sensitivity and specificity.</td></tr>
<tr><td>Full citation

Botsis, D., Kassanos, D., Antoniou, G., Pyrgiotis, E., Karakitsos, P., Kalogirou, D., Adenomyoma and leiomyoma: differential diagnosis with transvaginal sonography, Journal of Clinical</td><td>Sample size

N=194

Characteristics

The indication for surgery was an enlarged uterus with the following clinical findings: menorrhagia and/or dysmenorrhea (172 patients), pressure or</td><td>Tests

Index test

2D transvaginal ultrasound scan (2D-TVUS)

Reference standard

Histopathology (hysterectomy)</td><td>Methods

Ultrasound

Ultrasound examination was performed using a Toshiba SSA-340 A ECCOCEE scanner (Toshiba Medical Systems, Delft, The Netherlands) with a 5-MHz transvaginal probe. Five sonographic characteristics were evaluated: the location of the uterine mass, either anterior or posterior to the endometrium; the number of masses, 1, 2, or more than 2; the appearance of the margin of the mass, either distinct or</td><td>Results

2D-TVUS versus histopathology (hysterectomy)<table><tr><td></td><td>Confirmed adenomyosis</td><td>No adenomyosis</td><td>Total</td></tr><tr><td>Adenomyosis in index test</td><td>38*</td><td>14*</td><td>52*</td></tr><tr><td>No adenomyosis in index test</td><td>10*</td><td>132*</td><td>142*</td></tr></table></td><td>Limitations

QUADAS-2 a quality assessment tool for diagnostic accuracy studies:

Patient Selection

A. Risk of Bias

Was a consecutive or random sample of patients enrolled?</td></tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
Ultrasound, 26, 21-5, 1998 **Ref Id** 434058 **Country/ies where the study was carried out** Greece **Study type** Prospective cohort study **Aim of the study** To evaluate the capability of transvaginal sonography to differentiate adenomyomas from	pain consistent with a mass lesion (5), dyspareunia (21), pollakiuria and nocturia (6), and rapid tumor growth (2). The mean age of the 206 patients investigated was 46.7 years (range 35.7–51.8 years; SD 3.82). The mean weight of the patients was 70 kg (range 52–86 kg; SD 9.5). The mean weight of the uteri was 160 g (range 60–370 g; SD 61.4). The mean duration		indistinct; the echogenicity, hyperechoic, hypoechoic, or of mixed echogenicity; and the presence or absence of lacunae, with a lacuna defined as a hypoechoic area larger than 5 mm within the mass. The sonographic criteria for the diagnosis of adenomyosis were heterogeneous myometrial areas that were not encapsulated and that contained anechoic lacunae measuring 1–3 mm in diameter and an area characterized by irregular cystic spaces measuring 1–7 mm in diameter (honeycomb pattern) and disrupting the normal fine speckled echo pattern of the uterus. The sonographic examination was considered diagnostic of adenomyosis when at least 3 parameters were positive. Histopathology A histopathologic diagnosis of	<table><tr><td>Total</td><td>48</td><td>146</td><td>194</td></tr></table> Sensitivity* 79% (95% CI 65-90%) Specificity* 90% (95% CI 84-95%) Positive likelihood ratio* 8.26 (95% CI 4.91-13.87) Negative likelihood ratio* 0.23 (95% CI 0.13-0.40) Prevalence of adenomyosis 24.7% *Calculated by the NGA technical team	Unclear. (Not reported.) Was a case-control design avoided? Yes. Did the study avoid inappropriate exclusions? Unclear. (Women with uterine nodules of less than 2 cm in diameter were excluded [n=12] but it is unclear why.) Could the selection of patients have introduced bias? Unclear risk. B. Concerns regarding applicability:

Study details	Participants	Tests	Methods	Outcomes and results	Comments
leiomyomas. **Study dates** 1993 to 1994. **Source of funding** Not reported.	of menstruation in this group was 6.0 days (range 3–12 days; SD 1.83). **Inclusion Criteria** Women who underwent hysterectomy due to an enlarged uterus with clinical symptoms. **Exclusion Criteria** Uterine nodules less than 2 cm in diameter.		adenomyosis was made only when endometrial glands and stroma were found within the myometrium more than 1 high-power microscopic field below the basal endometrium. The severity of adenomyosis was graded as minimal when only the inner layer of the myometrium had been invaded, moderate when the middle layer had been penetrated, and marked or severe when all the layers were involved.		Not all women had HMB as a symptom 83% had HMB and/or dysmenorrhea, the proportion with HMB was not reported. Are there concerns that the included patients and setting do not match the review question? High concern. Index Test A. Risk of Bias Were the index test results interpreted without knowledge of the results of

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					the reference standard? Yes. If a threshold was used, was it pre-specified? Yes. (The diagnostic criteria of adenomyosis in the index test was defined.) Could the conduct or interpretation of the index test have introduced bias? Low risk. B. Concerns regarding applicability: The paper did not report who interpreted the index test or the level of experience of the person(s).

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					Are there concerns that the index test, its conduct, or interpretation differ from the review question? Unclear concern. Reference Standard A. Risk of Bias Is the reference standards likely to correctly classify the target condition? Yes. Were the reference standard results interpreted without knowledge of the results of

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					the index tests? Yes. Could the reference standard, its conduct, or its interpretation have introduced bias? Low risk. B. Concerns regarding applicability Are there concerns that the target condition as defined by the reference standard does not match the question? Low concern. Flow and Timing A. Risk of Bias

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					Was there an appropriate interval between index test and reference standard? Yes. Did all patients receive the same reference standard? Yes. Were all patients included in the analysis? No. (12 women were excluded due to uterine nodules less than 2 cm in diameter, reason unclear.) Could the patient flow have introduced bias? Unclear

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>risk.

Other information</td></tr>
<tr><td>Full citation

Exacoustos, C., Brienza, L., Di Giovanni, A., Szabolcs, B., Romanini, M. E., Zupi, E., Arduini, D., Adenomyosis : three-dimensional sonographic findings of the junctional zone and correlation with histology, Ultrasound in obstetrics & gynecology :</td><td>Sample size

N=74 women fit inclusion criteria but n=2 were later excluded due to morcellation of the uterus.

N=72 included in analysis

Characteristics

The mean age of the 72 patients included in the analysis was 46.7 (range 38–52) years. Indications for</td><td>Tests

Index test

2D transvaginal ultrasound scan (2D-TVUS); 3D-TVUS

Reference standard

Histopathology (hysterectomy)</td><td>Methods

Ultrasound

All patients underwent 2D, 3D and power Doppler TVUS of the pelvic organs in a single examination during the secretory phase of the menstrual cycle within 2 months
before surgery. Each scan was performed by one of three
expert sonographers, using an E8 (GE Healthcare, Zipf, Austria) ultrasound machine equipped
with a multifrequency 3D volume endovaginal probe (2.8–10 MHz). Power Doppler was used to evaluate
the vascularization of the myometrial tissue. All 2D and</td><td>Results

1) 2D-TVUS versus histopathology (hysterectomy)

<table><tr><td></td><td>Confirmed adenomyosis</td><td>No adenomyosis</td><td>Total</td></tr><tr><td>Adenomyosis in index test</td><td>24*</td><td>4*</td><td>28*</td></tr><tr><td>No adenomyosis in index test</td><td>8*</td><td>36*</td><td>44*</td></tr><tr><td>Total</td><td>32</td><td>40</td><td>72</td></tr></table>
Sensitivity* 75% (95% CI 57-89%)

Specificity* 90% (95% CI 76-97%)

Positive likelihood ratio 7.5 (95% CI 2.9-19.4)</td><td>Limitations

QUADAS-2 a quality assessment tool for diagnostic accuracy studies:

Patient Selection

A. Risk of Bias

Was a consecutive or random sample of patients enrolled? Yes.

Was a case-control design avoided? Yes.</td></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>the official journal of the International Society of Ultrasound in Obstetrics and Gynecology, 37, 471-479, 2011

Ref Id

370269

Country/ies where the study was carried out

Italy

Study type

Prospective cohort study

Aim of the study

To correlate with</td>
<td>surgery included menorrhagia or abnormal uterine bleeding in 55 (76%) patients, uterine prolapse in seven (10%) and ovarian pathology in 10 (14%). Mean body mass index (BMI) in the group of women with adenomyosis in histology was 24.3 (SD 3.3 and in the group of women without adenomyosis in histology was 24.5 (SD 2.9). Mean gravidity was</td>
<td></td>
<td>3D ultrasound evaluations and measurements were done during the same examination period and by the same operator.

The 2D-TVUS examination included evaluation and measurement of the pelvic organs. The uterus, endometrium and adnexa were evaluated for any abnormalities. The uterus and endometrium were measured and the uterine volume calculated by means of the ellipsoid formula (uterine longitudinal diameter × transverse diameter × anteroposterior diameter × 0.532). Any myometrial lesions (myomas and signs of adenomyosis) were described and measured. We determined the presence of certain TVS features associated with</td>
<td>Negative likelihood ratio 0.28 (95% CI 0.15-0.51)

2) 3D-TVUS versus histopathology (hysterectomy)
<table>
<tr><td></td><td>Confirmed adenomyosis</td><td>No adenomyosis</td><td>Total</td></tr>
<tr><td>Adenomyosis in index test</td><td>29*</td><td>5*</td><td>34*</td></tr>
<tr><td>No adenomyosis in index test</td><td>3*</td><td>35*</td><td>38*</td></tr>
<tr><td>Total</td><td>32</td><td>40</td><td>72</td></tr>
</table>
Sensitivity 91% (95% CI 74-97%)

Specificity 88% (95% CI 72-95%)

Positive likelihood ratio 7.3 (95% CI 3.2-16.6)

Negative likelihood ratio 0.11 (95% CI 0.03-0.31)

Prevalence of adenomyosis 44.4%</td>
<td>Did the study avoid inappropriate exclusions? Yes.

Could the selection of patients have introduced bias? Low risk.

B. Concerns regarding applicability:

Not all women included in the study had HMB. 81.3% of the women with histologically confirmed adenomyosis had HMB and 72.5% of the women without adenomyosis in histological examination</td>
</tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
histopathological features the adenomyosis-induced morphological alterations of the outer myometrium and the innermyometrium ('junctional zone', JZ) detectable on two- (2D) and three-dimensional (3D) transvaginal ultrasound imaging (TVS), and to evaluate their diagnostic accuracy for adenomyosis. **Study dates**	1.3 (SD 1.5) in the group with adenomyosis in histology and 1.5 (SD 1.3) in the non-adenomyosis group. Mean parity was 0.8 (SD 1.0) in the adenomyosis group and 1.2 (SD 0.9) in the non-adenomyosis group. 81.3% of the women in the adenomyosis group had HMB compared with 72.5% in the non-adenomyosis group. 84.4% of the women in the adenomyosis		adenomyosis: myometrial cysts and heterogeneous areas, myometrial hypoechoic linear striations, diffuse vascularity and asymmetry of the myometrial wall. Asymmetrical myometrial walls were defined as a regular enlarged uterus with asymmetry unrelated to leiomyoma, heterogeneous myometrium as an indistinctly defined myometrial area with decreased or increased echogenicity, myometrial hypoechoic linear striations as a pattern of thin acoustic shadowing not arising from echogenic foci and/or leiomyoma, and myometrial cyst as a round anechoic area within the myometrium. Overall diagnostic criteria of adenomyosis in the 2D-TVUS was based on the presence of ≥2 of the following	*Calculated by the NGA technical team	had HMB. Are there concerns that the included patients and setting do not match the review question? High concern. Index Test A. Risk of Bias Were the index test results interpreted without knowledge of the results of the reference standard? Yes. If a threshold was used, was it pre-specified? Yes. (Diagnostic criteria for adenomyosis in

Study details	Participants	Tests	Methods	Outcomes and results	Comments
September 2008 to January 2010. **Source of funding** Not reported.	group had dysmenorrhea compared with 47.5% in the non-adenomyosis group. **Inclusion Criteria** Premenopausal women who had benign pelvic pathology (diagnosed by ultrasound or office hysteroscopy) and were scheduled for hysterectomy. **Exclusion Criteria** Pregnant and postmenopausal women, those with		individual ultrasonographic features: myometrial cysts; asymmetrical myometrial cysts; hypoechoic striations; heterogenous myomerial cysts. Power Doppler was performed using fixed preinstalled settings: frequency, 6–9 MHz ('normal'); pulse repetition frequency, 0.6–0.3 kHz; gain, −4.0; wall motion filter, 'low 1' (40 Hz). If necessary, power Doppler gain was reduced until all color artifacts had disappeared. This modality was used to distinguish between a myometrial cyst and a vascular component, and between leiomyoma and focal adenomyosis. Localized adenomyosis and adenomyoma were characterized by the presence of rare, diffuse vessels, while fibroids		the index tests were defined.) Could the conduct or interpretation of the index test have introduced bias? Low risk. B. Concerns regarding applicability Are there concerns that the index test, its conduct, or interpretation differ from the review question? Low concern. Reference Standard A. Risk of Bias Is the reference standards likely

Study details	Participants	Tests	Methods	Outcomes and results	Comments
	reproductive tract cancer, those on GnRH analog therapy or other hormonal therapy, and those with fibroids >8 cm in maximum diameter or more than three fibroids >5 cmin maximum diameter on ultrasound examination prior to surgery. Two patients were later excluded due to morcellation of the uterus.		had flow aligned along the external myoma capsule, appearing on imaging as a vascular ring. Using 3D-TVUS, a volume of the uterus was then acquired in order to obtain the coronal view. Two to four static gray-scale volumes of the uterus were obtained from the sagittal plane and from the transverse plane. The volume acquisition technique was standardized according to the following criteria: frequency, 6–9 MHz; magnification of the uterus up to half of the screen; sweep angle, 120◦; sweep velocity, adjusted from medium to maximum quality; 3D volume box exceeding the uterus by 1 cm on each side. Overall diagnostic criteria of adenomyosis in the 3D-TVUS was based on the presence of ≥2 of the following ultrasonographic		to correctly classify the target condition? Yes. Were the reference standard results interpreted without knowledge of the results of the index tests? Yes. Could the reference standard, its conduct, or its interpretation have introduced bias? Low risk. B. Concerns regarding applicability Are there concerns that the target condition as

Study details	Participants	Tests	Methods	Outcomes and results	Comments
			features: JZmax ≥8 mm; JZmax − JZmin ≥4 mm; JZ ratio ≥50%; JZ alteration; myometrial cysts; asymmetrical myometrial cysts; heterogeneous myometrial cysts. Histopathology Hysterectomy was performed in a manner appropriate for their clinical condition (laparotomic, laparoscopic or vaginal hysterectomy). The entire uterus was sent to the pathologist, except in cases in which morcellation of the uterus had occurred. Histopathological examination was performed by a single pathologist, who was blinded to the sonographic data and who had been specifically asked to evaluate the JZ (innermyometrium) and the outer myometrium. Histological		defined by the reference standard does not match the question? Low concern. Flow and Timing A. Risk of Bias Was there an appropriate interval between index test and reference standard? Yes. Did all patients receive the same reference standard? Yes. Were all patients included in the analysis? No. (Two patients were excluded

Study details	Participants	Tests	Methods	Outcomes and results	Comments
			sections encompassing the full uterine wall thickness, from endometrium to serosa, were used for the study. In each case, at least eight slices were obtained, with at least one being from each of the fundus and the anterior, posterior and lateral walls of the uterus. Samples were also obtained from macroscopically abnormal areas of the myometrium. Adenomyosis was defined histopathologically by the presence of endometrial glands and stroma in the myometrium, located >2.5 mm beyond the endomyometrial junction. In some cases it remained diffuse pathology and was evaluated by grade according to depth and number of endometrial		due to a morcellation of the uterus, however, due to the small number, unlikely to affect the findings.) Could the patient flow have introduced bias? Low risk. **Other information**

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td>islets in the myometrium.
In others it was seen as a circumscribed nodular lesion mimicking an intramural myoma, which was defined as adenomyoma. For the purposes of statistical analysis in
this study, only the presence or absence of
adenomyosis was considered.</td><td></td><td></td></tr>
<tr><td>Full citation

Alborzi, S., Parsanezhad, M. E., Mahmoodian, N., Alborzi, S., Alborzi, M., Sonohysterography versus transvaginal sonography for screening of patients with abnormal</td><td>Sample size

N=81

Characteristics

Not reported.

Inclusion Criteria

Abnormal uterine bleeding.

Exclusion Criteria</td><td>Tests

Index test

2D transvaginal ultrasound scan (2D-TVUS)

Reference standard

Histopathological</td><td>Methods

Ultrasound

Transvaginal ultrasound scan (HS-2000, Honda-el., Toyohashi, Japan)
was performed using a 7.5 MHz transvaginal transducer by the first
author. The midline echo was considered to be normal when a
straight endometrial lining with well defined margins and without</td><td>Results

2D-TVUS versus histopathology (hysterectomy)
<table><tr><td></td><td>Confirmed adenomyosis</td><td>No adenomyosis</td><td>Total</td></tr><tr><td>Adenomyosis
in index test</td><td>5*</td><td>8*</td><td>13</td></tr><tr><td>No adenomyosis
in index test</td><td>4*</td><td>64*</td><td>68</td></tr></table></td><td>Limitations

QUADAS-2 a quality assessment tool for diagnostic accuracy studies:

Patient Selection

A. Risk of Bias

Was a consecutive or</td></tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
uterine bleeding, International Journal of Gynaecology & Obstetrics, 96, 20-3, 2007 **Ref Id** 400994 **Country/ies where the study was carried out** Iran **Study type** Prospective cohort study **Aim of the study** To compare the accuracy of saline infusion	Not reported.	specimen from hysteroscopy	echo dense foci was found. The most common ultrasonic finding of adenomyosis was simply diffuse uterine enlargement with no alteration in echotexture and contour. Focal adenomyosis was diagnosed when a poorly defined area of abnormal echotexture is present in the myometrium with increased or decreased echogenecity. Histopathology During hysteroscopy the uterine cavity was evaluated and findings were recorded. All myomas and polyps were removed by a resectoscope (Karl Storz GmbH, Tuttlingen, Germany). In all patients a relatively deep specimen from the anterior and posterior wall of the uterus was resected and	<table><tr><td>Total</td><td>9</td><td>72</td><td>81</td></tr></table> Sensitivity 55.6% (95% CI* 21-86%) Specificity 88.9% (95% CI* 79-95%) Positive likelihood ratio* 5.0 (95% CI 2.08-12.01) Negative likelihood ratio** 0.50 (95% CI 0.24-1.04) Prevalence of adenomyosis 11.1% *Calculated by the NGA technical team.	random sample of patients enrolled? Unclear. (Not reported.) Was a case-control design avoided? Yes. Did the study avoid inappropriate exclusions? Unclear. (No exclusions were reported. Inclusion criteria was not clearly defined either.) Could the selection of patients have introduced bias? Unclear risk. B. Concerns regarding

Study details	Participants	Tests	Methods	Outcomes and results	Comments
sonohysterography (SIS) with transvaginal sonography (TVS) for the screening of causes of abnormal uterine bleeding (AUB) in out-patients. **Study dates** June 2004 to November 2005. **Source of funding** Not reported.			sent to a pathologist for the diagnosis of adenomyosis.		applicability: The proportion of included patients with HMB is unclear. All included women had abnormal uterine bleeding but not specified further. Are there concerns that the included patients and setting do not match the review question? High concern. Index Test A. Risk of Bias Were the index test results interpreted

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					without knowledge of the results of the reference standard? Yes. If a threshold was used, was it pre-specified? Yes. (Diagnostic criteria for adenomyosis in the index test was defined.) Could the conduct or interpretation of the index test have introduced bias? Low risk. B. Concerns regarding applicability: The paper did not report who interpreted the index test or

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					what was the level of experience of the person(s). Are there concerns that the index test, its conduct, or interpretation differ from the review question? Unclear concer n. Reference Standard A. Risk of Bias Is the reference standards likely to correctly classify the target condition? Yes. Were the reference standard results

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					interpreted without knowledge of the results of the index tests? Yes. Could the reference standard, its conduct, or its interpretation have introduced bias? Low risk. B. Concerns regarding applicability Are there concerns that the target condition as defined by the reference standard does not match the question? Low concern. Flow and

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					Timing A. Risk of Bias Was there an appropriate interval between index test and reference standard? Yes. Did all patients receive the same reference standard? Yes. Were all patients included in the analysis? Yes. Could the patient flow have introduced bias? Low risk. **Other information** Inclusion and exclusion

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>criteria were not reported clearly. Characteristics of the included patients were not reported.</td></tr>
<tr><td>Full citation

Bazot, M., Darai, E., Rouger, J., Detchev, R., Cortez, A., Uzan, S., Limitations of transvaginal sonography for the diagnosis of adenomyosis, with histopathological correlation, Ultrasound in Obstetrics and</td><td>Sample size

N=129 who were divided into two groups:

Group 1 (n=23) women with recurrent menometrorrhagia but no evidence of leiomyomata and endometrial diseases on transabdominal examination.

Group 2 (n=106) all</td><td>Tests

Index test

2D transvaginal ultrasound scan (2D-TVUS); 2D transabdominal ultrasound scan (2D-TAUS)

Reference standard

Histopathology</td><td>Methods

Ultrasound

Sonographic examinations were performed with an Ultramark
HDI 3000 unit (Advanced Technology Laboratories, Bothell, WA, USA). Pelvic TAUS was performed using a wideband
2- to 4-MHz transducer, and transvaginal examination with a wide-band 5- to 9-MHz transducer. Color Doppler examination was performed using a pulse repetition frequency
of 1000–1500 Hz, a wall filter of 50 Hz, and a highpriority</td><td>Results

1) 2D-TAUS versus histopathology (hysterectomy)

Group 1
(women with recurrent menometrorrhagia but no evidence of leiomyomata and endometrial diseases on transabdominal examination)
<table><tr><td></td><td>Confirmed adenomyosis</td><td>No adenomyosis</td><td>Total</td></tr><tr><td>Adenomyosis in index test</td><td>12</td><td>1</td><td>13</td></tr><tr><td>No adenomyosis in index test</td><td>9</td><td>1</td><td>10</td></tr></table></td><td>Limitations

QUADAS-2 a quality assessment tool for diagnostic accuracy studies:

Patient Selection

A. Risk of Bias

Was a consecutive or random sample of patients enrolled? Yes.

Was a case-</td></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>Gynecology, 20, 605-611, 2002

Ref Id

369942

Country/ies where the study was carried out

France

Study type

Prospective cohort study

Aim of the study

To evaluate the diagnostic value of TAS and TVS for adenomyosis, and to identify factors influencing the sensitivity</td>
<td>other women.

Characteristics

The indications for surgery were menorrhagia and/or metrorrhagia (n = 92), endometrial carcinoma (n = 13), cervical intraepithelial neoplasia (n = 8), adnexal masses (n = 12), and genital prolapse (n = 13).

Mean age was 44.3 years (SD 4.8) in group 1 and 53.4 years (SD 11.1) in group 2. Mean gravidity was</td>
<td>(hysterectomy)</td>
<td>color setup. Each examination was interpreted in real time and videotaped by two investigators. The first investigator (M.B.) evaluated 79 patients, and the second (J.R.) the remaining 50 patients. The two investigators had, respectively, 8 and 3 years’ experience in female pelvic ultrasonography. During each sonographic examination, the uterine borders (regular or irregular), uterine size, myometrial echotexture, and the presence of associated abnormalities (including myomata) were noted.

Diagnostic criteria for adenomyosis by TAUS included an enlarged regular uterus with no evidence of leiomyoma and/</td>
<td>
<table>
<tr><td>Total</td><td>21</td><td>2</td><td>23</td></tr>
</table>
Sensitivity* 54.14% (95% CI 34.02-78.18%)

Specificity* 50.00% (95% CI 1.26-98.74%)

Positive likelihood ratio* 1.14 (95% CI 0.27-4.80)

Negative likelihood ratio* 0.86 (95% CI 0.20-3.73)

Group 2
(all other women)
<table>
<tr><td></td><td>Confirmed adenomyosis</td><td>No adenomyosis</td><td>Total</td></tr>
<tr><td>Adenomyosis in index test</td><td>2</td><td>3</td><td>5</td></tr>
<tr><td>No adenomyosis in index test</td><td>24</td><td>77</td><td>101</td></tr>
<tr><td>Total</td><td>26</td><td>80</td><td>106</td></tr>
</table>
</td>
<td>control design avoided? Yes.

Did the study avoid inappropriate exclusions? Yes.

Could the selection of patients have introduced bias? Low risk.

B. Concerns regarding applicability:

Not all of the included patients had HMB. 73.6% of the total sample (100% in group 1 and 67.9% in group 2) had menometrorrhagia.

Are there</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>and specificity of these methods in symptomatic unselected women.

Study dates

January 1996 to April 1998.

Source of funding

Not reported.</td>
<td>3.1 (SD 1.4) in group 1 and 2.2 (SD 1.5) in group 2. Mean parity was 2.4 (SD 1.1) in group 1 and 1.6 (SD 1.3) in group 2. In group 1 1 out of 23 women was menopausal, and in group 2, 38 out of 106 were menopausal. In group 1, 8.7% of the women had pelvic pain and 100% had menometrorrhagia, in group 2, 8.5% had pelvic pain and 67.9% had metromenorrhagia.</td>
<td></td>
<td>or presence of myometrial cysts.

Diagnostic criteria by TVUS were as follows: a globular and/or asymmetric uterus, a poorly defined focus of abnormal myometrial echotexture, distorted and heterogeneous myometrial echotexture, myometrial linear striations, and myometrial cysts. Globular and/or asymmetric uterus was defined as a regular enlarged uterus with possible myometrial asymmetry unrelated to leiomyoma. Heterogeneous myometrium was defined by the presence of an indistinctly defined myometrial area with decreased or increased echogenicity. Myometrial hypoechoic linear striations were defined as a radiate pattern of thin acoustic shadowing not arising from</td>
<td>Sensitivity* 7.69% (95% CI 0.95-25.13%)

Specificity* 96.25% (95% CI 89.43-99.22%)

Positive likelihood ratio* 2.05 (95% CI 0.36-11.61)

Negative likelihood ratio* 0.96 (95% CI 0.85-1.08)

2) 2D-TVUS versus histopathology (hysterectomy)

Group 1
(women with recurrent menometrorrhagia but no evidence of leiomyomata and endometrial diseases on transabdominal examination)
<table>
<tr><th></th><th>Confirmed adenomyosis</th><th>No adenomyosis</th><th>Total</th></tr>
<tr><td>Adenomyosis in index test</td><td>17</td><td>0</td><td>17</td></tr>
<tr><td>No adenomyos</td><td>4</td><td>2</td><td>6</td></tr>
</table>
</td>
<td>concerns that the included patients and setting do not match the review question? High concern.

Index Test

A. Risk of Bias

Were the index test results interpreted without knowledge of the results of the reference standard? Yes.

If a threshold was used, was it pre-specified? Yes. (A diagnostic criteria for adenomyosis in the index tests were defined.)</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td></td>
<td>Inclusion Criteria

Women scheduled for hysterectomy undergoing an ultrasound examination beforehand.

Exclusion Criteria

Surgery cancelled, myomectomy, endometrial resection.</td>
<td></td>
<td>echogenic foci and/or leiomyoma. Myometrial cyst was
defined as a round anechoic area of 1–7 mm diameter8,9. With the exception of diffuse heterogeneous myometrium that appeared non-specific for adenomyosis, the diagnosis was made when at least one of the above criteria was met.

Color Doppler was used to distinguish between a myometrial
cyst and a vascular component, and between supposed
leiomyoma and focal adenomyosis. Localized adenomyosis
and adenomyoma were characterized by the absence of
flow or by the presence of straight vessels traversing a hypertrophic
myometrium.

Adenomyosis was classified</td>
<td>
<table>
<tr><td>is
in index test</td><td></td><td></td><td></td></tr>
<tr><td>Total</td><td>21</td><td>2</td><td>23</td></tr>
</table>
Sensitivity* 80.95% (95% CI 58.09-94.55%)

Specificity* 100.00% (95% CI 15.81-100.00%)

Positive likelihood ratio* Not calculable (infinity)

Negative likelihood ratio* 0.19 (95% CI 0.08-0.46)

Group 2
(all other women)
<table>
<tr><td></td><td>Confirmed adenomyosis</td><td>No adenomyosis</td><td>Total</td></tr>
<tr><td>Adenomyosis
in index test</td><td>10</td><td>2</td><td>12</td></tr>
<tr><td>No adenomyosis</td><td>16</td><td>78</td><td>94</td></tr>
</table>
</td>
<td>Could the conduct or interpretation of the index test have introduced bias? Low risk.

B. Concerns regarding applicability

Are there concerns that the index test, its conduct, or interpretation differ from the review question? Low concern.

Reference Standard

A. Risk of Bias

Is the reference standards likely to correctly classify the</td>
</tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
			according to its uterine location. Its extent was evaluated according to inner, middle, and outer involvement by adenomyotic lesions. Finally, the location and the number of myometrial cysts were recorded. All these criteria were evaluated by TVUS. Histopathology Histopathological examination was performed by the same pathologist, who was blinded to the sonographic data. Gross and microscopic histopathological examinations were performed according to Molitor's method. Specimens were oriented by a fixed mark on the anterior uterine wall. Uterus weight, macroscopic appearance, and associated	<table><tr><td>in index test</td><td></td><td></td><td></td></tr><tr><td>Total</td><td>26</td><td>80</td><td>106</td></tr></table> Sensitivity* 38.46% (95% CI 20.23-59.43%) Specificity* 97.50% (95% CI 91.26-99.70%) Positive likelihood ratio* 15.38 (95% CI 3.60-65.74) Negative likelihood ratio* 0.63 (95% CI 0.46-0.86) Overall prevalence of adenomyosis 36.4%. Prevalence in Group 1 91.3%; prevalence in Group 2 24.5%. *Calculated by the NGA technical team	target condition? Yes. Were the reference standard results interpreted without knowledge of the results of the index tests? Yes. Could the reference standard, its conduct, or its interpretation have introduced bias? Low risk. B. Concerns regarding applicability Are there concerns that the target condition as defined by the reference

Study details	Participants	Tests	Methods	Outcomes and results	Comments
			pathological abnormalities were recorded. Fundal, anterior, posterior, right and left maximal uterine wall thicknesses were measured. Macroscopically, adenomyosis was diagnosed as an enlarged uterus, a globular and/or asymmetric uterus, and a dense anarchically fasciculated unlimited myometrium with small cavities (0.5–10 mm). Focal adenomyosis was defined by the presence of adenomyotic lesions restricted to one uterine wall (localized adenomyosis). Adenomyoma was defined as a circumscribed nodular lesion mimicking intramural myoma. In other cases, adenomyosis was		standard does not match the question? Low concern. Flow and Timing A. Risk of Bias Was there an appropriate interval between index test and reference standard? Yes. Did all patients receive the same reference standard? Yes. Were all patients included in the analysis? No. (N=23 patients from the original sample were excluded

Study details	Participants	Tests	Methods	Outcomes and results	Comments
			defined as diffuse pathology. Block sections were taken from the fundal, anterior, posterior, right and left uterine walls, and from macroscopically abnormal areas. The number of slides ranged from five to 15 depending on myometrial thickness. Histopathological diagnostic criteria for adenomyosis included the presence of ectopic endometrial tissue within the myometrium, located 2.5 mm beyond the endometrial−myometrial junction. Smooth-muscle cells surrounding ectopic endometrial areas were noted. Adenomyosis was classified according to the uterine		because the surgery was cancelled [n=6]; they underwent myomectomy [n=6]; or they underwent endomterial resectomy [n=11]. Could the patient flow have introduced bias? Unclear risk. **Other information**

Study details	Participants	Tests	Methods	Outcomes and results	Comments
			location, the depth of myometrial involvement, and the degree of involvement. Adenomyosis was graded according to the depth of myometrial involvement. Grades 1, 2, and 3 corresponded, respectively, to adenomyotic involvement of the inner third, two-thirds, and entire myometrium. Adenomyosis was also defined as mild, moderate, or severe according to the number of endometrial islets observed (one to three, four to nine, and ten or more foci, respectively).		
Full citation Dueholm, M., Lundorf, E., Hansen, E.	**Sample size** N= 108 **Characteristics**	**Tests** Index Test 2D transvaginal	**Methods** Two patients were excluded as their uteri were morcelated at hysterectomy	**Results** 1) 2D-TVUS versus histopathology (hysterectomy)	**Limitations** **QUADAS-2** a quality assessment

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>S., Sorensen, J. S., Ledertoug, S., Olesen, F., Magnetic resonance imaging and transvaginal ultrasonography for the diagnosis of adenomyosis, Fertility and Sterility, 76, 588-594, 2001

Ref Id

370238

Country/ies where the study was carried out

Denmark

Study type

Prospective</td>
<td>The indications for hysterectomy were abnormal uterine bleeding in 51 patients (48%), symptomatic myomas in 35 (33%), lower abdominal pain or endometriosis in 17 (16%), and dysplasia or prior borderline ovarian tumor in 3 patients (3%). Abnormal bleeding was present in 82 (77%) of the patients. The mean age (SD) was 44.7 years (SD 5.2;</td>
<td>ultrasound scan (2D-TVUS); MRI

Reference Test

Histopathological specimen from hysterectomy</td>
<td>(laparoscopically assisted vaginal hysterectomy), and therefore, standard pathologic examination could not be performed. Thus, 106 patients had MRI followed immediately by TVUS. Hysterectomy was completed within 2 weeks of these examinations. Findings were compared with the findings at pathologic examination as the true value. MRI, TVUS, and pathologic examinations were performed independently and without knowledge of the other investigators' findings and the findings were evaluated consecutively.

MRI

All MRI scans were evaluated by a single MRI specialist (EL). MRI was performed with 1.5- Tesla scanners (Signa, General Electric Medical Systems, Milwaukee, WI and Gyroscan ACS.NT, Philips). We acquired 4-mm slices with</td>
<td>
<table>
<tr><td></td><td>Confirmed adenomyosis</td><td>No adenomyosis</td><td>Total</td></tr>
<tr><td>Adenomyosis in index test</td><td>13</td><td>18</td><td>31</td></tr>
<tr><td>No adenomyosis in index test</td><td>6</td><td>33</td><td>39</td></tr>
<tr><td>Indefinite index test</td><td>3</td><td>33</td><td>36</td></tr>
<tr><td>Total</td><td>22</td><td>84</td><td>106</td></tr>
</table>
Indefinite findings included as negative in the following:

Sensitivity* 59.09% (95% CI 36.35 to 79.29%)

Specificity* 78.57%(95% CI 68.26 to 86.78%)

Positive likelihood ratio* 2.76 (95% CI 1.61 to 4.72)
</td>
<td>tool for diagnostic accuracy studies:

Patient Selection

A. Risk of Bias

Was a consecutive or random sample of patients enrolled? Yes.

Was a case-control design avoided? Yes.

Did the study avoid inappropriate exclusions? Unclear. (Inclusion and exclusion criteria not very well defined.)

Could the selection of</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>cohort study

Aim of the study

To compare the diagnostic potential of magnetic resonance imaging (MRI) and transvaginal ultrasonography (TVS) in the diagnosis of adenomyosis.

Study dates

September 1998 to February 2000.

Source of funding

Not reported.</td>
<td>range 28–58 years), the mean parity 1.73 (SD 1.18; range 0–4), and the mean number of pregnancies 2.68 (SD 1.59; range 0–7). The mean uterine volume was 298 (SD 271 mL; range 25– 1290 mL).

Inclusion Criteria

Premenopausal women undergoing hysterectomy for benign disease.

Exclusion</td>
<td></td>
<td>1-mm spacing in the sagittal, coronal, and axial planes relative to the orientation of the uterine cavity, using T2-weighted fast (turbo) spin echo sequences (TR/TEef, 3500–4000 mseconds/90 mseconds, echo train length 16) in all tree planes. We used surface coils (phase array pelvic coils) for data acquisition and completed the examination in 30 to 45 minutes. Junctional zone contours were described as uniform/not uniform in thickness. The thickness was measured at the thinnest (JZmin) and thickest (JZmax) part at the anterior and posterior wall in the sagittal slices. The difference between JZmax and JZmin (JZdif) was calculated for the anterior or posterior border. The largest parameter, either anterior or posterior, was used in all calculations. Diffuse adenomyosis was thought to be present at</td>
<td>Negative likelihood ratio* 0.52 (95% CI 0.31 to 0.87)

2) MRI versus histopathology (hysterectomy)
<table>
<tr><th></th><th>Confirmed adenomyosis</th><th>No adenomyosis</th><th>Total</th></tr>
<tr><td>Adenomyosis in index test</td><td>14</td><td>10</td><td>24</td></tr>
<tr><td>No adenomyosis in index test</td><td>6</td><td>63</td><td>69</td></tr>
<tr><td>Indefinite index test</td><td>2</td><td>11</td><td>13</td></tr>
<tr><td>Total</td><td>22</td><td>84</td><td>106</td></tr>
</table>
Indefinite findings included as negative in the following:</td>
<td>patients have introduced bias? Unclear risk.

B. Concerns regarding applicability:

Abnormal bleeding present in 77% of participants but unclear % of participants with HMB.

Are there concerns that the included patients and setting do not match the review question? High concern.

Index Test

A. Risk of Bias</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td></td>
<td>Criteria

Patients with previous transcervical endometrial resection, malignant diagnosis or acute or subacute indication for hysterectomy.</td>
<td></td>
<td>JZmax .15 mm. For a JZ thickness of 12–15 mm, adenomyosis was thought to be present when one of the criteria was met, such as a nonuniform, thickened JZ or focal not well-demarcated high or low intensity areas in the myometrium (12–14). The presence or absence of each criterion was specified in lesions suspect for adenomyosis.

Ultrasound

TVUS was always performed by the same experienced gynecologist (MD). TVUS was performed in two perpendicular planes with a commercially available scanner, Acuson 3.0 Sequoia 512 (Acuson Inc., Mountain View, CA) equipped with 5.0-, 6.0-, 7.0-, and 8.0-MHz transvaginal transducers and 8.0- and 5.0-MHz abdominal transducers. Presence of focal areas with not well-</td>
<td>Sensitivity* 63.64% (95% CI 40.66% to 82.80%)

Specificity* 88.10% (95% CI 79.19% to 94.14%)

Positive likelihood ratio* 5.35 (95% CI 2.76 to 10.36)

Negative likelihood ratio* 0.41 (95% CI 0.24 to 0.72)

3) MRI & 2D-TVUS versus histopathology (hysterectomy)
<table>
<tr><td></td><td>Confirmed adenomyosis</td><td>No adenomyosis</td><td>Total</td></tr>
<tr><td>Adenomyosis in index test</td><td>16</td><td>19</td><td>35</td></tr>
<tr><td>No adenomyosis in index test</td><td>2</td><td>28</td><td>30</td></tr>
<tr><td>Indefinite</td><td>4</td><td>37</td><td>41</td></tr>
</table>
</td>
<td>Were the index test results interpreted without knowledge of the results of the reference standard? Yes.

If a threshold was used, was it pre-specified? Yes. (Diagnostic criteria for adenomyosis with each test were pre-defined.)

Could the conduct or interpretation of the index test have introduced bias? Low risk.

B. Concerns regarding applicability</td>
</tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
			defined borders or abnormal echo texture was described. When these areas were present, the following criteria for adenomyosis were evaluated: presence of heterogeneity, increased or decreased areas of echogenicity, or presence of myometrial cysts (13). Images with measurements were taken, and a short digital video was recorded. **Histopathology** All hysterectomy specimens were examined by a single pathologist (ESH). The uterus was evaluated without fixation and its volume and weight was measured within 2 hours after hysterectomy. It was cut primarily in the mid-sagittal plane and histopathologic slices were obtained at 10-mm intervals parallel to this plane on the left and right side. All abnormalities were recorded. Adenomyosis was	<table><tr><td>index test</td><td></td><td></td><td></td></tr><tr><td>Total</td><td>22</td><td>84</td><td>106</td></tr></table> Indefinite findings included as negative in the following: Sensitivity* 72.73% (95% CI 49.78% to 89.27%) Specificity* 77.38% (95% CI 66.95% to 85.80%) Positive likelihood ratio* 3.22 (95% CI 2.01 to 5.15) Negative likelihood ratio* 0.35 (95% CI 0.18 to 0.70) Prevalence of adenomyosis 21% *Calculated by the NGA technical team	Are there concerns that the index test, its conduct, or interpretation differ from the review question? Low concern. Reference Standard A. Risk of Bias Is the reference standards likely to correctly classify the target condition? Yes. Were the reference standard results interpreted without knowledge of the results of the index tests?

Study details	Participants	Tests	Methods	Outcomes and results	Comments
			classified as diffuse when endometrial glands or stroma were distributed diffusely in the myometrium, and focal when circumscribed nodular aggregates were seen. This definition does not fully satisfy the diagnostic criteria of adenomyomas with compensatory hypertrophy of the surrounding myometrium (21). We described the presence of endometrial glands or stroma deep in the endometrial–myometrial junction and the diagnostic criterion of adenomyosis was satisfied when it exceeded one medium power (3100) field (i.e., ;2 mm deep into the endometrial–myometrial junction) (22). **Image Analysis** The quality of the images was evaluated, and cases where adenomyosis could not be unequivocally interpreted were described as indefinite		Yes. Could the reference standard, its conduct, or its interpretation have introduced bias? Low risk. B. Concerns regarding applicability Are there concerns that the target condition as defined by the reference standard does not match the question? Low concern. Flow and Timing A. Risk of Bias Was there an

Study details	Participants	Tests	Methods	Outcomes and results	Comments
			findings. Myomas were identified as well-circumscribed uterine masses. For myomas and focal areas with adenomyosis, we established the largest diameter in two perpendicular planes, localization and myometrial involvement. Images mapping myomas and adenomyosis at the different examinations were matched with the findings at pathology. At the end of the study, hard copies and videos from patients with false-negative findings of adenomyosis were revised for the presence of the different criteria of adenomyosis.		appropriate interval between index test and reference standard? Yes. (Hysterectomy performed within 2 weeks of tests.) Did all patients receive the same reference standard? Yes. Were all patients included in the analysis? No. (2 patients received the tests but not pathology due to uterus being morcelated at time of surgery.) Could the patient flow

<table>
<tr><th>Study details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>have introduced bias? Low risk. (Only two patients omitted after initial recruitment.)

Other information

Indefinite reporting of diagnosis for MRI and TVUS, included as a negative result.</td></tr>
<tr><td>Full citation

Vercellini, P., Cortesi, I., De Giorgi, O., Merlo, D., Carinelli, S. G., Crosignani, P. G.,</td><td>Sample size

N= 102

Characteristics

Mean age: 46 +/- 6 years</td><td>Tests

Index test

2D transvaginal ultrasound scan (2D-TVUS)</td><td>Methods

Ultrasound

In the week prior to hysterectomy, all women underwent TVUS using Ansaldo AU 440 (Ansaldo, Genoa, Italy) or AU 580 synchronous (Hitachi, Tokyo,</td><td>Results

2D-TVUS versus histopathology (hysterectomy)
<table><tr><td></td><td>Confirmed adenomyosis</td><td>No adenomyosis</td><td>Total</td></tr><tr><td>Adenomyosis</td><td>24</td><td>24</td><td>48</td></tr></table></td><td>Limitations

QUADAS-2 a quality assessment tool for diagnostic accuracy studies:</td></tr>
</table>

Study details	Participants	Tests	Methods	Outcomes and results	Comments
Transvaginal ultrasonography versus uterine needle biopsy in the diagnosis of diffuse adenomyosis, Human Reproduction, 13, 2884 **Ref Id** 512080 **Country/ies where the study was carried out** Italy **Study type** Prospective cohort study **Aim of the study**	Parity Parous: 86 Nulliparous: 16 **Inclusion Criteria** Premenopausal patients undergoing hysterectomy for menorrhagia and/or dysmennorrhoea; uterus < 12 week pregnancy. **Exclusion Criteria** Grossly distorted uterus due to multiple or large leiomyomata; known	Reference standard Histopathological specimen from hysterectomy	Japan) equipment and a transvaginal transducer of 6.5 MHz. The sonographer diagnosed adenomyosis by presence of indistinctly demarcated heterogeneous myometrial areas with distorted echotexture. Myometrial echotexture was defined as distorted by the presence of abnormally decreased or increased echogenicity and/or round anechoic areas. Only one expert sonographer interpreted the US examinations. In cases of doubtful interpretation at US, the findings were considered abnormal. Histopathology After removal of the uterus, the uterus was opened by pathologist at the left margin and fundus and four blocks of uterus wall were examined. A diagnosis of adenomyosis was made when the distance	<table><tr><td>in index test</td><td></td><td></td><td></td></tr><tr><td>No adenomyosis in index test</td><td>5</td><td>49</td><td>54</td></tr><tr><td>Total</td><td>29</td><td>73</td><td>102</td></tr></table> Sensitivity* 82.76% (95% CI 64.23-94.15%) Specificity* 67.12% (95% CI 55.13-77.67%) Positive likelihood ratio* 2.52 (95% CI 1.74-3.64) Negative likelihood ratio* 0.26 (95% CI 0.11-0.58) Prevalence of adenomyosis 28.4% *Calculated by the NGA technical team	Patient Selection A. Risk of Bias Was a consecutive or random sample of patients enrolled? Yes. Was a case-control design avoided? Yes. Did the study avoid inappropriate exclusions? Yes. Could the selection of patients have introduced bias? Low risk. B. Concerns regarding applicability:

Study details	Participants	Tests	Methods	Outcomes and results	Comments
To assess the reliability of transvaginal ultrasonography and uterine needle biopsy, used singly or in combination, in the diagnosis of diffuse adenomyosis. **Study dates** Not reported. **Source of funding** Not reported.	endocavitary or endometrial anomalies; received steroidal or gonadotrophin-releasing hormone agonist treatment in the preceeding 3 months.		between the lower border of the endometrium and the affected myometrial area was more than half of a low-power field. The pathologist was blind with respect to the sonographic diagnosis.		Proportion of women with HMB unclear (not reported). Are there concerns that the included patients and setting do not match the review question? High concern. Index Test A. Risk of Bias Were the index test results interpreted without knowledge of the results of the reference standard? Yes. If a threshold

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					was used, was it pre-specified? Yes. (Ultrasound criteria for diagnosis of adenomyosis defined.) Could the conduct or interpretation of the index test have introduced bias? Low risk. B. Concerns regarding applicability Are there concerns that the index test, its conduct, or interpretation differ from the review question? Low concern. Reference

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					Standard A. Risk of Bias Is the reference standards likely to correctly classify the target condition? Yes. Were the reference standard results interpreted without knowledge of the results of the index tests? Yes. Could the reference standard, its conduct, or its interpretation have introduced bias? Low risk. B. Concerns regarding

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					applicability Are there concerns that the target condition as defined by the reference standard does not match the question? Low concern. Flow and Timing A. Risk of Bias Was there an appropriate interval between index test and reference standard? Yes. (US completed in the week before surgery.) Did all patients receive the

Study details	Participants	Tests	Methods	Outcomes and results	Comments
					same reference standard? Yes. Were all patients included in the analysis? Yes. Could the patient flow have introduced bias? Low risk. **Other information**

1

Management of heavy menstrual bleeding

What is the most clinically and cost-effective treatment (pharmacological/surgical) for heavy menstrual bleeding in women with: suspected or confirmed fibroids; suspected or confirmed adenomyosis; no identified pathology?

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Abbott,J., Hawe,J., Hunter,D., Garry,R., A double-blind randomized trial comparing the Cavaterm and the NovaSure endometrial ablation systems for the treatment	**Sample size** n= 57 randomised (1 woman in each group withdrew after randomisation and before surgery) n= 55 available for analysis n=53 analysed at 6 months (cavaterm n=18 vs NovaSure n= 35) n= 54 analysed at 12 months (cavaterm n= 17 vs NovaSure= 37) **Characteristics**	**Interventions** NovaSure versus Cavaterm Women in the Cavaterm group underwent a mechanical pretreatment by curettage in the operating room immediately before their surgery. This was according to the general directions for use from respective manufacturers. All ablation	**Details** Randomisation Imbalanced randomisation of 2:1, NovaSure:Cavaterm. Randomisation was performed using computer generated sequences in blocks of 5. Allocation Concealment Concealment was achieved by placing the randomisation code into an opaque envelope. The study allocation was revealed after entry had been met and informed consent obtained. Blinding Patients, nursing staff, and the	**Results** Outcome: Patient Satisfaction At 6 months No difference in patient satisfaction for Cavaterm or NovaSure at 6 months, with patients being satisfied or very satisfied in 100% (18/18) vs 84% (31/37) of cases, respectively. 2 women (5%) in the NovaSure group were dissatisfied, and 1 woman (3%) very dissatisfied at 6 months.	**Limitations** **Cochrane risk of bias tool** Selection bias Random sequence generation: Low risk Allocation concealment: Low risk Performance bias Blinding of participants and personnel: Unclear risk Blinding

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
of dysfunctional uterine bleeding, Fertility and Sterility, 80, 203-208, 2003 **Ref Id** 98348 **Country/ies where the study was carried out** United Kingdom **Study type** RCT **Aim of the study**	**Baseline Characteristics** Cavaterm (n=18) vs Novasure (n=37) Mean age, y (SD): 40.5 (8.1) vs 40.5 (6.0) Parity median (range): 2 (1-4) vs 2 (0-4) Mean body mass index (SD): 22.9 (4.9) vs 26.9 (6.2) **Inclusion criteria** Women referred with abnormal uterine bleeding were invited to participate in the study if they had a pictorial blood loss assessment chart score >150, no intrauterine pathology demonstrated by inpatient or outpatient hysteroscopy, a normal endometrial biopsy, a uterine length of <12 cm, premenapausal	procedures were performed under general anaesthesia. Patients received a paracervical block of 10ml of 0.5% bupivicaine HCl and a single bolus of 1.2g I.V ampicillin and potassium clavulanate, unless they were allergic to peniccilin, in which case a third-generation cephalosporin was substituted.	patient's general practitioner were blinded as to the treatment arm. A research nurse, unaware of the treatment allocation, collected outcome data at 6 and 12 months. After the final assessment at 12 months, the treatment allocation was revealed to the patient. Follow-up The primary outcome measure for the study was amenorrhea after the surgical proceedure. Secondary outcomes included other effects of menstrual function, patient satisfaction and procedure acceptability, HRQoL, sexual health, operative details, morbidity, and re-intervention in the 12-month follow-up period. Outcome measures: After the surgical procedure, the operative notes were kept separate from the patient's file but were available in the case of an emergency. A separate record accompanying the patient	At 12 months Women in the cavaterm group, were either satisfied or very satisfied in 83% of cases (15/18). For the NovaSure group, women were satisfied or very satisfied in 92% (34/37) of cases and dissatisfied in 5% (2/37) of cases. No difference in satisfaction rates between the 2 groups. Outcome: Patient Acceptability Both procedures were acceptable to patients using a semantic differential technique. Patients were also asked to complete a VAS at 4 hours post-op; NovaSure was found to be significantly less painful than Cavaterm (VAS median, 48 vs 78,	of Patients, nursing staff, and the patient's general practitioner were blinded as to the treatment arm, however operator not blinded, unclear if this impacts on performance bias. Detection bias Blinding of outcome assessment: Low risk Blinding of outcome assessors was ensured (research nurse recording outcomes and patients themselves blinded) Attrition bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
To compare two second-generation endometrial ablation systems in women with dysfunctional uterine bleeding (DUB) who want conservative surgical treatment **Study dates** June 1999-May 2000 **Source of funding**	gonadotropin levels, normal pap smear, and if they had completed their family. **Exclusion criteria** Endometrial hyperplasia and malignancy, active pelvic inflammatory disease, palpable endometriosis, or full thickness uterine surgery.Novas		detailed than an endometrial ablation had been undertaken, any complications that occurred, and what medications had been given in the operating room. Patients were asked to complete an acceptability questionnaire at 4 hours after their proceedure. This questionnaire included a visual analogue scalepain scored measured at rest and was not adjusted for analgesia. Women were discharged home the same day and reviewed in the research clinic at 6 and 12 months. Menstrual blood loss was also assessed pre-op and 6-12 months post-op using a pictorial blood loss assessment chart. Women compelted the validated QoL: EurQOL-5D, SF-12, and sexual activity questionnaire at baseline, 6 months, and 12 months. Statistics The sample size for this study	p=0.01). Outcome: HRQoL EQ-5D Index Cavaterm original vs 12 months, mean difference (CI), P: -0.07 (-0.2, 0.23), NS NovaSure original vs 12 months, mean difference (CI), P: -0.14 (-0.2, -0.06), p= 0.001 Cavaterm vs Novasure at 12 months, mean difference (CI), P: -0.11 (-0.4, 0.27), NS EQ-5D vas Cavaterm original vs 12 months, mean difference (CI), P: -14 (-27, -1.14). p= 0.048 NovaSure original vs 12 months, mean difference (CI), P: -8.4 (-14.2, -2.5);	Incomplete outcome data: Low risk Low loss of follow-up (<20%) and ITT principles used Reporting bias Selective reporting: Low risk All outcomes reported Other bias Other sources of bias: - **Other information** Included in NMA only, Cavaterm not an intervention of interest according to protocol, therefore, not included in the

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Not disclosed			was calculated based on an ammenorrhea rate of 34% for Cavaterm. At the time of the study being performed, no large-scale study had been performed using the NovaSure. Initial results from an uncontrolled study report an 80% amenorrhea rate for NovaSure. To detect a similar difference (34% vs 80% at 12 months), with 80% power and a 2-sided type 1 error rate of 5% using a 2:1 randomisation, 51 women were required in a ratio of 32:17 SPSS for windows was used for stat analysis. Dichotomous data were analysed using the x2 test with Fishers extract correction if indicated. Continuous parametric data were analysed by students t-test, and nonparametric data by the Wilcoxon rank sum test for paired data and the Mann-Whitney U-Test for independent data. Significance for all analyses was set at the 5%	P=0.006 Cavaterm vs Novasure at 12 months, mean difference (CI), P: -2.1 (-5.9, 10.3); NS SF-12 PCS Cavaterm original vs 12 months, mean difference (CI), P: -4.2 (-9.4, -0.88);NS NovaSure original vs 12 months, mean difference (CI), P: -7.1 (-9.6, -4.7); P=<0.0001 Cavaterm vs Novasure at 12 months, mean difference (CI), P: -1.8 (-7.3, 3.6), NS SF-12 MCS Cavaterm original vs 12 months, mean difference (CI), P: -3.4 (-11.3, -4.1), NS	pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
			level.	NovaSure original vs 12 months, mean difference (CI), P: -5.1 (-9.1, -1.1), P=0.016 Cavaterm vs Novasure at 12 months, mean difference (CI), P: -8.1 (-15.7, -0.34), P=0.04	
Full citation Abdel Malak, K., Shawki, O., Management of menorrhagia with the levonorgestrel intrauterine system versus endometri	**Sample size** Please see Lethaby 2015 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
al resection, Gynecological surgery, 3, 275-80, 2006 **Ref Id** 483324 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Bongers,M.Y., Bourdrez, P., Mol,B.W., Heintz,A.P., Brolmann, H.A., Randomised controlled trial of bipolar radio-frequency endometrial ablation and balloon endometrial ablation, BJOG: An	**Sample size** N= 126 **Characteristics** Bipolar group N= 83 Mean age= 42.6 (4.9) PBAC score median= 515 (range= 150-3401) Dysmenorrhea= 51/83 Balloon group N= 43 Mean age= 43.1 (3.8)	**Interventions** Ablation techniques were performed by one gynaecologist. Patients received no medical pretreatment prior to surgery. Patients in both groups were treated in a day care program using spinal anesthesia or general. Novasure Ablation Technique -generator and disposable device (novacept) -constant power output generator (maximum delivery	**Details** Follow-up Patients were followed up at 3,6, and 12 month intervals after the initial treatment. Patients completed a PBAC and satisfaction, dysmenorrhea, clots and duration of menses were recorded. Those that went on to hysterectomy were recorded as not satisfied at all follow up visits. Statistics Analysis was performed according to ITT. Relative risk for hysterectomy was calculated using Cox regression analysis.	**Results** Outcome: Satisfaction at 12 months Bipolar group= 75/83 Balloon group= 35/43 Outcome: PBAC after treatment *reported graphically (values approximate) Bipolar group: Median= 5 (range 0-1000) Balloon group: Median= 40 (range 0-2000)	**Limitations** **Cochrane risk of bias tool** Selection bias Random sequence generation: Low risk, computer generated Allocation concealment: Low risk, opaque, sealed envelopes Performance bias Blinding: Low risk, patients were blinded to treatment allocation Detection bias Blinding: Low risk, assessors blinded

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
International Journal of Obstetrics and Gynaecology, 111, 1095-1102, 2004 **Ref Id** 98525 **Country/ies where the study was carried out** The Netherlands **Study type** RCT	PBAC score median= 660 (range= 188-3220) Dysmenorrhea= 29/43 **Inclusion criteria** -menorrhagia as indicated by PBAC score > 150 -SIS or diagnostic hysteroscopy was required to confirm a normal uterine cavity with histologically benign endometrium and cavity length 6-11cm -normal pap smear -negative chlamydia test -premenopausal FSH level less than 40 IU/L **Exclusion criteria** -documented	of 180 W) -vacuum pump is contained within the radio-frequency generator -when suction applied the endometrial lining is brought in contact with the electrode array Thermal Balloon Ablation technique -consists of generator and balloon catheter -latex balloon is filled with dextrose -fluid temperature increased to 87 degrees Celsius for 8 minutes			to treatment allocation Attrition bias Low risk, outcome data complete Reporting bias Low risk, outcomes stated in the objective were reported **Other information** After 44 patients, a technical failure in the NovaSure generator was discovered. Separate analysis reported for those women who were randomized after the failure of defective Novasure generator device had been

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study To compare the effectiveness of two second-generation ablation techniques, bipolar radiofrequency impedance-controlled endometrial ablation and balloon ablation, in the treatment for menorrhagia. **Study**	coagulopathies -patients treated with anticoagulants -prior uterine surgery (except low caesarean section) -desire to maintain fertility	-endometrial thinning was performed by aspiration curettage prior to the balloon treatment procedure			corrected. Same trial as Kleijn 2008. Included in the NMA. Compares to 2nd generation ablation techniques, therefore, not included in the pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
dates November 1999 - July 2001 **Source of funding** Novasure devices were free of charge and Thermach oice was discounted.					
Full citation Bonnar, J., Sheppard, B. L., Treatment of menorrhag	**Sample size** N= 76 **Characteristics** Mean age= 39 years (7) Mean height= 162 cm (7)	**Interventions** 3 different treatments taken from day 1 of bleeding for 5 days for three consecutive menstrual cycles.	**Details** Follow-up Menstrual blood loss measured by the Alkaline-Hematin method. Statistics	**Results** Outcome: Change in mean menstrual blood loss (A-H method) Ethamsylate group: Mean change= +8.0 mL (range 103 to 280) (n=27)	**Limitations** **Cochrane risk of bias tool** Selection bias Random sequence generation: unclear risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
ia during menstruation: randomised controlled trial of ethamsylate, mefenamic acid, and tranexamic acid, BMJ, 313, 579-82, 1996 **Ref Id** 483325 **Country/ies where the study was carried out** Ireland **Study**	Mean weight= 65 kg (10) **Inclusion criteria** -35 to 46 years complaining of heavy menstrual bleeding -organic causes excluded by gynaecological investigation (hysteroscopy, endometrial biopsy, pap swear) **Exclusion criteria** -history of renal or hepatic impairment -previous thromboembolic disease -inflammatory bowel disease -peptic or intestinal ulceration -coagulation or fibronolytic disease	Ethamsylate (not relevant for this review) 500 mg six hourly Mefenamic Acid 500 mg eight hourly Tranexamic Acid 1 gram six hourly	Paired and unpaired t tests used to compare blood loss in the three control and treatment cycles. Analysis was carried out using SAS.	Mefenamic acid group: Mean change= - 43.0 mL (range 82 to 179) (n=23) Tranexamic acid group: Mean change= - 89.0 (range 24 to 214) (n=26) Mean difference in change (95% CI) between mefenamic acid and tranexamic acid: -46 mL (-90 to -2 mL, p<0.05) Outcome: Treatment discontinuation- any reason Ethamsylate group: 11/27 Mefenamic acid group: 3/23 Tranexamic acid group: 4/26	Allocation concealment: unclear risk Performance bias Blinding: unclear if done but unlikely due to obvious difference between treatments Detection bias Blinding: unclear if done but unlikely due to obvious difference between treatments Attrition bias Outcome data complete Reporting bias Outcomes stated in the objective were reported

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
type RCT **Aim of the study** To compare the efficacy and acceptability of ethamsylate, mefenamic acid and tranexamic acid for treating menorrhagia. **Study dates** NR **Source of**				Outcome: Treatment discontinuation due to adverse event Ethamsylate group: 4/27 Mefenamic acid group: 1/23 Tranexamic acid group: 3/26 Outcome: Patient satisfaction Defined as those wishing to continue treatment at study end Ethamsylate group: 9/27 Mefanamic acid group: 17/23 Tranexamic acid group: 20/26	**Other information** Ethamsylate arm not relevant to review but used in NMA to provide data for the network. Included in NMA, this publication only reported on outcomes relevant for the NMA.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
funding Health Research Board of Ireland and Pharmacia, Sweden.					
Full citation Brun,J.L., Raynal,J., Burlet,G., Galand,B., Quereux,C., Bernard,P., Cavaterm thermal balloon endometrial ablation versus hysterosco	**Sample size** **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Included in NMA only, Cavaterm not an intervention of interest according to protocol, therefore, not included in the pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
pic endometrial resection to treat menorrhagia: the French, multicenter, randomized study, Journal of Minimally Invasive Gynecology, 13, 424-430, 2006 **Ref Id** 98554 **Country/ies where the study was carried out**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study type **Aim of the study** **Study dates** **Source of funding**					
Full citation Busfield,R.A., Farquhar, C.M., Sowter,M.C., Lethaby,A., Sprecher, M., Yu,Y., Sadler,L.C.,	**Sample size** N= 79 (LNG-IUS= 40, TBA= 39) **Characteristics** LNG-IUS group Age: 7 <40/ 21 40-44/ 14 45-49 BMI mean (SD)= 28.8 (8) PBAC score: 490 (419)	**Interventions** Treatments were performed in an outpatient setting during the first 10 days of menstrual cycle. Local anaesthetic (lignocaine) was injected into the cervix. All women underwent diagnostic hysteroscopy with 4	**Details** Follow-up Menstrual bleeding assessed with PBAC and quality of life assessed with SF-36 at pretreatment, 3, 6, 12, and 24 months. Standardized sanitary products used. Statistics Chi-squared, t test and Wilcoxon test used for statistical analysis.	**Results** Outcome: Patient Satisfaction at 24 months Those who felt treatment was a success LNG-IUS group: 34/40 TBA group: 25/39 Outcome: Treatment discontinuation due to adverse events	**Limitations** **Cochrane risk of bias tool** Selection bias Random sequence generation: Low risk, ccomputer generated blocks Allocation concealment: Low risk, sealed, opaque envelopes

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Brown,P., Johnson,N., A randomised trial comparing the levonorgestrel intrauterine system and thermal balloon ablation for heavy menstrual bleeding, BJOG: An International Journal of Obstetrics and Gynaecology, 113, 257-263, 2006	TBA group Age: 13 <40/ 16 40-44/ 12 45-49 BMI mean (SD)= 29.7 (5.4) PBAC score: 502 (422) **Inclusion criteria** -self-described HMB -completed their family -25-50 years -discrete episodes of bleeding occurring every 3-6 weeks **Exclusion criteria**	mm hysteroscope and 0.9% saline solution. Women who could not tolerate hysteroscopy were schedule to have procedure in theatres with general anaesthetic. TBA procedure Diclofenac given 1 hour before treatment. TBA used thermachoice as per manufacturers instructions. LNG-IUS Inserted as per manufacturers instructions.		LNG-IUS group: 8/40 (expulsion or removal due to pain) TBA group: NA Outcome: Post-op antibiotics for possible endometritis LNG-IUS group: NA TBA group: 5/39 Outcome: PBAC score at 24 months LNG_IUS group: Mean (SD)= 20.6 (28.8) TBA group: Mean (SD)= 75.4 (91.1) Outcome: Quality of life -	Performance bias Blinding: Unclear risk, blinding not possible Detection bias Blinding: High risk on subjective outcome, blinding not possible Attrition bias Low risk, outcome data complete Reporting bias Low risk, outcomes stated in the objective were reported **Other information** Patients with certain types of

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Ref Id 98567 **Country/ies where the study was carried out** New Zealand **Study type** RCT **Aim of the study** To compare LNG-IUS and thermal balloon ablation for the	-ultrasound abnormalities (submucosal fibroids, large fibroids, endometrial polyps) -laboratory abnormalities -hysteroscopic abnormalities -incidental adnexal abnormality on ultrasound -severe intermenstrual bleeding -severe dysmennorhea, premenstrual pain, chronic pelvic pain -medical contraindications -previous endometrial surgery -univestigated postcoital bleeding -untreated cervical cytology			Overall SF-36 score LNG-IUS group: Baseline mean (SD)= 63.7 (22.7) 24 months mean (SD)= 77.5 (20.1) TBA group: Baseline mean (SD)= 63.7 (14.4) 24 months mean (SD)= 74.9 (18.8) Outcome: Expulsion LNG-IUS group: by 3 months, 1 expulsion, by 12 months further 2 expulsions, by 24 months further 1 expulsion (reported narratively) TBA: N/A	pain excluded.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
treatment of heavy menstrual bleeding. **Study dates** March 1999 to July 2001 **Source of funding** NR					
Full citation Cooper,J., Gimpelson,R., Laberge,P., Galen,D., Garza-Leal,J.G., Scott,J.,	**Sample size** **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Included in NMA, this publication only reported on outcomes relevant for the NMA.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Leyland,N., Martyn,P., Liu,J., A randomized, multicenter trial of safety and efficacy of the NovaSure system in the treatment of menorrhagia, Journal of the American Association of Gynecologic Laparoscopists, 9, 418-428, 2002					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Ref Id 98673 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**					
Full citation Cooper,J. M.,	**Sample size** **Characteristics** **Inclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Included only in the NMA, microwave

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Anderson, T.L., Fortin,C.A., Jack,S.A., Plentl,M.B., Microwave endometrial ablation vs. rollerball electroablation for menorrhagia: A multicenter randomized trial, Journal of the American Association of Gynecologic Laparoscopists, 11, 394-403,	**Exclusion criteria**				ablation not an intervention of interest according to protocol, therefore not included in the pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
2004 **Ref Id** 98675 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**					
Full citation Cooper, K.	**Sample size** **Characteristics** **Inclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Included only in the

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
G., Bain, C., Parkin, D. E., Comparison of microwave endometrial ablation and transcervical resection of the endometrium for treatment of heavy menstrual loss: a randomised trial, Lancet (London, England), 354, 1859-63, 1999 **Ref Id**	**Exclusion criteria**				NMA, microwave ablation not an intervention of interest according to protocol, therefore not included in the pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
483327 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**					
Full citation Corson,S. L., A multicenter evaluation	**Sample size** Please see Lethaby 2013 Cochrane systematic review. **Characteristics**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
of endometrial ablation by Hydro ThermAblator and rollerball for treatment of menorrhagia, Journal of the American Association of Gynecologic Laparoscopists, 8, 359-367, 2001 **Ref Id** 98684 **Country/ies where the study**	**Inclusion criteria** **Exclusion criteria**				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
was carried out **Study type** **Aim of the study** **Study dates** **Source of funding**					
Full citation Corson,S. L., Brill,A.I., Brooks,P. G., Cooper,J. M., Indman,P. D.,	**Sample size** Please see Lethaby 2013 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Liu,J.H., Soderstrom,R.M., Vancaillie, T.G., One-year results of the vesta system for endometrial ablation, Journal of the American Association of Gynecologic Laparoscopists, 7, 489-497, 2000 **Ref Id** 98683 **Country/ies where the study**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
was carried out **Study type** **Aim of the study** **Study dates** **Source of funding**					
Full citation Crosignani, P. G., Vercellini, P., Mosconi, P., Oldani, S., Cortesi, I., De Giorgi, O.,	**Sample size** N=70 (LNG-IUS= 35, TCRE=35) **Characteristics** IUD group: Mean age= 43.8 years (3.8) Mean BMI = 25.3 (4.4)	**Interventions** LNG-IUS releases 20 ug levonorgestrel per day; inserted within 7 days of start of menstruation TCRE scheduled during	**Details** Follow-up Women had bi-monthly follow-up visits. Bleeding was assessed with PBAC. Quality of life was assessed with SF-36.	**Results** Outcome: Mean PBAC at 12 months LNG-IUS= 38.8 mL (37.1) Endometrial resection= 23.5 mL (32.6)	**Limitations** **Cochrane risk of bias tool** Selection bias Random sequence generation: unclear Allocation concealment: unclear

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Levonorgestrel-releasing intrauterine device versus hysteroscopic endometrial resection in the treatment of dysfunctional uterine bleeding, Obstetrics & Gynecology, 90, 257-63, 1997 **Ref Id** 483328 **Country/ies where the study**	PBAC score= 181.3 (59.4) Uterine volume= 181.3 mL (35.2) Endometrial resection: Mean age= 45.4 years (3.8) Mean BMI = 24.0 (3.0) PBAC score= 204.0 (82.9) Uterine volume= 122.4 mL (45.2) *All data mean (SD) **Inclusion criteria** -age 38 and over -referred to centre for hysterectomy for menorrhagia	the early proliferative stage of the cycle; roller-ball electrode used for the cornua and uterine fundus; 90-degree loop for the rest of the cavity Operations performed by one surgeon.		Outcome: Patient satisfaction at 12 months LNG-IUS: 29/34 satisfied or very satisfied TCRE: 33/35 satisfied or very satisfied Outcome: SF-36 at 12 months (mean (SD) Physical functioning LNG-IUS: 78.0 (22.4) TCRE: 9.2 (23.7) Role limitation (physical) LNG-IUS: 72.5 (33.7) TCRE: 74.2 (35.6) Bodily pain LNG-IUS: 58.9 (28.0) TCRE: 70.3 (23.3)	Performance bias Blinding: unclear risk, blinding not feasible due to the nature of the interventions but unclear how it might affect performance bias Detection bias Blinding: high risk, blinding not feasible due to the nature of the interventions, high risk of bias in subjective outcomes Attrition bias Low risk, outcome data complete Reporting bias Low risk, outcomes

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
was carried out Italy **Study type** RCT **Aim of the study** To compare the effect of a LNG-IUD with that of endometrial resection on menstrual bleeding, patient satisfaction, and quality of	-uterine volume less than 8-week pregnancy -negative pap smear in last 12 months -no evidence of atypical hyperplasia at endometrial biopsy -no adnexal tumours -normal uterine cavity at hysteroscopy **Exclusion criteria** -pregnant -breastfeeding -uncertain about wish for future pregnancy			General health perception LNG-IUS: 64.1 (18.6) TCRE: 70.3 (15.1) Vitality LNG-IUS: 56.3 (14.1) TCRE: 54.8 (20.7) Social functioning LNG-IUS: 69.8 (22.3) TCRE: 9.7 (24.1) Role limitation (emotional) LNG-IUS: 61.3 (35.6) TCRE: 72.4 (36.8) Mental health LNG-IUS: 60.1 (18.2) TCRE: 59.6 (20.5)	stated in the objective were reported **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
life in menorrhagia women during 12 months of follow-up. **Study dates** NR **Source of funding** Partially supported by the Italian National Research Council.				Outcome: Partial expulsion LNG-IUS: 2/34 TCRE: N/A	
Full citation Duleba, A. J.,	**Sample size** Please see Lethaby 2013 Cochrane systematic review.	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Heppard, M. C., Soderstrom, R. M., Townsend, D. E., A randomized study comparing endometrial cryoablation and rollerball electroablation for treatment of dysfunctional uterine bleeding, Journal of the American Association of Gynecologic Laparosco	**Characteristics** **Inclusion criteria** **Exclusion criteria**				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
pists, 10, 17-26, 2003 **Ref Id** 483330 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**					
Full citation	**Sample size**	**Interventions**	**Details**	**Results**	**Limitations**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Dunphy, B. C., Goerzen, J., Greene, C. A., de la Ronde, S., Seidel, J., Ingelson, B., A double-blind randomised study comparing danazol and medroxyprogesterone acetate in the management of menorrhagia, Journal of Obstetrics & Gynaecolo	**Characteristics** **Inclusion criteria** **Exclusion criteria**				**Other information** Only included in the NMA. Danazol not an intervention of interest according to protocol, therefore, not included in the pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
gy, 18, 553-5, 1998 **Ref Id** 483331 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**					
Full citation	**Sample size**	**Interventions**	**Details**	**Results**	**Limitations**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Endrikat, J., Shapiro, H., Lukkari-Lax, E., Kunz, M., Schmidt, W., Fortier, M., A Canadian, multicentre study comparing the efficacy of a levonorgestrel-releasing intrauterine system to an oral contraceptive in women with idiopathic	N=39 **Characteristics** LNG-IUS group: N=20 Mean age (SD)= 41.8 (4.3) Mean BMI (SD)= 24.3 (1.9) OC group: N=19 Mean age (SD)= 42.4 (4.4) Mean BMI (SD)= 22.6 (2.3) **Inclusion criteria** Participants were otherwise healthy women, aged 30 at entrty with a diagnosis of idiopathic menorrhagia (assessed by PBAC score 100 for 2 consecutive cycles) and with a normal or only slightly enlarged uterus.	For women randomized to undergo treatment with the LNG-IUS, it was inserted into the uterus by a physician within seven days of the start of the last menstrual period for a treatment period of 12 months. The system releases up to 20 ug LNG per 24 hours. Women randomized to treatment with a combined oral contraceptive (OC1/20) used a preparation containing norethindrone acetate and ethinyl estradiol (Minestrin, Parke-Davis Canada) and took	Follow-up The primary outcome measure was menstrual blood loss (MBL), and the secondary measures were treatment success (i.e., clinical outcome), hemoglobin concentration, and the menorrhagia severity score (to evaluate the effect of treatment on quality of life). In order to quantify baseline MBL, the pictorial blood loss assessment chart published by Higham was applied. Thereafter, MBL was quantified by pictorial blood assessment chart (PBAC).	Outcome: Median PBAC score LNG-IUS group: Baseline: 228 12 months: 13 OC group: Baseline: 290 12 months: 72 *uncertainty NR p=0.002; estimate for median difference –62; 95% CI–89 to –18 Outcome: Aberdeen Mean Menorrhagia Severity Score In subjects treated with LNG-IUS compared to subjects treated with OC1/20 was significantly	**Cochrane risk of bias tool** Selection bias Random sequence generation: unclear, patients randomized in order of enrolment Allocation concealment: unclear Performance bias Blinding: unclear, blinding not possible but unclear how it might affect performance bias Detection bias Blinding: high risk, blinding not possible, high risk of bias for

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
menorrhagia, Journal of Obstetrics & Gynaecology Canada: JOGC, 31, 340-7, 2009 **Ref Id** 483332 **Country/ies where the study was carried out** Canada **Study type** RCT **Aim of the**	**Exclusion criteria** -Primary exclusion criteria were the contraindications for LNG-US and combined oral contraceptive use. -Further exclusion criteria included metabolic and endocrine diseases, diagnostically unclassified genital bleeding, and a history of liver or vascular diseases. -In addition, concomitant use of medications that could influence the study objectives, including sex steroids, any treatment for menorrhagia (including tranexamic acid and non-steroidal antiinflammatory drugs), drugs that could affect bleeding patterns (platelet aggregation inhibitors, anticoagulants)	one tablet daily over 12 months. In each 28-tablet blister pack, the first 21 tablets (days 1 to 21) contained 1 mg norethindrone acetate and 20 µg ethinyl estradiol, and the last 7 tablets (days 22 to 28) contained placebo.		lower (p= 0.045, unadjusted) in the LNG-IUS group at 6 months (estimate for difference -6.37; 95% CI -12.61 to -0.14), while at other time points no significant difference was seen. Data displayed graphically and unable to extract data at other time points. Outcome: Discontinuation due to adverse events LNG-IUS: 1/20 OC: 5/19	subjective outcomes Attrition bias Low risk, outcome data complete Reporting bias Low risk, outcomes stated in the objective were reported **Other information** Included in NMA, this publication only reported on outcomes relevant for the NMA.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
study To evaluate the efficacy of a levonorgestrel-releasing intrauterine system (LNG-IUS) compared with a combined oral contraceptive containing 1 mg norethindrone acetate and 20 ethinyl estradiol (OC1/20) in reducing	and drugs known to induce or to inhibit liver enzymes was not permitted. -Women who had intramural or subserous fibroids of mean diameter 4 cm or submucosal fibroids, adenomyosis, or endometrial abnormalities (e.g., polyps or hyperplasia, verified by saline infusion sonography or hysteroscopy) or who were perimenopausal (as evidence by serum FSH levels 50 IU/L and serum estradiol levels 100 pmol/L) were also excluded.				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
menstrual blood loss (MBL) in women with idiopathic menorrhagia. **Study dates** NR **Source of funding** This study was supported by a grant from Bayer Schering Pharma AG, Berlin, Germany. Heather Shapiro					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
and Michel Fortier were supported by Bayer for their participation as clinical investigators. Eeva Lukkari-Lax, Michael Kunz and Jan Endrikat are employees of Bayer Schering Pharma.					
Full citation	**Sample size**	**Interventions**	**Details**	**Results**	**Limitations**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Fraser,I.S., Romer,T., Parke,S., Zeun,S., Mellinger, U., MacHlitt,A., Jensen,J.T., Effective treatment of heavy and/or prolonged menstrual bleeding with an oral contraceptive containing estradiol valerate and dienogest: A randomized, double-	N=231 **Characteristics** E2V/DNG Group: N= 149 Mean age= 39.5 (6.6) N with HMB= 136 (91.3%) Placebo group: N=82 Mean age= 38.5 (7.5) N with HMB= 76 (92.6%) **Inclusion criteria** -age 18 and over -heavy, prolongue and/or frequent menstrual bleeding (confirmed with 90-day run in) -willing to use barrier	Placebo or E2V/DNG which was administered using an estrogen step-down, progesterone step-up program: -3 mg E2V Days 1-2 -2 mg E2V/ 2 mg DNG Days 3-7 -2 mg E2V/ 3 mg DNG Days 8-24 -1 mg E2V Days 25-26 -Placebo Days 27-28 -No tablet free days between cycles -Given for the 3 cycles (90 day efficacy phase)	Follow-up 90-day run in period used to establish baseline menstrual blood loss (MBL). MBL was quanitified using AH method. Primary endpoint was response to treatment (return to normal bleeding). Secondary endpoint was change in MBL volume. Adverse events were reported. Statistics All outcomes were analyzed based on the ITT population. SAS software was used.	Outcome: Mean difference in MBL (SD) Mean in treatment cycle - mean in run-in period Treatment group= 458 mL (410) Placebo gruop= 93 mL (268) Outcome: Patient satisfaction at study end Patients reporting an overall improvement in bleeding symptoms Treatment group: 77.9% Placebo group: 45.1% Outcome: Discontinuation Treatment group: 32/149 Placebo: 17/82	**Cochrane risk of bias tool** Selection bias Random sequence generation: Low risk, computer-generated, permuted blocks Allocation concealment: unclear risk Performance bias Blinding: low risk, participants were blinded to treatment allocation Detection bias Blinding: low risk, investigators were blinded to treatment allocation Attrition bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
blind Phase III trial, Human Reproduction, 26, 2698-2708, 2011 **Ref Id** 287588 **Country/ies where the study was carried out** Europe and Australia **Study type** RCT **Aim of the**	contraception and willing to use and collect sanitary protection -normal endometrial biopsy **Exclusion criteria** -the use of medication intended to relieve HMB (sex steroids, NSAIDs, tranexamic acid) -abnormal transvaginal ultrasound -abnormal labaratory investigation -history of endometrial ablation -D and C in last 2 months -any organic cause of bleeding disorder -BMI over 32 -Age 35 and over who			Outcome: Discontinuation due to adverse events Treatment group: 14/149 Placebo group: 5/82	Low risk, outcome data complete Reporting bias Low risk, outcomes stated in the objective were reported **Other information** Included in NMA, this publication only reported on outcomes relevant for the NMA.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
study To investigate the efficacy and safety of estradiol valerate/dienogest (E2V/DNG) for the treatment of heavy menstrual bleeding without recognizable organic pathology. **Study dates** February 2006 to May 2008. **Source of funding**	smoke cigarettes -Any contraindication for the use of COCs				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Bayer HealthCare Pharmaceuticals.					
Full citation Hawe,J., Abbott,J., Hunter,D., Phillips,G., Garry,R., A randomised controlled trial comparing the Cavaterm endometrial ablation system with the	**Sample size** **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Only included in the NMA. Laser ablation not an intervention of interest according to protocol, therefore, not included in the pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Nd:YAG laser for the treatment of dysfunctional uterine bleeding, BJOG: An International Journal of Obstetrics and Gynaecology, 110, 350-357, 2003 **Ref Id** 99045 **Country/ies where the study was carried out**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study type **Aim of the study** **Study dates** **Source of funding**					
Full citation Higham, J. M., Shaw, R. W., A comparative study of danazol, a regimen of decreasing doses of danazol, and norethindr	**Sample size** **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** NMA only- Danazol

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
one in the treatment of objectively proven unexplained menorrhagia, American Journal of Obstetrics & Gynecology, 169, 1134-9, 1993 **Ref Id** 483334 **Country/ies where the study was carried out** **Study**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
type **Aim of the study** **Study dates** **Source of funding**					
Full citation Hurskainen, R., Teperi, J., Rissanen, P., Aalto, A. M., Grenman, S., Kivela, A., Kujansuu, E., Vuorma, S., Yliskoski,	**Sample size** Please see Lethaby 2015 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
M., Paavonen, J., Quality of life and cost-effectiveness of levonorgestrel-releasing intrauterine system versus hysterectomy for treatment of menorrhagia: a randomised trial, Lancet, 357, 273-7, 2001 **Ref Id** 483335 **Country/ie**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
s where the study was carried out **Study type** **Aim of the study** **Study dates** **Source of funding**					
Full citation Hurskainen, R., Teperi, J., Rissanen, P., Aalto, A. M., Grenman,	**Sample size** Please see Lethaby 2015 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
S., Kivela, A., Kujansuu, E., Vuorma, S., Yliskoski, M., Paavonen, J., Clinical outcomes and costs with the levonorgestrel-releasing intrauterine system or hysterectomy for treatment of menorrhagia: randomized trial 5-year follow-up,					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
JAMA, 291, 1456-63, 2004 **Ref Id** 483336 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**					
Full citation	**Sample size**	**Interventions**	**Details**	**Results**	**Limitations**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Irvine, G. A., Campbell-Brown, M. B., Lumsden, M. A., Heikkila, A., Walker, J. J., Cameron, I. T., Randomised comparative trial of the levonorgestrel intrauterine system and norethisterone for treatment of idiopathic menorrhag	N=44 **Characteristics** LNG-IUS group: N=22 Median age= 38.5 years (31-45) Baseline median MBL= 105 mL (82-780) Norethisterone group: N=22 Median age= 39 years (30-45) Baseline median MBL= 120 mL (82-336)	LNG-IUS fitted within first 7 days of start of period. Norethisterone was prescribed at a dose of 5 mg three times daily from day 5 to 26 of the cycle over 3 cycles.	Follow-up MBL assessed with alkaline-hematin method. Statistics Per-protocol and intention to treat analysis conducted. Wilcoxon rank sum test, Mann Whitney U test and t test planned to compare between groups.	Outcome: Discontinution due to adverse events LNG-IUS: 2/22 Norethisterone: 6/22 Outcome: MBL in ml (AH method) Baseline, median (range) LNG-IUS: 105 (82-780) Norethisterone: 120 (82-336) p=0.74 At 3rd treatment cycle (3 months), median (range) LNG-IUS: 6 (0-284) Norethisterone: median= 20 (range 4-137) p=0.03	**Cochrane risk of bias tool** Selection bias Random sequence generation: computer generated Allocation concealment: opaque, sealed envelopes Performance bias Blinding: unclear risk, blinding not feasible due to the nature of the interventions but unclear how it might affect performance bias Detection bias Blinding: high risk,

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
ia, British Journal of Obstetrics & Gynaecology, 105, 592-8, 1998 **Ref Id** 483337 **Country/ies where the study was carried out** UK **Study type** RCT **Aim of the study** To	**Inclusion criteria** -parous -age 18-45 -in good general health -normal pelvic exam -sound measurement <10 cm -negative cervical cytology -measured MBL > 80 mL **Exclusion criteria** -women treated with steroid hormones or anticoagulants within last 3 months -injectable hormones used within the last 12 months			Outcome: Satisfaction with treatment those reporting well or very well satisfied LNG-IUS: 14/22 Norethisterone: 8/18 (those reporting at 3 months Outcome: Expulsion LNG-IUS: 1/22 (during the third cycle of treatment) Norethisterone: N/A	blinding not feasible due to the nature of the interventions, high risk of bias for subjective outcomes Attrition bias Low risk, outcome data complete Reporting bias Low risk, outcomes stated in the objective were reported **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
compare the efficacy and acceptability of the levonorgestrel IUS and norethisterone for the treatment of idiopathic menorrhagia. **Study dates** NR **Source of funding** NR					
Full	**Sample size**	**Interventions**	**Details**	**Results**	**Limitations**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
citation Istre,O., Trolle,B., Treatment of menorrhagia with the levonorgestrel intrauterine system versus endometrial resection, Fertility and Sterility, 76, 304-309, 2001 **Ref Id** 226715 **Country/ies where the study was**	N= 60 (30 in each arm) **Characteristics** LNG-IUS Mean age (SD)= 41.4 years (3.8) Uterine sound measure= 7.5 mm (1.1) TCRE Mean age (SD)= 41.9 years (3.8) Uterine sound measure= 7.7 mm (1.1) **Inclusion criteria** -premenopausal -30 to 49 years -regular uterine cavity (length <= 10 cm) -no wish for future	LNG-IUS versus endometrial resection No pretreatment given to suppress the endometrium. Resection was performed without simultaneous laparoscopy. Cervical canal was dilated to Hegar 11 and a rigid resectoscope was passed into the uterine cavity. Glycine 1.5% was infused for irrigation. A diathermal current of 120 W was used for resection of fibroids and endometrium. 80 W was used for homeostasis.	Follow-up Menstrual blood loss was assessed using PBAC. Other symptoms were assessed using visual analogue scale. Statistics SAS program was used. Continuous variables assessed with t test or Wilcoxon rank sum test. Categorical variables were tested with Fisher's exact test.	Outcome: Discontinuation due to AE LNG-IUS: 6/30 TCRE: NA Outcome: Menstrual blood loss (mean PBAC score (SD)) LNG-IUS: Baseline= 420 (352) 12 months= 42 (99) TCRE: Baseline= 404 (480) 12 months= 7 (15)	**Cochrane risk of bias tool** Selection bias High risk of bias- patients assigned to groups in order of enrolment Performance bias Blinding: unclear but unlikely due to obvious difference between treatments Detection bias Blinding: unclear but unlikely due to obvious difference between treatments Attrition bias Low risk, outcome data complete

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
carried out Norway **Study type** RCT **Aim of the study** Treatment of menorrhagia with levonorgestrel intrauterine system (LNG IUS) and transcervical resection. **Study dates** NR	pregnancy SIS or hysteroscopy performed to exclude pathology **Exclusion criteria** -breast feeding -presences of subserous myomas > 40 mm -current or recent PID -abnormal pap smear -known endometriosis -breast cancer -history of DVT -thromboembolism or liver disease -hormone therapy during 3 months prior to surgery				Reporting bias Low risk, outcomes stated in the objective were reported **Other information** Included in NMA, this publication only reported on outcomes relevant for the NMA.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Source of funding Supported by Leiras Oy, Turku, Finland					
Full citation Kaunitz, A. M., Bissonnette, F., Monteiro, I., Lukkari-Lax, E., Muysers, C., Jensen, J. T., Levonorgestrel-releasing intrauterine system	**Sample size** Please see Lethaby 2015 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
or medroxyprogesterone for heavy menstrual bleeding: a randomized controlled trial, Obstetrics and gynecology, 116, 625-32, 2010 **Ref Id** 483339 **Country/ies where the study was carried out** **Study type**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study **Study dates** **Source of funding**					
Full citation Kittelsen, N., Istre, O., A randomized study comparing levonorgestrel intrauterine system (LNG IUS) and transcervical resection	**Sample size** Please see Lethaby 2015 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
of the endometrium (TCRE) in the treatment of menorrhagia: Preliminary results, Gynaecological Endoscopy, 7, 61-5, 1998 **Ref Id** 483340 **Country/ies where the study was carried out** **Study type**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study **Study dates** **Source of funding**					
Full citation Kriplani, A., Kulshrestha, V., Agarwal, N., Diwakar, S., Role of tranexamic acid in management of dysfunctional uterine bleeding in	**Sample size** **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Included in NMA, this publication only reported on outcomes relevant for the NMA.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
comparison with medroxyprogesterone acetate, Journal of Obstetrics & Gynaecology, 26, 673-8, 2006 **Ref Id** 483341 **Country/ies where the study was carried out** **Study type** **Aim of the study**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study dates **Source of funding**					
Full citation Meyer, W. R., Walsh, B. W., Grainger, D. A., Peacock, L. M., Loffer, F. D., Steege, J. F., Thermal balloon and rollerball ablation to treat menorrhag	**Sample size** Please see Lethaby 2013 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
ia: a multicenter comparison, Obstetrics & Gynecology, 92, 98-103, 1998 **Ref Id** 483343 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
funding					
Full citation Pellicano, M., Guida, M., Acunzo, G., Cirillo, D., Bifulco, G., Nappi, C., Hysteroscopic transcervical endometrial resection versus thermal destruction for menorrhagia: a prospectiv	**Sample size** **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Included in NMA, this publication only reported on outcomes relevant for the NMA.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
e randomized trial on satisfaction rate, American Journal of Obstetrics & Gynecology, 187, 545-50, 2002 **Ref Id** 483345 **Country/ies where the study was carried out** **Study type** **Aim of the study**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study dates **Source of funding**					
Full citation Perino, Antonio, Castelli, Antonio, Cucinella, Gaspare, Biondo, Andrea, Pane, Antonella, Venezia, Renato, A randomized comparison of endometrial laser	**Sample size** **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Only included in the NMA. Laser ablation not an intervention of interest according to protocol, therefore, not included in the pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
intrauterine thermotherapy and hysteroscopic endometrial resection, Fertility and sterility, 82, 731-4, 2004 **Ref Id** 483346 **Country/ies where the study was carried out** **Study type** **Aim of the**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
study **Study dates** **Source of funding**					
Full citation Rauramo, Ilkka, Elo, Iina, Istre, Olav, Long-term treatment of menorrhagia with levonorgestrel intrauterine system versus endometrial resection,	**Sample size** N= 59 **Characteristics** LNG-IUS group: Mean age (SD)= 41.4 years (3.8) Weight= 73.4 kg (12.9) Uterine sound measure median= 7.0 cm (range 5.2-10.0) TCRE group: Mean age (SD)= 42.1 years	**Interventions** The endometrial resections were performed under spinal anesthesia by the same surgeon (O.I.) who also inserted all the levonorgestrel intrauterine systems. The technique has been described in detail previously.	**Details** Randomisation This study was an open, randomized 3-year trial. Patients with menorrhagia were assigned randomly to either the levonorgestrel intrauterine system (n = 30) or endometrial resection (n = 29). Follow-up Pictorial blood loss assessment charts were used to measure menstrual blood loss. A pictorial blood-loss assessment chart score exceeding 75 (representing menstrual blood loss >=60 mL) was used to	**Results** Outcome: Treatment Discontinuation due to adverse event LNG-IUS: 9/30 TCRE: N/A Outcome: Median menstrual blood loss (PBAC) LNG-IUS: Baseline: 261.5 (60-1503) 3 years: 7.0 (0-101)	**Limitations** **Cochrane risk of bias tool** Selection bias Random sequence generation: using the SAS/PLAN procedure Allocation concealment: sealed envelopes used Performance bias Blinding: unclear risk,

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Obstetrics and gynecology, 104, 1314-21, 2004 **Ref Id** 483348 **Country/ies where the study was carried out** Norway **Study type** RCT **Aim of the study** To compare the long-	(3.6) Weight= 70.4 kg (13.8) Uterine sound measure median= 8.0 cm (range 6.0-10.0) **Inclusion criteria** -aged from 30 to 49 years, -expressed no further desire for children, -had idiopathic menorrhagia needing treatment, -exhibited a normal uterine cavity, -They were not pregnant, breastfeeding, or menopausal, as evidenced by a follicle-stimulating hormone (FSH) level not exceeding 30 IU/L and a serum estradiol (E2) level less than 20 nmol/L **Exclusion criteria**		diagnosis the patient as having menorrhagia. Discontinuations and cases requiring repeat operations were evaluated. The patients were followed at the outpatient clinic, with visits scheduled at 6 weeks and at 6, 12, 18, 24, and 36 months after transcervical resection of the endometrium or insertion of the levonorgestrel intrauterine system. Statistical analysis The following nonparametric methods were used for analysis: Wilcoxon rank-sum test to compare differences between the groups at baseline and for analyzing the treatment by time interaction; Friedman's 2-way analysis of variance for repeated measures, and Wilcoxon signed rank test for intra-group comparisons. Serum ferritin and blood hemoglobin were tested in similar manner as menstrual blood loss. The alpha level was	TCRE: Baseline: 311.0 (81-2506) 3 years: 4.0 (0-182) Outcome: Post-procedure infection LNG-IUS: 5/30 (PID or endometritis) TCRE: 4/29 (PID or myometritis) Outcome: Expulsion LNG-IUS: 1/30 TCRE: N/A	blinding not possible, unclear how it might affect performance bias Detection bias Blinding: high risk, blinding not possible, high risk of bias for subjective outcomes Attrition bias Low risk, outcome data complete Reporting bias Low risk, outcomes stated in the objective were reported **Other information** In the levonorgestrel intrauterine system

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
term efficacy of the LNG-IUS and transcervical resection of the endometrium in the treatment of menorrhagia. **Study dates** March 1993-October 1995 **Source of funding** Sponsored by Schering Ag, Berlin,	-subserous or intramural fibroids (myomata) with a diameter more than 40 mm -submucosal fibroids confirmed by ultrasonography, -current genital infection or pelvic inflammatory disease within the last 6 months, -Pap test classified as cervical intraepithelial neoplasia 2 or higher, -manifest endometriosis or adenomyosis, -a history of or active thromboembolic disorder, -undiagnosed abnormal uterine bleeding, -acute liver disease or liver tumor, -breast cancer, -or use of injectable		controlled at the overall level main effects and was set at P < .05. The treatment by time interaction for menstrual blood loss was performed using multiple pairwise comparisons between the groups. The Bonferroni procedure should have been applied and, consequently, for the 3 comparisons the significance level should have been set to 0.0167. The data program used was SAS (SAS Institute Inc., Cary, NC). All analyses were based on the intent-to-treat population.		group, 19 of 30 women (63,3%) completed the 36-month follow-up. In the resection group, the procedure was effective during the 3-year study period in 22 of 29 women (75.9%).

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Germany	hormones during the preceding 12 months				
Full citation Reid, Peter C., Virtanen-Kari, Susanna, Randomised comparative trial of the levonorgestrel intrauterine system and mefenamic acid for the treatment of idiopathic menorrhag	**Sample size** N= 51 (LNG-IUS= 25, mefenamic acid= 26) **Characteristics** There were no significant differences between the treatment groups in any of the baseline parameters measured. Mean age in the LNG-IUS group was 39.4 years (SD 4.4) and 38.5 years (SD 4.2) in the oral mefenamic acid group. **Inclusion criteria** -age 18–47 -good general health with regular, ovulatory, menstrual cycles of 21–35	**Interventions** Women were randomised to receive either oral mefenamic acid 500 mg three times daily for the first four d ays of the menstrual cycle or to have a LNG-IUS inserted for the study period of six cycles. The LNG-IUS comprises a T-shaped polyethylene frame and a levonorgestrel-containing cylinder covered with a membrane regulating the release of the hormone. The total	**Details** Follow-up To assess MBL and TMFL subjects were given Tampax super tampons and/or Kotex simplicity size two sanitary towels which had been individually weighed in a self - sealing plastic bag. Statistical analysis The primary outcome measure was compared between treatment groups at baseline, after three cycles and after six cycles using the Wilcoxon rank sum test. Change in MBL between baseline and other time points (three cycles and six cycles) was tested between the treatment groups using the Wilcox on rank sum test. The	**Results** Outcome: Median menstrual blood loss (PBAC) LNG-IUS group: Baseline: 240 (range: 91-545) 6 months: 25 (0-402) Mefenamic acid group: Baseline: 233 (range: 77-469) 6 months: 159 (50-307) Outcome: Adverse event: Infection Chlamydial endometritis:	**Limitations** **Cochrane risk of bias tool** Selection bias Random sequence generation: SAS/PLAN method Allocation concealment: opaque, sealed envelopes Performance bias Blinding: unclear risk, blinding not possible, unclear how it might affect performance bias Detection bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
ia: a multiple analysis using total menstrual fluid loss, menstrual blood loss and pictorial blood loss assessment charts, BJOG : an international journal of obstetrics and gynaecology, 112, 1121-5, 2005 **Ref Id** 483349 **Country/ies where**	days -objective, idiopathic menorrhagia (MBL 80 mL). -Screening investigations included haemoglobin, ferritin, mid-luteal phase progesterone , mid-luteal endometrial biopsy to assess ovulation, thyroid and liver function tests, pelvic ultrasound and cervical smear **Exclusion criteria** -undiagnosed abnormal bleeding, -were anovulatory, -had submucosal fibroids or fibroids with a total volume of >5cm -a uterine sound of >10 cm, -abnormal cervical cytology, -untreated hypertension,	amount of levonorgestrel in the cylinder is 52 mg and its initial release rate is 20 Ag per 24 hours.	time effect was analysed using Friedman's two-way ANOVA separately for each treatment group. In case of statistically significant time effects the change from baseline to the other time points was tes ted using the Wilcoxon signed rank test. The median (Wilcoxon median) differences between the treatment groups for the difference between baseline and three cycles and correspondingly between baseline and six cycles were estimated together with 95% confidence intervals	LNG-IUS group: 1 case Mefenamic acid group: none Outcome: Adverse event: Expulsion LNG-IUS: 1 case Mefenamic acid group: none	Blinding: high risk, blinding not possible, high risk of bias for subjective outcomes Attrition bias Low risk, outcome data complete Reporting bias Low risk, outcomes stated in the objective were reported **Other information** First-line treatment only.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
the study was carried out UK **Study type** RCT **Aim of the study** To compare the efficacy and tolerability of the levonorgestrel intrauterine system (LNG IUS) with mefenamic acid in the	-abnormal thyroid or liver function tests, -asthma, an IUCD in situ, -had been treated for menorrhagia or used hormonal contraceptives within the previous four months				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
management of objective idiopathic menorrhagia. **Study dates** May 1996 to December 1998 **Source of funding** The authors would like to thank Schering Oy, Finland, for funding of this study. Kimberly Clark for donating					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
sanitary protection.					
Full citation Sambrook, A. M., Cooper, K. G., Campbell, M. K., Cook, J. A., Clinical outcomes from a randomised comparison of Microwave Endometrial Ablation with Thermal Balloon endometri	**Sample size** **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Only included in the NMA. Microwave ablation not an intervention of interest according to protocol, therefore, not included in the pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
al ablation for the treatment of heavy menstrual bleeding, BJOG : an international journal of obstetrics and gynaecology, 116, 1038-45, 2009 **Ref Id** 483351 **Country/ies where the study was carried out** **Study type**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study **Study dates** **Source of funding**					
Full citation Shaaban, Mamdouh M., Shabaan, Mamdouh M., Zakherah, Mahmoud S., El-Nashar, Sherif A., Sayed, Gamal H., Levonorgestrel-	**Sample size** Please see Lethaby 2015 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
releasing intrauterine system compared to low dose combined oral contraceptive pills for idiopathic menorrhagia: a randomized clinical trial, Contraception, 83, 48-54, 2011 **Ref Id** 483352 **Country/ies where the study was carried**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
out **Study type** **Aim of the study** **Study dates** **Source of funding**					
Full citation Soysal, Mehmet, Soysal, Seyide, Ozer, Suzan, A randomized controlled trial of levonorges	**Sample size** N= 72 **Characteristics** TBA group: Mean age= 44.1 (2.4) PBAC score= 417 (81.4) Uterine volume= 111.3 mL (24)	**Interventions** Two monthly injected doses of GnRH analog goserelin acetate given prior to TBA. TBA performed under local intracervivcal and paracervical anesthesia supplemented with conscious sedation.	**Details** Follow-up PBAC score used to assess menstrual blood loss. Quality of life evaluated with SF-36. HADS used to measure anxiety and depression. Statistical analysis Analysis was using SPSS. Student's t test, Mann-Whitney U test, Fisher's exact test, chi-	**Results** Outcome: Patient Satisfaction at 12 months Assessed by those who would recommend or highly recommend the treatment TBA: 26/35 LNG-IUD: 22/32	**Limitations** **Cochrane risk of bias tool** Selection bias Random sequence generation: computer generated Allocation concealment: opaque envelopes

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
trel releasing IUD and thermal balloon ablation in the treatment of menorrhagia, Zentralblatt fur Gynakologie, 124, 213-9, 2002 **Ref Id** 483353 **Country/ies where the study was carried out** Turkey	LNG-IUS group: Mean age= 43.8 (2.7) PBAC score= 408 (101) Uterine volume= 108 mL (21.7) **Inclusion criteria** -over 40 years of age -with no further desire for childbearing -dysfunctional menorrhagia (diagnosis of exclusion) -refused or did not respond to medical treatment All patients underwent complete physical examination and routine laboratory evaluation, transvaginal ultrasonography, diagnostic hysteroscopy, endometrial biopsy and pap smear.	Thermal balloon was introduced into the uterine cavity, instilled with 5% dextrose and temperature increased to 87 degrees celcius for 8 minutes. LNG-IUS was inserted during the first seven days of menstruation. Delivers 20 ug levnorogestrel to the endometrial surface. Nothing was administered to promote endometrial thinning to the group.	squared test and others used where appropriate.	Outcome: Quality of Life at 12 months (median (IQR)) TBA N= 33, LNG-IUD N= 32 Physical functioning TBA= 75 (42.5-40) LNG-IUS= 72.5 (53.7-91.2) Role limitation physical TBA= 50 (-25- 125) LNG= 25 (-25 - 75) Pain TBA= 51 (20-82) LNG= 51 (30-72) General health TBA= 47 (19.5-74.5) LNG= 52 (25.5-78.5)	Performance bias Blinding: unclear but unlikely due to obvious difference between treatments Detection bias Blinding: unclear but unlikely due to obvious difference between treatments Attrition bias Low risk, outcome data complete Reporting bias Low risk, outcomes stated in the objective were reported **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study type RCT **Aim of the study** To compare the treatment of menorrhagia either with a levonorgestrel-releasing intrauterine device or with endometrial thermal balloon ablation. **Study dates**	**Exclusion criteria** -patients with congenital and acquired uterine abnormalities -pelvic inflammatory disease -breast cancer -premalignant and malignant uterine diseases -any concurrent medical disorders -uterine volume greater than an 8 week pregnancy -obvious pathologies -myomas greater than 2 cm in diameter			Vitality TBA= 45 (10-80) LNG= 45 (26.2-63.7) Social functioning TBA= 50 (12.5-87.5) LNG= 50 (3.7-96.8) Role limitation emotional TBA=33.3 (-33.3- 99.9) LNG= 33.3 (-58.3-124.9) Mental health TBA= 52 (22-82) LNG= 52 (25-79)	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
August 1999 to November 2001 **Source of funding** NR					
Full citation Van Zon-Rabelink, I. A., Vleugels, M. P., Merkus, H. M., De Graaf, R., Efficacy and satisfactio n rate comparing endometri	**Sample size** Pleasee see Lethaby 2013 Cochrane systematic review (van Zon-Rabelink 2003). **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
al ablation by rollerball electrocoagulation to uterine balloon thermal ablation in a randomised controlled trial, European Journal of Obstetrics, Gynecology, & Reproductive Biology, 114, 97-103, 2004 **Ref Id** 483354 **Country/ies where**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
the study was carried out **Study type** **Aim of the study** **Study dates** **Source of funding**					
Full citation Vercellini, P., Oldani, S., Yaylayan, L., Zaina, B., De Giorgi, O., Crosignani	**Sample size** **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Only included in the NMA. Compares two 1st generation ablation techniques, therefore, not included in the pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
, P. G., Randomized comparison of vaporizing electrode and cutting loop for endometrial ablation, Obstetrics and gynecology, 94, 521-7, 1999 **Ref Id** 483355 **Country/ies where the study was carried out** **Study type**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study **Study dates** **Source of funding**					
Full citation Abu Hashim, H., Alsherbini, W., Bazeed, M., Contraceptive vaginal ring treatment of heavy menstrual bleeding: a randomize	**Sample size** N=95 original sample randomised (CVR n=48, norehisterone n=47) N=95 women received treatment (CVR n=48, norehisterone n=47) N=95 women follow-up at 3 months (CVR n=48, norehisterone n=47) **Characteristics** Age in years CVR: 27.8 (4.9), Norehisterone: 28.2 (4.4); p	**Interventions** Patients were randomly allocated (1:1) to contraceptive vaginal ring (CVR) or norehisterone group. In CVR group, patients received verbal and written instructions on the use of the ring, including how and when they should insert and remove it. For the first cycle,	**Details** Sample size calculation Sample size was calculated based on an expected PBAC score of 156.6 after 3 months of cyclical progestogens therap. A total of 64 women (32 in each arm) were required to detect a 50-point difference in PBAC score between treatments, with a power of 90%, using a two-tailed unpaired Student's t test with a 5% significance level (Type I error). Randomisation and allocation concealment	**Results** Outcome: PBAC score (mean and SD) At baseline CVR: 287.8 (77.4) norehisterone acetate: 302.4 (84.6) At 3 months CVR: 90.2 (24.4) norehisterone acetate: 92.3 (26.7)	**Limitations** **Cochrane risk of bias tool** Selection bias Random sequence generation: Low risk Allocation concealment: Low risk Performance bias Blinding of participants and personnel: Unclear

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
d controlled trial with norethisterone, Contraception, 85, 246-52, 2012 **Ref Id** 454593 **Country/ies where the study was carried out** Egypt **Study type** Multicenter prospective randomise	value .96 Parity 1> CVR: 5 (10.4), Norehisterone: 6 (12.8); p value .71 2> CVR: 14 (29.2), Norehisterone: 10 (21.3); p value .47 3≥ CVR: 29 (60.4), Norehisterone: 31 (65.9); p value .33 BMI (Kg/m^2): CVR: 24.8 (3.8), Norehisterone: 25.4 (3.2); p value .39 Blood pressure (mmhg) Systolic: CVR: 110.8 (8.1), Norehisterone: 111.5 (7.8); p value .38	women inserted the ring between Days 1 and 5 of the menstrual cycle, according to the instructions in the package insert. Treatment continued for three cycles. Each cycle consisted of 3 weeks of ring use followed by a 1-week ring-free period. Women were advised to apply the blue and white stickers at the end of the package insert on their calendar to remember when to insert and remove the CVR. Norehisteron e acetate tablets were prescribed at a dose of 5 mg three times	Women were randomized according to a computer generated random numeric table prepared by an independent statistician with concealment of treatment allocation by use of sealed opaque envelopes that were given to a third party (nurse) who assigned patients to study arms: Group A (CVR) or B (norethisterone acetate) Blinding The treatment was revealed to the patient because of the different nature of treatments. Outcome assessors, that is, those performing laboratory investigations and statistical analysis, were blinded to the treatment groups Follow-up The primary outcome measure was menstrual blood loss at the end of the study (Cycle 3) assessed by PBAC. Secondary	Outcome: Health related quality of life score (HRQoL-4) At baseline Self-rated health (≥ very good) (n%): CVR: 2 (4.1), norehisterone: 2 (4.2) Number of days feeling physically unwell (mean and SD) CVR: 7.4 (1.8), norehisterone: 7.5 (2.1) Number of days feeling mentally unwell (mean and SD) CVR: 5.8 (1.7), norehisterone: 6.2 (1.6) Number of lost days (no regular activity) (mean and SD) CVR: 6.4 (2.1),	risk blinding was not possible due to the nature of the interventions, however, not clear if it can introduce performance bias. Detection bias Blinding of outcome assessment: Low risk Blinding of outcome assessors was ensured (laboratory investigators and analyst were biased to treatment group) Attrition bias Incomplete outcome data:

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
d controlled trial **Aim of the study** The objective of this prospective, randomized trial is to compare the efficacy of the CVR (contraceptive vaginal ring) and norethisterone acetate for treatment of idiopathic HMB	Diastolic: CVR: 74.2 (5.1), Norehisterone: 72.7 (5.8); p value .43 Cycle length: CVR: 26.9 (3.7), Norehisterone: 27.2 (4.4); p value .61 Duration of menses (days) CVR: 8.8 (2.7), Norehisterone: 8.4 (2.6); p value .74 Hemoglobin (g/dl) CVR: 10.5 (1.3), Norehisterone: 10.7 (1.2); p value .72 Ferritin (mcg/dl) CVR: 18.4 (3.3),	daily from days 5 to 26 of the cycle over three cycles. Male condom was used for contraception during treatment.	outcome measures were duration of menses, hemoglobin, serum ferritin, HRQoL-4 questionnaire, presence of side effects and overall satisfaction with treatment at the end of the study. Patient in both groups were followed up monthly during the treatment period when PBAC score, duration of bleeding and any adverse effects were noted to assess the patients' response to treatment. To increase the reliability of the measurements, the participants were instructed on how to complete the PBAC, and all participants completed two menstrual cycles during the screening phase of the study. In addition, to optimize the accuracy of the PBAC assessment, the same sanitary pads were used to ensure uniform size and absorbency level. Blood was taken at the beginning and end of the study to measure hemoglobin and	norehisterone: 6.3 (2.3) At 3 months Self -rated health (≥ very good) (n%): CVR: 17 (35.4), norehisterone: 14 (29.7) Number of days feeling physically unwell (mean and SD) CVR: 3.3 (1.1), norehisterone: 3.5 (1.3) Number of days feeling mentally unwell (mean and SD) CVR: 4.7 (1.2), norehisterone: 5.1 (1.3) Number of lost days (no regular activity) (mean and SD) CVR: 1.7 (1.2), norehisterone: 2.6 (1.4)	Low risk No loss to follow up in both treatment group at 3 months Reporting bias Selective reporting: Low risk All outcomes reported Other bias Other sources of bias: **Other information** Included in NMA, this publication only reported on outcomes relevant for the NMA.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
during the fertile age. **Study dates** July 2008-September 2010 **Source of funding** No funding provided for this study. CVR(NuvaRing) provided by Organon Egypt and sanitary pad by Procter & Gamble, Egypt	Norehisterone: 17.1 (2.9); p value .42 **Inclusion criteria** 1) HMB based on a PBAC score over 185 (mean of two control cycles), 2) parous women desiring contraception and willing to use a male condom if required, 3) aged between 20 and 35 years in good general health with a regular menstrual cycle with evidence of ovulation diagnosed when midluteal phase serum progesterone level was ≥5 ng/mL, 4) a normal pelvic examination with a sound measurement of the uterus of <10 cm,		serum ferritin levels. The Health-Related Quality of Life 4 (HRQoL-4) questionnaire was administered at baseline and also at 3 months to assess quality of life in the previous 30 days. The questionnaire includes the following four questions: health as self-assessed, number of days feeling physically unhealthy, number of days feeling mentally unhealthy and lost days (defined as days when work or other daily activities are not possible). Also, at the end of the study (Cycle 3), women's overall satisfaction with their treatment was assessed and rated on a four-level scale questionnaire (very satisfied, satisfied, uncertain and dissatisfied), and they were given the option of continuing with the treatment. Statistical analysis Intention to treat used. Means were compared between the two	Outcome: Patient satisfaction n(%) Very satisfied CVR: 34(70.8%) norehisterone: 20 (42.5%)	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	5) no pathology identified in pelvic ultrasound, 6) normal histology on endometrial biopsy, 7) negative cervical smear and no contraindication to either the CVR or norethisterone **Exclusion criteria** 1) pregnancy 2) age >35 years 3) obesity (body mass index >30 kg/m2) 4) smokers 5) current intrauterine contraceptive device users 6) abnormal uterine bleeding not fully investigated 7) hormone therapy or any medication that might affect		study groups using the unpaired Student's t test, while proportions were compared using the χ2 test. Comparison inside each group was based on the change in mean using a paired t test for continuous variables and the McNemar test for categorical variables. P value of less than .05 was considered statistically significant.		

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	the menstrual blood loss within the previous 3 months (e.g., antifibrinolytics, steroid hormones or anticoagulants) 8) women who used injectable hormones for contraception during the previous 12 months 9) use of drugs that interfere with contraceptive hormone metabolism 10) previous endometrial resection/ablation and other pathology (e.g., patients with fibroids of any size, adenomyosis, endometriosis, pelvic inflammatory disease, endometrial hyperplasia in the biopsy or incidental adnexal abnormality on ultrasound) or HMB of endocrine or systemic origin (e.g., thyroid disease and coagulopathies)				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	11) Patients unwilling to use contraception or medical management				
Full citation Athanatos, D, Pados, G, Venetis, Ca, Stamatopoulos, P, Rousso, D, Tsolakidis, D, Stamatopoulos, Cp, Tarlatzis, Bc, Novasure impedance control system versus microwave	**Sample size** **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Only included in the NMA. Microwave ablation not an intervention of interest according to protocol, therefore, not included in the pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
endometrial ablation for the treatment of dysfunctional uterine bleeding: a double-blind, randomized controlled trial, Clinical and experimental obstetrics & gynecology, 42, 347-51, 2015 **Ref Id** 549813 **Country/ies where**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
the study was carried out **Study type** **Aim of the study** **Study dates** **Source of funding**					
Full citation Clark, Tj, Samuel, N, Malick, S, Middleton, Lj, Daniels, J, Gupta, Jk, Bipolar radiofrequ	**Sample size** **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Included in the NMA. Compares two 2nd generation ablation techniques, therefore, not included in the pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
ency compared with thermal balloon endometrial ablation in the office: a randomized controlled trial, Obstetrics and Gynecology, 117, 109-18, 2011 **Ref Id** 549921 **Country/ies where the study was carried out**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study type **Aim of the study** **Study dates** **Source of funding**					
Full citation de Bruijn, A. M., Ankum, W. M., Reekers, J. A., Birnie, E., van der Kooij, S. M., Volkers, N. A.,	**Sample size** N=177 original sample randomised (UAE n=88, hysterestomy n=89) N=156 women received treatment (UAE n=81, hysterestomy n=75) N=131 women responded to follow-up questionnaire at 10 years post-treatment (UAE n=63, hysterestomy n=68)	**Interventions** Patients were randomly (1:1) allocated to uterine artery embolization (UAE) or hysterectomy. UAE and hysterectomy were performed according to protocol and professional standards (details	**Details** (Some of the information here taken from Hehenkamp 2005) Randomisation Women were randomly assigned (1:1) to UAE or hysterectomy, using a computer-based minimisation sceheme ('balancing procedure') and stratified for study centre. The randomisation result was recorded electronically.	**Results** Outcome: Health-related Quality of Life SF-36 mental component summary Change from baseline at 1 year follow-up UAE: 6.33* Hysterectomy: 7.67* Change score between groups (95% CI): 1.34 (-	**Limitations** **Cochrane risk of bias tool** Selection bias Random sequence generation: Low risk Allocation concealment: Low risk Performance bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Hehenkamp, W. J., Uterine artery embolization vs hysterectomy in the treatment of symptomatic uterine fibroids: 10-year outcomes from the randomized EMMY trial, American Journal of Obstetrics & GynecologyAm J Obstet Gynecol, 5, 5, 2016	**Characteristics** **Baseline characteristics** Age in years, mean (SD) UAE: 44.6 (4.8) Hysterestomy: 45.4 (45.4) BMI, mean (SD) UAE: 26.7 (5.6) Hysterestomy: 25.4 (4.0) Parity ≥1, % UAE: 65.9 Hysterestomy: 77.5 Black ethnicity, % UAE: 27.3 Hysterestomy: 22.5 Caucasian ethnicity, % UAE: 61.4 Hysterestomy: 64.0	described in another publication).	Allocation concealment Not reported but according Gupta et al., 2014 Cochrane Systematic Review including other publications from the EMMY trial, a telephone randomisation was used. Blinding Not possible due to the nature of the interventions. Follow up A questionnaire was mailed to the participants when the last included patient had reached 10 years of follow-up. The 10-year questionnaire evaluated the following subjects: additional interventions between 5-10 years of follow-up, health-related quality of live (HRQOL), urinary and defecation function, menopausal	2.3 to 5.32), p=0.505 Change from baseline at 2 years follow-up UAE: 5.80* Hysterectomy: 7.26* Change score between groups (95% CI): 1.47 (-2.78 to 5.71), p=0.496 Change from baseline at 5 years follow-up UAE: 6.31* Hysterectomy: 6.87* Change score between groups (95% CI): -0.56 (-5.07 to 3.95), p=0.806 Change from baseline at 10 years follow-up UAE: 4.41* Hysterectomy: 4.54* Change score difference	Blinding of participants and personnel: Unclear risk, blinding was not possible due to the nature of the interventions, however, not clear if it can introduce performance bias. Detection bias Blinding of outcome assessment: High risk, blinding not possible due to the nature of the interventions, therefore, there is a high risk of bias on subjective outcomes (quality of life and satisfaction). Attrition bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Ref Id 549973 **Country/ies where the study was carried out** Netherlands **Study type** Multicentre RCT (EMMY trial) **Aim of the study** The purpose of this study was to compare	Other ethnicity, % UAE: 11.4 Hysterestomy: 13.5 Marital status single, % UAE: 18.2 Hysterestomy: 14.8 Married, % UAE: 62.5 Hysterestomy: 61.4 Divorced, % UAE: 13.6 Hysterestomy: 17.0 Unemployed, % UAE: 22.7 Hysterestomy: 21.6 Current smoker, % UAE: 23.9		symptoms, menstrual characteristics (bleeding symptoms since UAE or no symptoms due to successful UAE or menopause), and satisfaction. Of these the following are of interest to this review: HRQOL and satisfaction. Health status and HRQOL was evaluated using the Medical Outcome Study Short Form (SF)-36. The SF-36 generates 2 summary scores: The physical component summary (PCS) and the mental component summary (MCS). The scores range from 0-100 and were validated for the Dutch population. Higher scores represent better physical or mental functioning.	between groups (95% CI): 0.13 (-4.08 to 3.82), p=0.947 SF-36 physical component summary Change from baseline at 1 year follow-up UAE: 7.32* Hysterectomy: 10.13* Change score between groups (95% CI): 2.81 (-0.59 to 6.21), p=0.104 Change from baseline at 2 years follow-up UAE: 9.42* Hysterectomy: 9.32* Change score between groups (95% CI): -0.096 (-2.98 to 2.79), p=0.948	Incomplete outcome data: Unclear risk, 74% of the participants randomised and 84% of the participants receiving treatment had data at 10 years follow-up. Reporting bias Selective reporting: Low risk Other bias Other sources of bias: - **Other information** Please see other publications from the EMMY trial: Hehenkamp et al., 2005;, Volkers et al., 2007; Hehenkamp et al.,

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
clinical outcome and health-related quality of life 10 years after uterine artery embolization or hysterectomy in the treatment of heavy menstrual bleeding caused by uterine fibroids in a randomized controlled trial. **Study dates**	Hysterestomy: 25.8 Previous treatment, % None UAE: 12.5 Hysterestomy: 16.9 Hormonal UAE: 67.0 Hysterestomy: 66.3 Nonsteroidal antiinflammatory drugs/tranexamic acid UAE: 51.1 Hysterestomy: 46.1 Iron supplement/blood transfusion UAE: 56.8 Hysterestomy: 58.4 Surgical procedures		Satisfaction was assessed by inquiring whether the patients would recommend the primary treatment to a friend and whether or not they would indeed have chosen the assigned treatment again if they would have the opportunity to do so. Finally, patients were asked to indicate how satisfied they were with the received treatment on a 7-point Likert scale: very satisfied, satisfied, fairly satisfied, not satisfied/not unsatisfied, fairly unsatisfied, unsatisfied, or very unsatisfied. Statistical analysis Differences in HRQOL between the groups were assessed with the	Change from baseline at 5 years follow-up UAE: 8.47* Hysterectomy: 7.20* Change score between groups (95% CI): 1.26 (-2.16 to 4.70), p=0.468 Change from baseline at 10 years follow-up UAE: 7.31* Hysterectomy: 7.04* Change score difference between groups (95% CI): 0.26 (-3.93 to 4.46), p=0.900 *A statistically significant ($p<0.05$) change from baseline the within-group analysis.	2007; Hehenkamp et al., 2007; van der Krooj et al., 2010; Volkers et al., 2008.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
2002 through 2004, this publication reports follow-up at 10 years. **Source of funding** The EMMY study is funded by ZonMweThe Netherlands Organization for Health Research and Development (grant application no. 945-	UAE: 19.3 Hysterestomy: 12.4 Symptoms, % Menorrhagia UAE: 100 Hysterestomy: 100 Dysmenorrhea UAE: 53.4 Hysterestomy: 56.2 Pain (not during menstruation) UAE: 17.0 Hysterestomy: 15.7 Anaemia UAE: 48.9 Hysterestomy: 47.2 Pressure symptoms		unpaired Student t tests. Repeated measurement analysis was used to evaluate longitudinal differences (MCS, PCS, UDI, DDI, and Wiklund scores) between the treatment strategies with time as a repeated factor (covariance structure: unstructured). P <.05 (2-sided) was considered statistically significant in all analyses.	Outcome: Patient satisfaction At 1 year follow-up Very satisfied UAE: 29/81 Hysterectomy: 48/75 Satisfied UAE: 21/81 Hysterectomy: 14/75 Moderately satisfied UAE: 18/81 Hysterectomy: 3/75 Not satisfied or unsatisfied UAE: 5/81 Hysterectomy: 3/75 Moderately unsatisfied	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
01-017) and supported by Boston Scientific Corp, The Netherlands.	UAE: 26.1 Hysterestomy: 28.1 **Inclusion criteria** (1) premenopausal status, (2) diagnosis of uterine fibroids by ultrasonography, (3) heavy menstrual bleeding as the predominant symptom, (4) no other treatment option than hysterectomy, and (5) no wish to conceive in the future. **Exclusion criteria** (From Hehenkamp et al., 2005) (1) preservation of the uterus was warranted for future pregnancy, (2) renal failure (creatitine			UAE: 3/81 Hysterectomy: 1/75 Unsatisfied UAE: 1/81 Hysterectomy: 1/75 Very unsatisfied UAE: 1/81 Hysterectomy: 0/75 Satisfied (combining very satisfied, satisfied and moderately satisfied)** UAE: 68/81 Hysterectomy: 65/75 At 2 year follow-up Very satisfied UAE: 34/81	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	>150 mmol/L), active pelvic infection, or clotting disorders were clinically established, (3) they were allergic to contrast material, (4) uterine malignancy was suspected, (5) submucosal fibroids with 50% of their diameter within the uterine cavity or dominant pedunculated serosal fibroids were present.			Hysterectomy: 45/75 Satisfied UAE: 29/81 Hysterectomy: 16/75 Moderately satisfied UAE: 11/81 Hysterectomy: 5/75 Not satisfied or unsatisfied UAE: 2/81 Hysterectomy: 3/75 Moderately unsatisfied UAE: 3/81 Hysterectomy: 0/75 Unsatisfied UAE: 1/81 Hysterectomy: 1/75	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				Very unsatisfied UAE: 0/81 Hysterectomy: 3/75 Satisfied (combining very satisfied, satisfied and moderately satisfied)** UAE: 74/81 Hysterectomy: 66/75 At 5 year follow-up Very satisfied UAE: 37/81 Hysterectomy: 42/75 Satisfied UAE: 27/81 Hysterectomy: 20/75 Moderately satisfied	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				UAE: 4/81 Hysterectomy: 4/75 Not satisfied or unsatisfied UAE: 1/81 Hysterectomy: 3/75 Moderately unsatisfied UAE: 3/81 Hysterectomy: 0/75 Unsatisfied UAE: 3/81 Hysterectomy: 1/75 Very unsatisfied UAE: 0/81 Hysterectomy: 0/75 Satisfied (combining very satisfied, satisfied and moderately satisfied)**	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				UAE: 67/81 Hysterectomy: 66/75 At 10 year follow-up Very satisfied UAE: 34/81 Hysterectomy: 32/75 Satisfied UAE: 22/81 Hysterectomy: 24/75 Moderately satisfied UAE: 5/81 Hysterectomy: 7/75 Not satisfied or unsatisfied UAE: 2/81 Hysterectomy: 2/75	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				Moderately unsatisfied UAE: 0/81 Hysterectomy: 0/75 Unsatisfied UAE: 0/81 Hysterectomy: 2/75 Very unsatisfied UAE: 0/81 Hysterectomy: 0/75 Satisfied (combining very satisfied, satisfied and moderately satisfied)** UAE: 61/81 Hysterectomy: 63/75 **Calculated by the NGA technical team.	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Dickersin, K, Munro, Mg, Clark, M, Langenberg, P, Scherer, R, Frick, K, Zhu, Q, Hallock, L, Nichols, J, Yalcinkaya, Tm, Hysterectomy compared with endometrial ablation for dysfunctional uterine bleeding: a randomized	**Sample size** Please see Fergusson 2013 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
controlled trial, Obstetrics and Gynecology, 110, 1279-89, 2007 **Ref Id** 549993 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Ergun, B, Bastu, E, Kuru, O, Sen, S, Kilic, Y, Dural, O, Comparison of rollerball endometrial ablation and levonorgestrel releasing intrauterine system in the management of abnormal uterine bleeding,	**Sample size** Please see Lethaby 2015 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Included in NMA, this publication only reported on outcomes relevant for the NMA.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
International journal of gynaecology and obstetrics, 119, S672, 2012 **Ref Id** 550028 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Ergun, B, Kuru, O, Sen, S, Kilic, Y, Comparison between roller-ball endometrial ablation and levonorgestrel intrauterine system (LNG-IUS) in the treatment of abnormal uterine bleeding, Turk Jinekoloji	**Sample size** Please see Lethaby 2015 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Included in NMA, this publication only reported on outcomes relevant for the NMA.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
ve Obstetrik Dernegi Dergisi, 8, 259-63, 2011 **Ref Id** 550030 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Ergun, B., Kuru, O., Sen, S., Kilic, Y., Bastu, E., Roller-ball endometrial ablation versus levonorgestrel releasing intrauterine system in the management of abnormal uterine bleeding, Gineco.ro, 8, 199-201, 2012 **Ref Id**	**Sample size** Please see Lethaby 2015 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Included in NMA, this publication only reported on outcomes relevant for the NMA.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
550031 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**					
Full citation Fergusson, Rosalie J, Lethaby, Anne,	**Sample size** **Crosgnani 1997** N=92 **Dickerson 2007**	**Interventions** **Dickersin 2007** 1) resectoscopic endometrial ablation with el	**Details** **Dickerson 2007** Design: RCT, multicentre, parallel group Outcomes: Pain, bleeding and	**Results** **Comparison: Endometrial resection/ablation vs. hysterectomy**	**Limitations** **Quality of the Cochrane SR:** Systematic review assessed with

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Shepperd, Sasha, Farquhar, Cindy, Endometrial resection and ablation versus hysterectomy for heavy menstrual bleeding, Cochrane Database of Systematic Reviews, 2013 **Ref Id** 550047 **Country/ies where the study was**	N=237 **Sesti 2011** N=68 **Zupi 2003** N=203 **Dwyer 1993** N=196 **Characteristics** **Crosignani 1997** Population: 92 Women 42 to 49 years of age, with menorrhagia not responding to medical treatment and requiring hysterectomy, recruited from an outpatient clinic Setting: Italy **Dickerson 2007**	ectrodesiccation/coagulation or vaporisation OR ablation with thermal balloon (1st or second generation ablation/resection) 2) vaginal, laparoscopic or abdominal hysterectomy under general or regional anaesthesia. In both groups, women > 45 y ears were allowed oophorectomy Duration of trial: e nrolme nt was staggered, with some women having data for five years Prior experience of the surgeon not mentioned	fatigue at one year; Other outcomes at different time points: QOL outcomes, sexual function, employment, housework, leisure activities, out-of-pocket costs, h ealth provider visits, surgical complications, additional surgery **Sesti 2011** Design: RCT, single centre. parallel-group Outcomes: Menstrual bleeding (PBAC score) at three, six, 12 and 24 months; Quality of life (SF-36 score) at 24 months; Improvement in bleeding patterns (f requency and duration of bleeding) at three, six, 12 and 24 months; Haemoglobin le vels at three, six, 12 and 24 months; intensity of postoperative pain; early postoperative complications **Zupi 2003** Design: RCT, single centre,	Outcome: PBAC NMA outcome Outcome: Satisfaction NMA outcome Outcome: Blood transfusion (perioperative) Zupi 2003 Ablation group: 0/89 Hysterectomy group: 2/92 Sesti 2011* Not observed in either group (narratively reported) Dwyer 1993* Resection: 2/99 Hysterectomy: 6/97 Outcome: uterine perforation (perioperative)	AMSTAR checklist. Total score: 11/11 **Quality of the individual studies:** Risk of bias assessment taken from Cochrane SR (Cochrane risk of bias tool). **Dickerson 2007** Random sequence generation: low risk Allocation concealment: low risk Blinding: high risk Incomplete outcome data: unclear (no reasons given for dropouts)

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
carried out **Study type** Cochrane review of RCTs. **Aim of the study** The objective of this review is to compare the effectiveness, acceptability and safety of techniques of endometrial destruction	Population: 237 Women with dysfunctional bleeding (not explained by pathology, drugs, e tc.), most of whom were younger than 45 years of age (85%), recruited from 25 clinical centres (proportion of women with HMB not reported*) Setting: US and Canada *extracted from individual RCT **Sesti 2011** Population: 68 Women 35 to 50 years of age with heavy menstrual bleeding, who had failed appropriate first-line oral medical th erapy and required surgical treatment Setting: Italy **Zupi 2003**	**Sesti 2011** 1) endometrial ablation via Thermachoice III thermal balloon ablation 2) laparoscopic subtotal hysterectomy Duration of follow-up: 24 months All surgery was performed by the same two surgeons; however, prior experience of the surgeon not mentioned **Zupi 2003** 1) pretreatment with	parallel-group Outcomes: Pain (immediately after surgery and then for a week); Duration of vaginal bleeding; Date resumed normal activities, sexual intercourse, work; Quality of life (S F-36); Further surgery; Operative outcomes (duration of surgery, blood loss, complications, hospital stay) **Crosignani 1997** Design: Single-centre, parallel-group with no blinding, randomisation by computer-generated sequence using numbered opaque sealed envelopes Outcomes: Participant satisfaction with treatment; Improvement in MBL; Quality of life; Duration of surgery (minutes); Duration of hospital stay (days); Return to work (weeks); Requirement for further surgery	Dickersin 2007 Ablation group: 3/110 (1st generation: 1/53, 2nd generation: 2/57*) Hysterectomy group: 0/118 Dwyer 1993 Resection: 4/99 (narratively) Hysterectomy: none reported Outcome: thromboembolic event (perioperative) Dickersin 2007 Ablation group: 0/110 Hysterectomy group: 2/118 Outcome: readmission/return to theatre	Selective reporting: low risk other: low risk **Sesti 2011** Random sequence generation: low risk Allocation concealment: low risk Blinding: high risk Incomplete outcome data: low risk Selective reporting: low risk other: low risk **Zupi 2003** Random sequence generation: low risk Allocation

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
by any means versus hysterectomy by any means for the treatment of heavy menstrual bleeding. **Study dates** Search performed in 2013. **Source of funding** Not reported.	Population: 203 Women with mean age of 43 years with menometrorrhagia unresponsive to medical treatment, recruited between March 1995 and February 1997 Setting: Italy **Dwyer 1993** Population: 196 women with menorrhagia, mean age of 40 years, recruited from an outpatient gynaecology clinic at a teaching hospital in Bristol, UK Setting: UK **Inclusion criteria** **Dickerson 2007** 18 years of age or older; premenopausal; dysfunctional uterine bleeding for at least six	GnRHa one month before surgery, then hysteroscopic endometrial resection 2) laparoscopic supracervical hysterectomy Duration: two years (follow-up at three months, at one and two years) All surgeons were proficient in both endometrial resection and laparoscopic hysterectomy **Crosignani 1997** 1) hysteroscopic endometrial resection 2) vaginal	**Dwyer 1993** Design: Single-centre, parallel-group, no blinding, randomisation by sealed numbered envelopes in variable blocks of 20, 30 and 50 Outcomes: Satisfaction with surgery at four months; Satisfaction with surgery at 2.8 years; Change in menstrual blood loss after surgery (subjective) at four months; Change in menstrual blood loss after surgery (subjective) at 2.8 years; Quality of life at 2.8 years; Postoperative complications; Duration of hospital stay (days); Duration of surgery (minutes); Return to work (weeks); Requirement for further surgery within one year; Requirement for further surgery at 2.8 years; Total health service resource cost at four months; Total health service resource cost at 2.8 years	Dickersin 2007 Ablation group: 0/110 Hysterectomy group: 3/118 Sesti 2011* Not observed in either group (narratively reported) Dwyer 1993, return to theathre within 24h Resection: none reported Hysterectomy: 2/97 Dwyer 1993, readmission within 4-6 weeks Resection: 2/99 Hysterectomy: 4/97 Outcome: Quality of Life (SF-36) NMA outcome	concealment: unclear Blinding: high risk Incomplete outcome data: low risk Selective reporting: unclear (no prior protocol identified) other: low risk **Crosignani 1997** Random sequence generation: low risk Allocation concealment: low risk Blinding: high risk, not feasible for a comparison of surgical techniques Incomplete outcome data: low

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	months (defined as one or more of excess duration, amount or unpredictability); refractory to medical treatment for at least three months **Sesti 2011** PBAC score ≥ 100 (average of two consecutive cycles), completed family, normal smear, pelvic ultrasound scan and endometrial biopsy **Zupi 2003** ception; normal endometrial histology and Pap smear within the previous six months; uterus not greater than 12 weeks of pregnancy in size; without submucosal fibroids, adnexal masses or endometriosis **Crosignani 1997**	hysterectomy Duration: two years of follow-up Prior experience of the surgeon not mentioned **Dwyer 1993** 1) transcervical endometrial resection, n = 99 2) abdominal hysterectomy, n = 97 Duration: four months of follow-up, 2.8 years of follow-up Prior experience of the surgeon not mentioned		Outcome: Duration of hospital stay Dickersin 2007 Ablation group: mean (SD)= 0.05 (0.25), N= 110 (1st generation: 0.04 (0.19) N= 53, 2nd generation: 0.05 (0.29), N=57*) Hysterectomy group: mean (SD)= 1.86 (0.97), N=118 Zupi 2003 Ablation group: mean (SD)= 1.3 (1.1), N= 89 Hysterectomy group: mean (SD)= 1.6 (1.5), N=92 Dwyer 1993 Resection: median 2 (range 1 to 8), n=99	risk Selective reporting: unclear (no prior protocol identified, study did not measure adverse events) other: low risk **Dwyer 1993** Random sequence generation: unclear risk, randomisation sequence not described Allocation concealment: low risk Blinding: high risk, not feasible for a comparison of surgical techniques Incomplete outcome data: low

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	≤ 50 years, mobile uterus with volume < 12 weeks in gestational size and<380 mL on ultrasound, negative cervical smear, no evidence of a typical hyperplasia at endometrial biopsy, no adnexal tumours at clinical and ultrasound examination **Dwyer 1993** < 52 years of age, complaint of menorrhagia that could not be controlled by conservative means, candidates for abdominal hysterectomy **Exclusion criteria** **Dickerson 2007** postmenopausal; bilateral oophorectomy; pregnant;			Hysterectomy: median 6 (5 to 10), n=97 Outcome: Infection (abdominal wound infection) Dickersin 2007* Ablation group: NA Hysterectomy group: 5/118 Outcome: Infection (urinary tract infection) Dickersin 2007* Ablation group: 2/110 (1st generation: 1/53, 2nd generation: 1/57*) Hysterectomy group: 6/118 Zupi 2003* Endometrial resection: 1/89	risk Selective reporting: unclear (no prior protocol identified) other: low risk **Other information** Studies not included in current review beause of incorrect PICO: Gannon 1991, Pinion 1994

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	wishing to retain fertilty; refusal to consider surgery **Sesti 2011** previous endometrial resection/ablation, previous levonorgestrel intrauterine system, any uterine pathology on pelvic ultrasound scan or hyster oscopy, any pathology whereby hy sterectomy was indicated, uninvestigated abnormal bleeding or postmenopausal bleeding **Zupi 2003** no further exclusion criteria reported **Crosignani 1997** known PID or endometriosis, urinary stress incontinence, moderate/ severe genital prolapse, clotting disorders, use of IUD or drugs that			Hysterectomy: 1/92 Dwyer 1993* Resection: 0/99 Hysterectomy: 12/97 Outcome: Infection (endometritis) Dickersin 2007* Ablation group: 1/110 Hysterectomy group: NA *data extracted from individual RCT Outcome: Infection (pelvic infection) Dwyer 1993* Resection: 2/99 Hysterectomy: 5/97 Outcome: Infection (wound infection)	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	may affect MBL, unstable general conditions, submucosal myomas >3cm in diameter or >50% intramural extension **Dwyer 1993** uterine size ≤ 12 gestational weeks, additional symptoms or other pathology, making hysterectomy the preferred treatment			Dwyer 1993* Resection: 0/99 Hysterectomy: 11/97 *Data extracted from the original paper by the NGA technical team.	
Full citation Ghazizadeh, S, Bakhtiari, F, Rahmanpour, H, Davari-Tanha, F, Ramezanzadeh, F, A	**Sample size** Randomised N =104 (TCRE= 52, LNG-IUS =52) Loss to follow up (TCRE= 5, LNG-IUS=7) Total at 1 year follow up= (TCRE= 47, LNG-IUS= 45) *TCRE(trans-cervical resection of the*	**Interventions** Patients were randomly allocated (1:1) to LNG-IUS or TCRE group In LNG-IUS group, LNG-IUS was inserted within 7 days of the start of menstruation by a single gynecologist,	**Details** Sample size calculation Sample of 52 patients each were divided into two groups based on previous study from the literature in which a 97% and 94% reduction in menstrual blood loss was reported in the LNG-IUS and TCRE groups, respectively, as well as differences > 0.09 SD between	**Results** Outcome: PBAC score (Mean & SD) Baseline LNG-IUS: 595 (165) TCRE: 596 (185) At 6 months	**Limitations** **Cochrane risk of bias tool** Selection bias Random sequence generation: Low risk Allocation concealment: Low risk Performance bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
randomized clinical trial to compare levonorgestrel-releasing intrauterine system (Mirena) vs trans-ervical endometrial resection for treatment of menorrhagia, International journal of women's health, 3, 207-11, 2011 **Ref Id**	*endometrium), LNG-IUS (levonorgestrel intrauterine system)* **Characteristics** **Baseline characteristics value are given as mean (SD)** Age in years LNG-IUS: 40.2 (4.3) TCRE: 41.5 (4.4) BMI (Kg/m^2) LNG-IUS: 28.3 (4.2) TCRE: 26.7 (3.3) Duration of complaint (years) LNG-IUS: 3.35 (0.32) TCRE: 41.5 (4.4)	based on the need for cervical dilatation on IUD insertion or not, which was classified as difficult or easy respectively. Any complications such as uterine perforation, hemorrhage, and abdominal cramps were recorded and the patients were observed for 1 hour before discharge. In the TCRE group, the operation was performed under general anesthesia 5 weeks after endometrial preparation with a single injection of triptorelin 3.76 mg and by a single operator. A Storz rigid resectoscope	the means of the two groups (quantitative variables), with a statistical power of 80% and a 95% confidence level Randomisation and allocation concealment Series of sealed, opaque, sequentially numbered, envelopes prepared by an independent statistician, revealing the treatment code in a 1:1 individual randomization ratio. This was predetermined by computer-generated random number tables, which were in balanced blocks of 20. Blinding The treatment was revealed to the patient because of the different nature of treatments. Blinding of outcome assessor not reported and most probably not done Follow-up	LNG-IUS: 60.4 (110.7) TCRE: 70.7 (115.6) Final follow up at 12 months Not reported Outcome: Patient satisfaction (mean and SD) at 12months LNG-IUS: 3.08 (1.26) TCRE: 2.5 (1.59) Outcome: Expulsion at 12 months LNG-IUS: 9 out of 45 (20%) Outcome: Discontinued	Blinding of participants and personnel: Unclear risk Blinding was not possible due to the nature of the interventions, however, not clear if it can introduce performance bias. Detection bias Blinding of outcome assessment: High risk Blinding of outcome assessors not reported and most probably not done, high risk of bias for subjective outcomes Attrition bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
550090 **Country/ies where the study was carried out** Iran **Study type** Randomised controlled trial **Aim of the study** The aim of this study is to compare the efficacy, adverse effects,	Bleeding duration (day) LNG-IUS: 10.1 (4.2) TCRE: 14.5 (9.2) PBAC score LNG-IUS: 595 (165) TCRE: 596 (185) Menstrual interval (days) LNG-IUS: 25.6 (4.7) TCRE: 21.7 (6.6) **Inclusion criteria** 1) 35–45 years old 2) had heavy menstrual	with a 4-mm resection loop was passed into the uterine cavity. Glycine 1.5% was infused for irrigation with an infusion pressure of 100 mmHg. A mixed diathermy current of 120 W was used After the procedure, all patients were advised to keep a menstrual record including length of menstrual cycles, days of bleeding, number of stained towels in one day, amount of staining and note any adverse effects namely spotting, abdominal cramps and pains, breast	The primary outcomes included the menstrual pattern namely amenorrhea and reduction in bleeding score (PBAC). The secondary outcome was the rate of patient satisfaction. Statistical analysis Normal distribution of the data was verified using the Kolmogorov– Smirnov test. The variables were described as mean and SD. The statistical differences between the groups were tested using Student's unpaired t test, Mann–Whitney test, and Chi square test. Significance level was established as P> 0.05.	treatment LNG-IUS: 6 out of 45 5 for continued menorrhagia and 1 for unacceptable spotting and weight gain Outcome: Uterine perforation LNG-IUS: none TCRE: "1 case of uterine perforation with no haemorrhagic complication needed intervention"	Incomplete outcome data: High risk Data reported based on participants who completed 1 year follow up. No ITT or other post-hoc analysis done to adjust for missing data. No further information on missing participants. Reporting bias Selective reporting: High risk PBAC score reported at baseline and 6 month but not at 12 month.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
and rate of satisfaction and acceptability of LNG-IUS and TCRE in the treatment of menorrhagia **Study dates** Not reported **Source of funding** Not reported	loss based on a PBAC (score> 100) 3) no history of medical treatment for at least 6 months before the trial **Exclusion criteria** 1) A previous history of deep venous thrombosis, thromboembolism, liver disease, pelvic disease, active genital tract infection, abnormal endometrial histology, abnormal cervical cytology, previous endometrial resection and ablation, or any other pathology such as uterine prolapse or large myomas and pregnancy 2) Patients who were uncertain about their future wish for pregnancy were also excluded	tenderness, headaches, acne, mood changes, and weight gain			Other bias Other sources of bias: Unclear **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Ghazizadeh, S Panahi Z Ghanbari Z Menshadi At Farahmandian T Javadian P, Comparative efficacy of novasure, the levonorgestrel-releasing intrauterine system, and hysteroscopic endometri	**Sample size** Please see Marjoribanks 2016 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Included in NMA, this publication only reported on outcomes relevant for the NMA.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
al resection in the treatment of menorrhagia: A randomized clinical trial, Journal of Gynecologic Surgery, 30, 215-8, 2014 **Ref Id** 550091 **Country/ies where the study was carried out** **Study type**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study **Study dates** **Source of funding**					
Full citation Goshtasebi, A., Moukhah, S., Gandevani, S. B., Treatment of heavy menstrual bleeding of endometrial origin: randomized controlled	**Sample size** n= 90 randomised (MPA n= 44 vs TA n= 46) In the TA group 38 (82.6%) and in the MPA group 33 (71.7%) patients completed the 3-month follow-up. MPA group drop-outs 3 spotting, 7 irregular bleeding, 1 breast fibrocystic change TA group drop-outs 3 nausea and vomiting, 3 headache, 2 vertigoBaseli	**Interventions** Medroxyprogesterone acetate (MPA) 5mg every 12 hours, for 21 days from day 5 of menses Tranexamic acid (TA) 500mg every 6 hours for 5 days from day 1 of menses. During 3 consecutive menstrual periods	**Details** Randomisation Parallel technique. Block randomisation was used. Allocation concealment No details Blinding No details Follow-up Data on clinical outcomes were obtained at the baseline of one control menstrual cycle, and 1,	**Results** Outcome: PBAC See NMA Outcome: Quality of life SF-36 See NMA Outcome: HRQoL - Condition-Specific HMB Questionnaire (Menorrhagia Questionnaire) TA (n=46) vs MPA (n=44) Before treatment Mean	**Limitations** **Cochrane risk of bias tool** Selection bias Random sequence generation: Unclear risk, details not reported. Allocation concealment: Unclear risk, not reported. Performance bias Blinding of

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
trial of medroxyprogesterone e acetate and tranexamic acid, Archives of Gynecology & Obstetrics, 288, 1055-60, 2013 **Ref Id** 454606 **Country/ies where the study was carried out** Iran **Study type**	**Characteristics** **Baseline Characteristics** Age n (%) 20-30 years: 13 (28.3) vs 14 (31.8) 31-40 years: 19 (41.3) vs 18 (40.9) 41-45 years: 14 (30.4) vs 12 (27.3) p value= 0.91 Parity n (%) <1: 20 (43.5) vs 21 (47.7) >2: 26 (56.7) vs 23 (52.3) p value= 0.68 Education n (%) 0-8 years: 16 (34.8) vs 15		2, and 3 months after treatment. For symptom change as a result of therapy, several measurement tools were used. Statistical Analysis SPSS. Comparisons between groups were performed using t test, paired t test, x2, mann-whitney, wilcoxon signed-ranked test, and repeated measure analysis. Statistical significance level was set at 0.05.	(SD): 44.36 (15.47) vs 40.1 (13.22) After treatment Mean (SD): 27.16 (14.69)* vs 29.41 (16.14)** *p<0.05 compared with TA before treatment **p<0.01 compared with MPA group before treatment Mean difference: -17.2 vs -10.68, p-value 0.52	participants and personnel: Unclear risk, not reported Detection bias Blinding of outcome assessment: Unclear risk, not reported Attrition bias Incomplete outcome data: Low risk Low loss of follow-up (<20%) and ITT principles used. Reporting bias Selective reporting: Low risk Other bias Other sources of bias: -

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
RCT **Aim of the study** This study aimed at comparing the efficacy of medroxyprogesterone acetate (MPA) and tranexamic acid (TA) for treating heavy menstrual bleeding of endometrial origin (HMB) **Study dates** January 2010 -	(34.1) 9-12 years: 19 (41.3) vs 22 (50) > 13 years: 11 (23.9) vs 7 (15.9) p value= 0.57 Occupation n (%) Student/employee: 12 (26.1) vs 19 (43.2) Housewife: 34 (73.9) vs 25 (56.8) p value= 0.08 **Inclusion criteria** Aged 20-45 years, who complained of regular HMB with BMI (19-29 kg/m). **Exclusion criteria**				**Other information** Included in NMA, this publication only reported on outcomes relevant for the NMA.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
December 2011 **Source of funding** None declared	Cases with organic causes of HMB. Women with iron deficiency anaemia. Previous thromboembolic disease. History of chronic diseases known to interfere with menstural bleeding like leiomyoma, history of anticoagulant agents, oral contraceptive or other hormonal drug use, and woemn with an IUD in situ were excluded from the study				
Full citation Gupta, J. K., Daniels, J.	**Sample size** Please see Lethaby 2015 Cochrane systematic review.	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Included in NMA, this publication only

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
P., Middleton, L. J., Pattison, H. M., Prileszky, G., Roberts, T. E., Sanghera, S., Barton, P., Gray, R., Kai, J., A randomised controlled trial of the clinical effectiveness and cost-effectiveness of the levonorgestrel-releasing intrauterine system	**Characteristics** **Inclusion criteria** **Exclusion criteria**				reported on outcomes relevant for the NMA. Same trial as Gupta 2013.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
in primary care against standard treatment for menorrhagia: The ECLIPSE trial, Health Technology Assessment, 19, 1-118, 2015 **Ref Id** 550121 **Country/ies where the study was carried out** **Study type**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study **Study dates** **Source of funding**					
Full citation Gupta, Janesh K, Sinha, Anju, Lumsden, M A, Hickey, Martha, Uterine artery embolization for symptomatic uterine fibroids,	**Sample size** **EMMY 2010** N=177 randomised (n=88 UAE, n=89 hysterectomy) **FUME 2012** N=163 randmised (n=82 UAE, n=81 myomectomy) **Jun 2012** N=127 randomised (n=63 UAE, n=64 surgery) **Mara 2008** N=121 randomised (n=58	**Interventions** **EMMY 2010** 1) UAE 2) hysterectomy Duration: Recruitment took place between March 2002 and February 2004 with follow-up of 5 years reported. **FUME 2012**	**Details** **EMMY 2010** Design: RCT (Attending gynaecologist contacted the trial bureau by telephone, where the participant was registered and randomly assigned (1:1) to UAE or hysterectomy, using a computer-based minimization scheme ('balancing procedure'), and stratified for study centre. The randomisation result was recorded electronically.) Outcomes: Evaluation of re-intervention rates at 5 years: menstrual characteristics,	**Results** Outcome: Satisfaction with treatment up to 24 months **Comparison: UAE versus hysterectomy** **EMMY 2010** UAE: 68/81 Hysterectomy: 65/75 **Pinto 2003** UAE: 28/36 Hysterectomy: 15/17	**Limitations** **Quality of Cochrane SR:** Systematic review assessed using AMSTAR checklist. Total score: 11/11 **Quality of individual studies:** Risk of bias assessment taken from Cochrane SR (Cochrane risk of bias tool).

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Cochrane Database of Systematic Reviews, 2014 **Ref Id** 550123 **Country/ies where the study was carried out** **Study type** Cochrane systematic review of RCTs **Aim of the study** To review the	UAE, n=63 myomectomy) **Pinto 2003** N=57 randomised (n=38 told of UAE and hysterectomy, n=19 told of hysterectomy only) **REST 2011** N=157 randomised (n=106 UAE, n=51 surgery) **Ruuskanen 2010** N=57 ransomised (n=27 UAE, n=30 hysterectomy) **Characteristics** **EMMY 2010** The mean age was 44.6 years (UAE group) and 45.4 years (hysterectomy group) . Participants suffered from menorrhagia for a median of 24 months. The majority of women had multiple fibroids. Fibroid	1) UAE (performed by or supervised by same experienced interventional radiologist) 2) myomectomy (without preoperative gonadotrophin releasing hormone agonists) Duration: Not stated. **Jun 2012** 1) UAE 2) surgery: hysterectomy or myomectomy ("The method of hysterectomy or myomectomy was not specified; the choice between	menorrhagia, quality of life measures Patient satisfaction measured by asking women whether they would undergo the same treatment again. **FUME 2012** Design: RCT (Sealed opaque envelopes, random numbers generated by computer. Blocks of 10.) Outcomes: Primary endpoint: quality of life measures at one year using the Uterine Fibroid Symptom and Quality of Life (UFS-QOL) questionnaire. Other endpoints: evaluation of reintervention rates at 2 years, complications **Jun 2012** Design: RCT (Randomisation	**Ruuskanen 2010** UAE: 24/27 Hysterectomy: 29/30 **Comparison: UAE versus hysterectomy or myomectomy** **Jun 2012** UAE: 52/62 Hysterectomy or myomectomy: 45/62 **REST 2011** UAE: 84/95 Hysterectomy or myomectomy: 42/45 **Comparison: UAE versus myomectomy** **Mara 2008** UAE: 46/52 Myomectomy: 51/58	**EMMY 2010** Random sequence generation (selection bias): Low risk (Randomly assigned (1:1) using a computer-based minimization scheme) Allocation concealment (selection bias): Low risk (Telephone randomisation) Blinding (performance bias and detection bias) Objective outcomes: Unclear risk (No blinding, but unclear how much this would affect relatively objective outcomes

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
benefits and risks of uterine artery embolization (UAE) versus other medical or surgical interventions for symptomatic uterine fibroids. **Study dates** Search up to 17 April 2014 **Source of funding** None reported.	volumes were higher in the hysterectomy group. Setting: the Netherlands **FUME 2012** The mean age was 44 years (UAE group) and 43 years (hysterectomy group). The UAE group had slightly larger fibroid volumes. Setting: England **Jun 2012** Not reported. Setting: China **Mara 2008** The mean age was 32.4 years (UAE group) and 32.0 years (myomectomy group). Of the 121 participants, 110 were symptomatic (90.9%), 66 were nulligravidae (54.5%),	these options depended on whether the patient wished to retain her uterus for fertility or other reasons." All the hysterectomies and myomectomies were performed through an abdominal incision.) Duration: Recruitment took place between October 2006 to September 2009 **Mara 2008** 1) UAE (bilateral) 2) myomectomy (laparoscopic or open, the type and route of access were left at the discretion of the	was performed in a 1:1 ratio according to a computer-generated schedule.) Outcomes: Primary outcome measure: quality of life (36-Item Short-Form General Health Survey (SF-36) and complications. The SF-36 scores were presented at 6 month follow-up while the complications were reported after a maximum follow-up of 42 months. Secondary outcome measures: hospital stay, recovery time, satisfactory rate, recommending rate, pain at 24 hours and additional invasive procedures including hysterectomy or repeated embolization. Patient satisfaction measured by asking women whether they would undergo the same treatment again. **Mara 2008**	Outcome: Satisfaction with treatment at 5 years **Comparison: UAE versus hysterectomy** **EMMY 2010** UAE: 68/81 Hysterectomy: 66/75 **Comparison: UAE versus hysterectomy or myomectomy** **REST 2011** UAE: 83/93 Hysterectomy or myomectomy: 40/46 Outcome: Adverse event - Need for blood transfusion **Comparison: UAE versus hysterectomy**	(e.g. live birth, complications, re-intervention)) Blinding (performance bias and detection bias) Subjective outcomes: High risk (No blinding which was likely to affect subjective outcomes (e.g. satisfaction rate, quality of life) Incomplete outcome data (attrition bias) All outcomes: High risk (After randomisation, 92% of randomised women were analysed in the UAE group (81/88) and 84,3% in the hysterectomy group (75/89). At 5

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	35 were sterile (28.9%; 11 in embolization and 24 in myomectomy group; P < 0.05), 18 had miscarried in the past (14.9%) and 51 had another subfertility factor other than myoma (42.1%). Setting: Czech republic **Pinto 2003** Women aged 35 to 57 years. Setting: Spain **REST 2011** Women over the age of 18 were enrolled. Setting: UK **Ruuskanen 2010** All Caucasians. Setting: Finland **Inclusion criteria**	attending gynaecologist) Duration: Not reported in systematic review **Pinto 2003** 1) UAE 2) hysterectomy Duration: Recruitment took place between April 1999 to June 2001 with intended 2 years of follow-up **REST 2011** 1) UAE 2) Surgery (n=43 hysterectomies, n=8 myomectomies). "The method of	Design: RCT (Randomization was performed by means of a computer-generated random numbers. Patients with odd integers were placed into the embolization group and those with even numbers into the myomectomy group.) Outcomes: Early post-operative complications during the first 30 days; Symptomatic effectiveness; Post-procedural follicle stimulating hormone levels; Late complications after 30 days of the procedure; Reproductive outcome following both procedures **Pinto 2003** Design: RCT (Method of randomisation: Zelen design which is random allocation prior to seeking consent. The randomisation was stratified 2:1 in favour of UAE and generated	**EMMY 2010** UAE: 0/81 Hysterectomy: 10/75 **Pinto 2003*** **Intra- and postprocedural (within 30 days) blood transfusion** UAE: 0/40 Hysterectomy: 6/20 **Comparison: UAE versus myomectomy** **Mara 2008** UAE: 0/58 Hysterectomy: 2/63 Outcome: Adverse event - Unscheduled re-admission rate within 4-6 weeks	years, there were further dropouts: 85% in the UAE group (75/ 88) and 78.7% in the hysterectomy group (70/89)) Selective reporting (reporting bias): Low risk (Protocol not available but all expected outcomes reported) Other bias: Low risk (No other potential source of bias identified) **FUME 2012** Random sequence generation (selection bias): Low risk ("Women were randomised using the sealed opaque envelope

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	Inclusion criteria for the Cochrane review: All randomised controlled trials (RCTs) of uterine artery embolization versus other interventions. Women with symptomatic uterine fibroids, with either subjective or objective symptoms (expected to be predominantly heavy menstrual bleeding with or without intermenstrual bleeding, but also including pain and bulk-related symptoms), or both. Bilateral UAE using permanent embolic material versus any other surgical intervention as a primary treatment for symptomatic fibroids, for example myomectomy or hysterectomy. UAE was evaluated as a single therapy, not combined with	hysterectomy or myomectomy was not specified; the choice between these options depended on whether the patient wished to retain her uterus for fertility or other reasons". All the hysterectomies and myomectomies were performed through an abdominal incision. Duration of trial: recruitment took place between November 2000 to May 2004 with long term follow-up of 5 years **Ruuskanen 2010** 1) UAE (Shortly after selective	by computer sealednumber envelopes.) Outcomes: Evaluation of efficiency: total length of hospital stay after UAE and hysterectomy; Evaluation of safety: complications resulting from both the procedures; Evaluation of effectiveness: cessation of bleeding after UAE Patient satisfaction measured by asking women whether they would undergo the same treatment again. **REST 2011** Design: RCT (Randomisation was performed by means of a computer-generated schedule. Permuted blocks). This was stratified by centre and women were randomly assigned (2:1) to UAE or surgery (hysterectomy or moyomectomy). The method of surgery was not specified.	**Comparison: UAE versus hysterectomy** **EMMY 2010** UAE: 39/81 Hysterectomy: 19/76 **Pinto 2003*** UAE: 2/40 Hysterectomy: 1/20 **Comparison: UAE versus myomectomy** **Mara 2008** UAE: 2/58 Myomectomy: 1/63 Outcome: Length of hospital stay in days, mean (SD) **Comparison: UAE versus hysterectomy**	technique, using random numbers generated by computer") Allocation concealment (selection bias): Low risk ("Women were randomised using the sealed opaque envelope technique, using random numbers generated by computer") Blinding (performance bias and detection bias) Objective outcomes: Unclear risk (Unclear risk No blinding, but unclear how much this would affect relatively objective outcomes (e.g. live

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	surgery. We excluded trials of the occlusion of uterine arteries by any means other than embolization. **Includion criteria in individual studies:** **EMMY 2010** 1) the clinical diagnosis of uterine fibroids confirmed by ultrasonography; 2) menorrhagia (subjectively reported by the patient as increased or prolonged menstrual blood loss which caused dysfunction in daily life) was their predominant complaint, among other possibly fibroid-related signs and symptoms; 3) they were premenopausal; and 4) they were to be	catheterization of both uterine arteries from right femoral artery access, embolization was performed with calibrated microsphere particles (550-700 µm; EmboSphere; BioSphere Medical, Louvres, France) until near-stasis was observed in the ascending segment of the uterine artery. In tortuous, small or spastic uterine arteries, catheterization was performed with a 2.1- French microcatheter to ensure free-flow embolization. An Angio-Seal closure device was routinely used. The same interventional	Outcomes: Primary outcome measure: quality of life (36-Item Short-Form General Health Survey [SF-36]). Secondary outcome measures: time until resumption of usual activities (we have used the data for when women started driving their car as a resumption to normal activities), satisfaction score, pain score at 24 hours, any complications and treatment failure. Ovarian failure has also been reported at 1 year. Pregnancy outcomes were reported at 5 year follow-up. The study was not set up or powered to assess this outcome and there were only 8 myomectomies in the surgical group of 51 women. The original target of 200 women was reduced to 150 because of difficulties in recruitment which reduced the power to 80%. The data were presented in median and	**EMMY 2010** UAE: 2 (2.1) (n=81) Hysterectomy: 5.1 (1.3) (n=75) **Pinto 2003** UAE: 1.71 (1.59) (n=38) Hysterectomy: 5.85 (2.52) (n=19) **Ruuskanen 2010** UAE: 1.3 (0.4) (n=27) Hysterectomy: 3.5 (1.5) (n=26) **Comparison: UAE versus hysterectomy or myomectomy** **Jun 2012** UAE: 4.2 (2.7) (n=62) Hysterectomy or myomectomy: 7.6 (4.8) (n=62)	birth, complications, reintervention) Blinding (performance bias and detection bias) Subjective outcomes: High risk (No blinding, which was likely to affect subjective outcomes (e.g. satisfaction rate, quality of life)) Incomplete outcome data (attrition bias) All outcomes: High risk (After randomisation, 23% of randomised women excluded from analysis in the UAE group (19/82) and 27% in the myomectomy group (22/81))

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	scheduled for a hysterectomy **FUME 2012** symptomatic uterine fibroids confirmed by ultrasonography > 3cm in diameter; they were seeking treatment and treatment was considered justified by the physician, they wished to preserve their uterus, and would otherwise have been offered myomectomy performed via open abdominal surgery **Jun 2012** women with fibroids (>4cm) that could be adequately	radiologist performed all interventions (HM, with 2 years' experience in UAE at the beginning of the trial). After the intervention, women were observed in a recovery room for 4-6 h, after which they were transferred to the gynaecology ward for further care.) 2) hysterestomy (The type of hysterectomy and route of access were not standardised and left to the discretion of the attending gynaecologist, in order to maintain the protocol as close to that of daily practice as possible.	interquartile ranges as the milestone data were very skewed. After contacting the authors they released the mean and standard deviations of the data on the understanding that these data are included in this review with this caveat. **Ruuskanen 2010** Design: Single-centre RCT (Enrolled and assigned eligible participants to UAE or hysterectomy using sealed envelopes (1:1 ratio). Recruitment and randomisation were performed at the same gynaecology outpatient clinic visit.) Outcomes: The primary endpoint was improvement of symptoms; secondary endpoints were procedural characteristics, major complications, time to discharge from hospital, length of sick leave, re-interventions required,	**REST 2011** UAE: 1.6 (0.8) (n=100) Hysterectomy or myomectomy: 4.7 (1.9) (n=49) **Comparison: UAE versus myomectomy** **FUME 2012** UAE: 2 (2.73) (n=63) Myomectomy: 6 (2.73) (n=59) **Mara 2008** UAE: 2.5 (1.3) (n=58) Myomectomy: 3.6 (1.7) (n=63) Outcome: Health-related Quality of Life (USF-QOL) at one year, mean (SD)	Selective reporting (reporting bias): High risk (No suggestion of selective reporting. Fertility as an outcome was not collected as the ethics committee did not approve UAE for women who wished to conceive. Findings for QoL differed according to whether change scores or end scores were used, but both were reported in the review) Other bias: High risk (There were baseline differences between the groups in QoL and

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	visualized with the use of magnetic resonance imaging causing symptoms of menorrhagia or pelvic pain and pressure which justified surgical treatment **Mara 2008** 1) age up to 40 years; 2) planned pregnancy; 3) ultrasound verified intramural fibroids of at least 4 cm in greatest diameter (in the case of more fibroids, the largest being at least 4 cm); 4) serum concentration of FSH under 30 IU/L (on the third day of the menstrual cycle) **Pinto 2003**	Hysterectomy was performed as an abdominal hysterectomy, vaginal hysterectomy or laparoscopic-assisted hysterectomy. General anaesthesia was used in all operations.) Duration: Not reported in the systematic review	and satisfaction with treatment at 2 year follow-up The following symptoms were recorded: duration and severity of menstrual flow (no periods,mild,moderate,severe;withmoderateor severeindicating menorrhagia), dysmenorrhoea, pressure symptoms of the bladder, bowel, or back, increased urinary frequency, urinarystressincontinence, andnon-menstrualrelatedlowerabdominal pain.Menstrual flowwasrecordedseverewhenitpreventedeverydayactivities,causedanaemia,andextra large pads or tampons (change every 1 to 2 h) were needed. Complete blood count, ferritin, haematocrit, follicle-stimulating hormone and estrogen levels were ordered. Patient satisfaction measured by asking women whether they would undergo the same treatment again.	**Comparison: UAE versus myomectomy** USF-QOL End scores **FUME 2012** UAE: 72.9 (24.9) (n=63) Myomectomy: 86.3 (20.1) (n=59) USF-QOL Change scores **FUME 2012** UAE: 32.3 (28.8) (n=63) Myomectomy: 39.9 (27.3) (n=59) Outcome: Quality of life (SF-36) **Comparison: UAE versus surgery (hysterestomy or myomectomy)** Physical function within 1	although these were reported as not statistically significant, these do represent high risk) **Jun 2012** Random sequence generation (selection bias): Low risk (“Patients were randomly assigned to study groups according to a computer-generated schedule”) Allocation concealment (selection bias): Unclear risk (No details provided) Blinding (performance bias and detection bias) Objective

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	women with bleeding uterine fibroids who were candidates for hysterectomy **REST 2011** women with fibroids (>2cm) that could be adequately visualized with the use of magnetic resonance imaging causing symptoms of menorrhagia or pelvic pain and pressure which justified surgical treatment. **Ruuskanen 2010** women's subjective symptoms, which had to be severe enough to warrant consideration of hysterectomy, and only women agreeing to hysterectomy, if necessary, were included in the study			year, mean (SD) **Jun 2012** UAE: 68.4 (6.1) (n=62) Surgery: 60.1 (5.5) (n=62) **REST 2011** UAE: 92 (14) (n=106) Surgery: 89 (20) (n=51) Physical function at 5 years, mean (SD) **REST 2011 (from Moss 2011)*** UAE: 90 (18) (n=96) Surgery: 87 (24) (n=48) Social function within 1 year, mean (SD) **Jun 2012** UAE: 63 (10.2) (n=62) Surgery: 55 (11.2) (n=62)	outcomes: Unclear risk (No blinding, but unclear how much this would affect relatively objective outcomes (e.g. live birth, complications, re-intervention)) Blinding (performance bias and detection bias) Subjective outcomes: High risk (No blinding, which was likely to affect subjective outcomes (e.g. satisfaction rate, quality of life)) Incomplete outcome data (attrition bias) All outcomes: Low risk (After randomisation, 98.4% (62/63) were

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	Exclusion criteria Exclusion criteria for the individual studies: **EMMY 2010** 1) preservation of the uterus was warranted for future pregnancy; 2) renal failure(creatinine >150 mmol/L),active pelvic infection, or clotting disorderswere clinically established; 3) they were allergic to contrast material; 4) uterine malignancy was suspected; 5) submucosal fibroids with 50% of their diameter within the uterine cavity or dominant pedunculated serosal fibroids were present			**REST 2011** UAE: 84 (23) (n=106) Surgery: 87 (26) (n=51) Social function at 5 years, mean (SD) **REST 2011 (from Moss 2011)*** UAE: 86 (23) (n=96) Surgery: 85 (29) (n=48) Mental health within 1 year, mean (SD) **Jun 2012** UAE: 71.9 (6.2) (n=62) Surgery: 57.9 (8.9) (n=62) **REST 2011** UAE: 76 (17) (n=106) Surgery: 76 (21) (n=51) Mental health at 5 years,	analysed in the UAE group and 96.9% (62/ 64) in the surgical group) Selective reporting (reporting bias): Low risk (Protocol not available but all expected outcomes reported) Other bias: Unclear risk (Power calculations not carried out) **Mara 2008** Random sequence generation (selection bias): Low risk ("Patients marked with odd integers were placed into the E group (embolization) and patients given even numbers by the

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	FUME 2012 fibroids attached to the uterus by a narrow pedicle, or the whole fibroid mass being so large that it extended beyond the level of the umbilicus, or documented allergy to radiographic contrast medium, or a history of recent or ongoing pelvic inflammatory disease. Women also were excluded if they were not prepared to accept surgery as a treatment option, if they were pregnant, or if they were actively planning or trying to conceive.			mean (SD) **REST 2011 (from Moss 2011)*** UAE: 76 (17) (n=96) Surgery: 74 (24) (n=48) Emotional role within 1 year, mean (SD) **Jun 2012** UAE: 69.6 (6.7) (n=62) Surgery: 58.5 (6.8) (n=62) **REST 2011** UAE: 81 (35) (n=106) Surgery: 87 (30) (n=51) Emotional role at 5 years, mean (SD) **REST 2011 (from Moss 2011)*** UAE: 82 (35) (n=96) Surgery: 85 (34) (n=48)	computer were located into the Mgroup (myomectomy). In other words, a random number hasbeengenerated anew for every new patient; none of the researchers could therefore either know or predict the next number (there was no pre-created list of numbers).") Allocation concealment (selection bias): Low risk ("Patients marked with odd integers were placed into the E group (embolization) and patients given even numbers by the computer were located into the

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	Jun 2012 contraindication to MRI, severe allergy to iodinated contrast media, recent or ongoing pelvic inflammatory disease, pregnancy and any contraindication to surgery **Mara 2008** 1) type 0 and type 1 submucosal myomas and subserous myomas; 2) size of largest fibroid greater than 12 cm in greatest diameter on ultrasound or a uterus greater than the 4th month of pregnancy on palpation; 3) previous surgical or medical treatment;			Vitality within 1 year, mean (SD) **Jun 2012** UAE: 66.2 (6) (n=62) Surgery: 55.3 (9.8) (n=62) **REST 2011** UAE: 62 (21) (n=106) Surgery: 67 (22) (n=51) Vitality at 5 years, mean (SD) **REST 2011 (from Moss 2011)*** UAE: 63 (22) (n=96) Surgery: 63 (25) (n=48) **Comparison: UAE versus hysterectomy** **EMMY 2010 (from Hehenkamp 2008)*** Mental component	Mgroup (myomectomy). In other words, a random number hasbeengenerated anew for every new patient; none of the researchers could therefore either know or predict the next number (there was no pre-created list of numbers).") Blinding (performance bias and detection bias) Objective outcomes: Unclear risk (No blinding, but unclear how much this would affect relatively objective outcomes (e.g. live birth, complications, re-intervention)) Blinding

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	4) suspected uterine sarcoma; 5) significant illness that would contraindicate pregnancy; 6) lack of consent **Pinto 2003** wish to retain fertility; fibroids larger than 10 cm in diameter, any contraindication to surgery; sensitivity to iodine-based contrast material **REST 2011** Contraindication to MRI, severe allergy to iodinated contrast media, subserosal			summary change score from baseline at 6 weeks, mean UAE: 2.65 Hysterectomy: 2.78 p=0.953 Physical component summary change score from baseline at 6 weeks, mean UAE: 3.09 Hysterectomy: -5.96 p<0.0001 Mental component summary change score from baseline at 6 months, mean UAE: 7.03 Hysterectomy: 7.09 p=0.976	(performance bias and detection bias) Subjective outcomes: High risk (No blinding, which was likely to affect subjective outcomes (e.g. satisfaction rate, quality of life)) Incomplete outcome data (attrition bias) All outcomes: Low risk (After randomisation, 100% (58/58) were analysed in the UAE group and 98.4% (6263) in the myomectomy group. At 12 months there were 2 further dropouts in the UAE group giving a follow-up rate of 96.6%)

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	pedunculated fibroids, recent or ongoing pelvic inflammatory disease and any contraindication to surgery **Ruuskanen 2010** suspected genital tract malignancy, adnexal pathological features (suspected tumour or sactosalpinx), acute pelvic inflammatory disease, fertility preservation, uterovaginal prolapse requiring treatment, previous reactions to contrast media, renal impairment, and leiomyomas suitable for hysteroscopic			Physical component summary change score from baseline at 6 months, mean UAE: 8.05 Hysterectomy: 10.21 p=0.192 Mental component summary change score from baseline at 18 months, mean UAE: 7.01 Hysterectomy: 7.09 p=0.969 Physical component summary change score from baseline at 18 months, mean UAE: 7.94 Hysterectomy: 10.45	Selective reporting (reporting bias): Low risk (Protocol not available but all expected outcomes reported) Other bias: Low risk (No other potential source of bias identified) **Pinto 2003** Random sequence generation (selection bias): Low risk ("The random patient assignments were generated by computer and kept in sealed, numbered envelopes") Allocation

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	myomectomy (single leiomyoma over 50% in the cavum uteri and 5 cm or less in size)			p=0.131 Mental component summary change score from baseline at 24 months, mean UAE: 5.80 Hysterectomy: 7.26 p= 0.496 Physical component summary change score from baseline at 24 months, mean UAE: 9.42 Hysterectomy: 9.32 p=0.948 Outcome: Adverse event - Infection **Comparison: UAE versus myomectomy**	concealment (selection bias): Low risk ("The random patient assignments were generated by computer and kept in sealed, numbered envelopes") Blinding (performance bias and detection bias) Objective outcomes: Unclear risk (No blinding, but unclear how much this would affect relatively objective outcomes (e.g. live birth, complications, re-intervention)) Blinding (performance bias and detection bias)

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				Mara 2008* Need for antibiotics within 30 days post-procedure UAE: 8/58 Myomectomy: 6/63 **FUME 2012 (from Manyonda 2012)*** Urinary tract infection UAE: 0/63 Myomectomy: 8/59 Pneumonia UAE: 0/63 Myomectomy: 1/59 Sepsis UAE: 1/63 Myomectomy: 1/59 **Comparison: UAE versus hysterectomy**	Subjective outcomes: High risk (No blinding, which was likely to affect subjective outcomes (e.g. satisfaction rate, quality of life)) Incomplete outcome data (attrition bias) All outcomes: High risk (The analysis is different for different outcomes. Per protocol analysis used) Selective reporting (reporting bias): Low risk (Protocol not available but all expected outcomes reported) Other bias: Low risk (No other potential source of

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				Pinto 2003* Urinary tract infection within 30 days post-procedure UAE: 2/40 Hysterectomy: 2/20 Vulvovagitinis within 30 days post-procedure UAE: 1/40 Hysterectomy: 0/20 Surgical wound abscess within 30 days post-procedure UAE: 0/40 Hysterectomy: 3/20 Intra-abdominal abscess within 30 days post-procedure UAE: 0/40 Hysterectomy: 1/20	bias identified) **REST 2011** Random sequence generation (selection bias): Low risk (randomly assigned [2:1] using a computer generated schedule) Allocation concealment (selection bias): Low risk (remote telephone randomisation) Blinding (performance bias and detection bias) objective outcomes: Unclear risk (no blinding, but unclear how much this would

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				EMMY 2010 (from Hehenkamp 2005)* Urinary tract infection during hospital stay UAE: 0/81 Hysterectomy: 3/75 Urinary tract infection up to 6 weeks post-discharge UAE: 5/81 Hysterectomy: 2/75 Endometritis during hospital stay UAE: 0/81 Hysterectomy: - Endometritis up to 6 weeks post-discharge UAE: 2/81 Hysterectomy: -	affect relatively objective outcomes [e.g live birth, complications, re-intervention]) Blinding (performance bias and detection bias) subjective outcomes: High risk (no blinding, which was likely to affect subjective outcomes (e.g. satisfaction rate, quality of life) Incomplete outcome data (attrition bias) all outcomes: Low risk (after randomisation, 89.6% [95/106] were analysed in the UAE group and 88.2% [45/51] in the surgical group)

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				Pneumonia during hospital stay UAE: 0/81 Hysterectomy: 0/75 Pneumonia up to 6 weeks post-discharge UAE: 1/81 Hysterectomy: 0/75 Intra-abdominal infection during hospital stay UAE: 0/81 Hysterectomy: 0/75 Intra-abdominal infection up to 6 weeks post-discharge UAE: 0/81 Hysterectomy: 0/75 Sepsis during hospital stay	Selective reporting (reporting bias): Low risk (protocol not available but all expected outcomes reported) Other bias: low risk (no other potential source of bias identified) **Ruuskanen 2010** Random sequence generation (selection bias): Unclear risk (Insufficient details reported, states "The same gynaecologist discussed treatment options with the patient and enrolled and assigned eligible

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				UAE: 0/81 Hysterectomy: 0/75 Sepsis up to 6 weeks post-discharge UAE: 1/81 Hysterectomy: 0/75 **Comparison: UAE versus hysterectomy** **REST 2011 (from Edwards 2007)*** Wound infection (during hospital stay) UAE: N/A Surgical group: 2/51 Outcome: Adverse event - Venous thrombosis **Comparison: UAE versus hysterectomy**	participants to UAE or hysterectomy using sealed envelopes (1:1 ratio).") Allocation concealment (selection bias): Unclear risk (Insufficient details reported, states "The same gynaecologist discussed treatment options with the patient and enrolled and assigned eligible participants to UAE or hysterectomy using sealed envelopes (1:1 ratio).") Blinding (performance bias and detection bias) Objective

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				Pinto 2003* Deep venous thrombosis UAE: 1/40 Hysterectomy: 1/20 **EMMY 2010 (from Hehenkamp 2005)*** Thrombosis during hospital stay UAE: 0/81 Hysterectomy: 0/75 Thrombosis up to 6 weeks post-discharge UAE: 0/81 Hysterectomy: 0/75 Pulmonary embolism during hospital stay UAE: 1/81 Hysterectomy: 1/75	outcomes: Unclear risk (Carried out in same gynaecology outpatient clinic) Blinding (performance bias and detection bias) Subjective outcomes: High risk (No blinding, which was likely to affect subjective outcomes (e.g. satisfaction rate, quality of life)) Incomplete outcome data (attrition bias) All outcomes: Low risk (After randomisation, 96.35 (26/27) were analysedintheUAE groupand96.7%(29 / 30) in the hysterectomy group. One patient

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				Pulmonary embolism up to 6 weeks post-discharge UAE: 0/81 Hysterectomy: 0/75 **Comparison: UAE versus myomectomy** **FUME 2012 (from Manyonda 2012)*** Pulmonary embolus UAE: 0/63 Myomectomy: 1/59 Outcome: Adverse event - Long-term complications **Comparison: UAE versus hysterectomy** **Ruuskanen 2010*** Urinary stress incontinence at 2-year	from the UAE group withdrew consentforfollow-up1dayafterUAE,an done patient from the hysterectomy group died from cerebral infarct 13 months after the hysterectomy) Selective reporting (reporting bias): Low risk (Protocol not available but all expected outcomes reported) Other bias: Unclear risk (Power calculation not carried out) **Other information** EMMY 2010 references included

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				follow-up UAE: 7/27 Hysterectomy: 13/30 Outcome: Adverse event - Death **Comparison: UAE versus hysterectomy** **EMMY 2010 (from Hehenkamo 2005)*** UAE: 0/81 Hysterectomy: 0/75 *Data extracted from the original paper by the NGA tehcnical team.	in the Cochrane systematic review relevant for the current review: Hehenkamp 2005; Hehenkamp 2008; van der Kooij 2010; Volkers 2007. FUME 2012 reference included in the Cochrane systematic review relevant for the current review: Manyonda 2012 REST 2011 reference included in the Cochrane systematic review relevant for the current review: Edwards 2007; Moss 2011) Studies included in the SR that are not

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
					relevant to the current review: REST 2011 (Rashid 2010), as there are no outcomes of interest
Full citation Hehenkamp, W. J., Volkers, N. A., Birnie, E., Reekers, J. A., Ankum, W. M., Symptomatic uterine fibroids: treatment with	**Sample size** Please see Gupta 2014 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
uterine artery embolization or hysterectomy--results from the randomized clinical Embolisation versus Hysterectomy (EMMY) Trial, Radiology, 246, 823-32, 2008 **Ref Id** 550146 **Country/ies where the study was carried out**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study type **Aim of the study** **Study dates** **Source of funding**					
Full citation Jain, P., Rajaram, S., Gupta, B., Goel, N., Srivastava, H., Randomized controlled trial of thermal	**Sample size** N=40 n=20 TBA; n=20 vaginal hysterectomy (VH) **Characteristics** Age in years, mean ± SD (range): TBA - 44.25 ± 3.41 (40-50); VH - 43.95 ± 1.95 (40-47) Parity, mean ± SD (range): TBA - 2.85 ± 1.2 (1-7); VH - 3.25 ± 1.2 (1-6)	**Interventions** Thermal Balloon Ablation (TBA) versus vaginal hysterectomy (VH) Both TBA and vaginal hysterectomy were performed under spinal anesthesia in the postmenstrual phase of the cycle. TBA was performed	**Details** Sample size calculation A sample size of 40 was considered adequate assuming that 40% of women in the vaginal hysterectomy group and 8% in the TBA group would experience adverse effects (minor and major), and a reduction in the PBAC score of 342 in women undergoing TBA, with 80% power	**Results** Outcome: UFS-TS (Uterine Fibroid Symptom Transformed Score) At baseline TBA: 60.43% VH: 61.85% At 6 months post-surgery TBA: 7.79% VH: 2.02%	**Limitations** **Cochrane risk of bias tool** Selection bias Random sequence generation: Low risk Allocation concealment: Unclear risk, not reported. Performance bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
balloon ablation versus vaginal hysterectomy for leiomyoma -induced heavy menstrual bleeding, International Journal of Gynaecology & Obstetricslnt J Gynaecol Obstet, 135, 140-144, 2016 **Ref Id** 550189 **Country/ies where the study**	BMI, mean ± SD (range): TBA - 26.63 ± 4.52 (20.0-36.6); VH - 25.53 ± 3.52 (20-31.6) PBAC score at baseline, mean ± SD (range): TBA - 624.4 ± 280.1 (192-974); VH - 668.3 ± 199.2 (300-965) Duration of symptoms in years, mean ± SD (range): TBA - 1.73 ± 1.41 (0.25-5); VH - 1.62 ± 1.15 (0.5-4) Symptom severity score at baseline, mean ± SD (range): TBA - 27.4 ± 3.3 (23-37); VH - 27.8 ± 2.6 (23-32) HRQoL score at baseline, mean ± SD (range): TBA - 102.9 ± 9.4 (80-114); VH - 106.9 ± 5.3 (87-114) Haemoglobin g/L, mean ± SD (range): TBA - 108.8 ±	using the LiNAMenotreat system (LiNA Medical, Glostrup, Denmark), which consists of a reusable Menotreat system controller and a singleuse Menotreat balloon set with an inflatable silicon balloon catheter. Thorough curettagewas performed to reduce the endometrial thickness before TBA. The balloon was inflated with normal saline at 85°C ± 3°C with the pressure maintained at 200 ± 10 mm Hg for 11 minutes ± 5 seconds. The maximal uterine cavity length for	at a 5% level of significance. Randomisation Participants were randomly allocated into two groups (TBA and vaginal hysterectomy) in a 1:1 ratio using computer-generated random number tables. Allocation concealment Not reported Blinding Participants, investigators, and data analysts were not masked to group assignment. Examinations before interventions A detailed history was obtained from all participants. A physical examination was also performed, alongwith PBAC scoring. All requisite preoperative investigations were	Difference in mean change: 7.18% (95% CI 1.29 to 13.07, p=0.018) Outcome: Increase in mean HR-TS HR-TS (Health-related Transformed Score) from baseline to 6 months post-surgery TBA: 58.17% ± 9.06% VH: 64.04% ± 3.63% Difference in mean change: -5.87 (95% CI -10.29 to -1.45, p=0.011) Outcome: Adverse events - Blood transfusion TBA: 0/20 VH: 12/20 p<0.001	Blinding of participants and personnel: Unclear risk, blinding was not possible due to the nature of the interventions, however, not clear if it can introduce performance bias. Detection bias Blinding of outcome assessment: High risk, blinding not possible due to the nature of the interventions, therefore, there is a high risk of bias on subjective outcomes (quality of life) but low risk of bias in objective outcomes such as adverse events.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
was carried out India **Study type** RCT **Aim of the study** To compare the efrficacy of thermal balloon ablation (TBA) with that of vaginal hysteroscopy in the treatment of leiomyoma-induced	15.2 (82.0-146.0); VH - 101.9 ± 13.9 (84.0-137.0) Leiomyoma size in cm, mean ± SD: TBA - 2.74 ± 0.84; VH - 3.86 ± 0.94 No. of leiomyomas, mean ± SD (range): TBA - 1.35 ± 0.1 (1-2); VH - 1.45 ± 0.6 (1-3) Endometrial thickness in mm, mean ± (range): TBA - 7.81 ± 3.09 (4-17.8); VH - 8.31 ± 2.30 (4-15) **Inclusion criteria** Women older than 40 years of age who had no desire for future childbearing; heavy menstrual bleeding (pictorial blood loss assessment chart [PBAC] score ≥100); a uterine size up to that of 14 weeks of pegnancy; leiomyomas of ≤5 cm in diameter; and a uterocervical length of ≤12	TBA was 12 cm as recommended by the manufacturer. Vaginal hysterectomy was performed using the standard technique.	undertaken, including hemoglobin tests, cervical smear tests, ultrasonography, endometrial histologic examinations, and pre-anesthetic evaluation. Follow-up The Uterine Fibroid Symptom and Quality of Life (UFS-QOL) questionnaire was used to assess the quality of life before and after the procedures. The UFS-QOL consists of the symptom severity score (SSS) and the health-related quality of life (HR-QOL) score. SSS includes questions pertaining to severity of symptoms, and the HR-QOL score includes questions pertaining to concern, energy, activities, control, self-consciousness,	Outcome: Adverse events - Internal organ injury "No cervical lacerations, uterine perforations, vessel injuries, or injuries to viscera (enterotomy, ureteric injusry, cystotomy) were noted in either group." Outcome: Adverse events - Length of hospital stay in hours (mean) TBA: 36.65 VH: 87.60 p<0.001 Mean difference 50.9 (95% CI 46.2 to 55.69) Outcome: Adverse events	Attrition bias Incomplete outcome data: Low risk, all eligible participants were followed up. Reporting bias Selective reporting: Low risk Other bias Other sources of bias: - Overall assessment: Serious risk of bias **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
heavy menstrual bleeding. **Study dates** November 12th 2012 to October 31st 2014 **Source of funding** Not reported.	cm. **Exclusion criteria** Women with acute pelvic inflammatory disease or pelvic pathology (e.g. adenomyosis, gyaecologic cancers [including endometrial malignancy], atypical endometrial hyperplasia, and submucosal leiomyomas.		and sexual functions. The SSS and HR-QOL score were applied to formulas to obtain corresponding transformed scores indicating severity (Uterine Fibroid Symptom Transformed Score [UFS-TS]) and quality of life (Health-Related Transformed Score [HR-TS]), respectively, in terms of percentages. Intraoperative variables—including blood loss, duration of surgery, need for blood transfusion, complications, and technical difficulty— were compared in both groups. Duration of hospital stay, and early and late postoperative complications—including infection, fever, endometritis, pneumonia, thromboembolism, hematoma, cellulitis, and abscess formation—were noted and compared in both groups. The frequency of	- early or late complications "There were no early or late complications, such as urinary tract infections, fever, endometritis, pneumonia, thromnoemolism, haematoma, or cardiorespitaroty arrest, in either group."	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
			adverse events such as hematometra and postablation tubal sterilization syndrome was noted in women who underwent TBA. Follow-up was performed at 1, 3, and 6 months after surgery to assess menstrual blood loss (PBAC score) in women in the TBA group and hemoglobin levels in both groups. Six months after surgery, improvement of symptoms and UFS-QOL scores (SSS and HR-QOL scores) was assessed in allwomen.Women in the TBA groupwere also assessed at 12 and 24 months after surgery for recurrence of HMB. The primary outcome measure was the number of women with HMB in the TBA group 6 months after surgery for uterine leiomyomas. Secondary outcome measures		

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
			were improvement in hemoglobin levels, intraoperative and postoperative events, and UFS-QOL scores in both groups. Statistical analysis Statistical analyses were by intention to treat. The χ2 test was used to study baseline variables and symptoms; the unpaired t test was used to compare changes in UFS-QOL. The McNemar test was used to compare symptom scores. P values and mean differences with 95% confidence intervals (CIs) were used to determine significance. P<0.05 was considered significant.		
Full citation	**Sample size** N=95 original sample	**Interventions** The women in the	**Details** Sample size calculation	**Results** PBAC score (mean & SD)	**Limitations** **Cochrane risk of**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Khajehei, M, Abdali, K, Tabatabaee, H, The effect of mefenamic acid and naproxen on heavy menstrual bleeding: A placebo-controlled study, South African journal of obstetrics and gynaecology, 19, 31-4, 2013 **Ref Id** 550227 **Country/ie**	Randomised (Mefenamic acid=40, Naproxen=40, Placebo=40) Loss to follow up in 3 months (Mefenamic acid=8, Naproxen=7, Placebo=12) Analysed at 1 month (Mefenamic acid=37, Naproxen=36, Placebo=37) Analysed at 2 month (Mefenamic acid=35, Naproxen=35, Placebo=32) Analysed at 3 months (Mefenamic acid=32, Naproxen=33, Placebo=28) **Characteristics** **Baseline characteristics not reported except as a narrative summary.** The mean age of those who	first group received tablets containing 250 mg mefenamic acid 4 times a day, those in the second group tablets containing 250 mg naproxen 4 times a day, and those in the third group placebo tablets 4 times a day. The placebo, mefenamic acid and naproxen tablets were identical in appearance and their packages were coded according to the content by a person who was not in the research team, so they could not be identified by either the researchers or the participants until after completion of the study and	Not reported Randomisation and allocation concealment The nominated women were randomly allocated to one of the three study groups in the following way: first, each questionnaire was assigned a number. Then three numbers were selected randomly in order to designate the first person in each group. After that, the 117 remaining questionnaires were divided into 39 groups consisting of three questionnaires in each group. Next, we randomly assigned each of these three questionnaires to one of the three study groups. At the end, there were three groups of 40 participants. Blinding The placebo, mefenamic acid and naproxen tablets were identical in appearance and their	Baseline Mefenamic acid: 118.2 (3.4) Naproxen: 117.6 (7.8) Placebo: 119.6 (5.9) At 1 month follow up Mefenamic acid: 81.4 (4.5) Naproxen: 58.3 (5.1) Placebo: 115.8 (8.6) At 2 month follow up Mefenamic acid: 68.2 (8.5) Naproxen: 47.4 (4.9) Placebo: 110.7 (6.5)	**bias tool** Selection bias Random sequence generation: High Risk Allocation concealment: High Risk Participant were allocated to one of the group based on the judgment of clinician (list of random numbers) although it was stated that allocation was completely random. Performance bias Blinding of participants and personnel: Low Risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
s where the study was carried out Iran **Study type** Randomised placebo controlled trial **Aim of the study** To compare the efficacy of mefenamic acid and naproxen in reducing heavy menstrual bleeding	completed the study was 30.6 years (standard deviation (SD)±1.6 years; range 19 - 43 years). Socio-demographic data (age, education, job, marital status, gravidity) were evaluated at baseline, and there were no statistically significant differences in any baseline parameters between the groups. **Inclusion criteria** 1) age 20 - 45 years 2) normal findings on cervical smear test 3) normal ovulatory cycles 4) no history of renal or hepatic impairment, thromboembolic disease, inflammatory bowel disease, peptic or intestinal ulceration, or coagulation or fibrinolytic disorders	statistical analysis, when the codes were broken. All participants completed the PBAC prospectively during the intervention cycles, and they were asked to record any adverse effects. The participants were advised to take the tablets with food and a sufficient amount of water, and to use the pads that had been provided during both the control and intervention cycles. They were visited between cycles to make sure that they were not having any serious problems and to answer their	packages were coded according to the content by a person who was not in the research team, so they could not be identified by either the researchers or the participants until after completion of the study and statistical analysis, when the codes were broken. All participants completed the PBAC prospectively during the intervention cycles, and they were asked to record any adverse effects. Follow-up Of the initial 120 participants, 93 completed the trial (32 in the mefenamic acid group, 33 in the naproxen group and 28 in the placebo group). Of the 8 participants in the mefenamic acid group who dropped out, 3 stopped using the study medication and 5 were lost to follow-up; in the naproxen group 4 stopped using the study medication and 2 were lost to	At 3 month follow up Mefenamic acid: 63.4 (7.2) Naproxen: 43.2 (4.0) Placebo: 113.1 (5.6)	Pills were identical in appearance and their packages were coded according to the content by a person who was not in the research team, so they could not be identified by either the researchers or the participants until after completion of the study and statistical analysis, when the codes were broken Detection bias Blinding of outcome assessment: Low risk Blinding of outcome assessors was ensured as

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study dates 2008-2009 **Source of funding** Deputy for Research of Shiraz University of Medical Sciences	5) normal results for blood tests (including prothrombin time, partial thromboplastin time and thyroid-stimulating hormone) 6) not taking any hormones or NSAID **Exclusion criteria** 1) infertility 2) being overweight or obese (body mass index (BMI) >25 kg/m2) or underweight (BMI <18.5 kg/m2) 3) polycystic ovarian syndrome 4) vaginitis and/or pelvic inflammatory disease 5) uterine polyps and/or fibroids 6) use of the ICUD 7) being peri-menopausal	questions. After completion of the 3 intervention cycles, all the participants were met for a final visit and to collect the questionnaires.	follow-up; and in the placebo group 8 did not proceed due to the drug's ineffectiveness and 4 were lost to follow-up. However, the primary intention-to-treat analysis was based on data from 120 women Outcome measure: The primary outcome measure was menstrual blood loss at the end of the study assessed by PBAC. Stistical analysis One-way ANOVA to compare menstrual blood loss in the three groups before and during the intervention. Descriptive statistics were used to summarise demographic data and adverse events. A p-value of <0.05 was considered statistically significant.		stated previously Attrition bias Incomplete outcome data: High risk Loss to follow up was approximately 17.5% for mefenamic acid, 20% for naproxen and 30% for placebo. No further information on differential follow up. Study states that ITT was used but reviewer is unclear on whether the reported data is based on ITT Reporting bias Selective reporting: High risk Outcomes were not

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	(increased serum follicle-stimulating hormone levels indicating the approach of menopause)				clearly reported in methodology. No data for one of the outcome (Hemoglobin conc entration) Other bias Other sources of bias: High risk Serious consideration on the quality of the data. Researchers were also unable to control use of the pads provided or adherence to the medications, so had to rely on information given by the participants. **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
					Included in NMA, this publication only reported on outcomes relevant for the NMA.
Full citation Kiseli, M Kayikcioglu F Evliyaoglu O Haberal A, Comparison of Therapeutic Efficacies of Norethisterone, Tranexamic Acid and Levonorge	**Sample size** N= 84 randomised NETA (norehisterone acid)= 28 Tranexamic acid=28 LNG-IUS=28 Follow up at 6 months N= 62 NETA (norehisterone acid)= 20 Tranexamic acid=22 LNG-IUS=20	**Interventions** Patients recruited to one of the following 3 groups: oral NETA (5 mg 3 times daily, total dose 15 mg/day) for 10 days between the 14th and 23rd day of menstrual cycle, oral tranexamic acid (1 g 4 times daily, total dose of 4 g/day) for the first 4 days of the cycle, and LNG-IUS releasing 20 µg levonorgestrel per day, which was	**Details** Sample size calculation A sample size was claculted (minimum 60) to detect at least a 57.0 difference in PBAC scores between any of the 2 groups with a power of 95% at the 5% significance level. Sample size estimation was performed using NCSS and PASS 2000 software Randomisation and allocation concealment Randomization was performed with computer-generated codes. Blinding	**Results** Outcome: PBAC scores (median and interquartile range) Baseline NETA, 290 (87.50) Tranexamic acid, 300 (174) LNG-IUS, 300 (91.75) At 1 month NETA, 245 (115) Tranexamic acid, 235 (131.25) LNG-IUS, 208 (190)	**Limitations** **Cochrane risk of bias tool** Selection bias Random sequence generation: Unclear Allocation concealment: Unclear Inadequate information to make judgment for either high or low risk of bias Performance bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
strel-Releasing Intrauterine System for the Treatment of Heavy Menstrual Bleeding: A Randomized Controlled Study, Gynecologic and Obstetric Investigation, 81, 447-53, 2016 **Ref Id** 550239 **Country/ies where the study was**	**Characteristics** Demographic data based on the participant which completed the study Age, mean ± SD NETA: 43.1±6.4 Tranexamic acid: 41.7±4.0 LNG-IUS: 41.4±6.5 Duration of complaint, months, median (min–max) NETA: 5.5 (1–48) Tranexamic acid: 21 (1–60) LNG-IUS: 15 (2–60) PBAC score, median (IQR)	applied during the first few days of menstruation. Oral tranexamic acid and NETA were given for 6 menstrual cycles. Randomization was performed with computer-generated codes. None of the recruited patients were symptomatic because of anemia (Hb >10 g/dl), and oral iron preparations were not prescribed. Patients were examined in the first, third and sixth months of the treatment. Side effects of the medications were recorded. Additionally, patients were asked to respond 'yes' or	Neither patients nor researchers were blinded to treatment Follow-up Twelve patients 3 patients NETA, 4 patients tranexamic acid and 5 patients in LNG-IUS were lost to follow-up. Five patients in group 1 and 2 patients in group 2 used the medications inappropriately. 5 patients in NETA and 2 patients in tranexamic acid used the medications inappropriately and were dropped. 1 patient reported that the intrauterine device had dropped in the fifth month and 2 patients asked for removal of the LNG-IUS because of intolerable pelvic pain and heavy bleeding in the second month. Final outcome based on 62 participants. The primary outcome measure was PBAC score, HQOL and patient satisfaction.	At 3 month NETA, 178 (132.50) Tranexamic acid, 188 (154.25) LNG-IUS, 88 (132.5) At 6 month NETA, 165 (115) Tranexamic acid, 150 (132.50) LNG-IUS, 45 (57.50) Outcome: QOL parameters before and after treatment in 4 domains: pre-treatment and post treatment values (Mean ±SD) Physical domain Pretreatment	Blinding of participants and personnel: Unclear risk blinding was not possible due to the nature of the interventions, however, not clear if it can introduce performance bias Detection bias Blinding of outcome assessment: High Risk Outcome assessors were not blind Attrition bias Incomplete outcome data: High Loss to follow up

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
carried out Turkey **Study type** Randomised controlled trial **Aim of the study** To compare the therapeutic efficacies of norethisterone acid (NETA), tranexamic acid and levonorgestrel-releasing	NETA: 290 (87.5) Tranexamic acid: 300 (174) LNG-IUS: 300 (91.8) Body weight NETA: 72.5(16.8) Tranexamic acid: 71.5 (15.3) LNG-IUS: 70.5 (20.0) **Inclusion criteria** 1) Premenopausal patients (18–45 years) with complaints of regular but heavy periods 2) mean PBAC scores of ≥ 100 during 2 consecutive	'no' if they were satisfied or not satisfied with the treatment. The first month of treatment was defined as the period of 1 month beginning from the application of LNG-IUS	QOL evaluation was performed according to the World Health Organization Quality of Life-Short Form, Turkish version (WHOQOL-BREF TR), which consists of 26 questions. The participants were asked 7 questions regarding their physical health, 6 about their psychological status, 3 about their social support and 8 relating to their environment. The Turkish version has an additional national item contributing the environmental domain of the scale. Each facet of the WHOQOL-BREF TR is measured using a 5-point Likert scale about the respondents' feelings over the previous 2 weeks. The range of scores was between 1 and 100, with higher scores indicating better QOL. Forms were filled out by the patients privately, with the	NETA: 12.94±3.46 Tranexamic acid: 12.68±2.57 LNG-IUS: 12.46±2.42 Post-treatment NETA: 14.17±2.11 Tranexamic acid: 14.88±2.92 LNG-IUS: 14.14±2.27 Psychological domain Pretreatment NETA: 12.43±2.52 Tranexamic acid: 12.03±2.83 LNG-IUS: 12.43±2.76 Post-treatment NETA: 12.93±2.41 Tranexamic acid:	reported in all three groups. No analysis performed to account for loss to follow up. Final value was based on participants which completed the study Reporting bias Selective reporting: Low All outcomes were reported Other bias Other sources of bias: **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
intrauterine system (LNG-IUS) in treating idiopathic heavy menstrual bleeding (HMB) **Study dates** Not reported **Source of funding** Authors declare no financial support re ceived for this trial	periods *Patients with fibroids smaller than 2 cm and not distorting the endometrial cavity were accepted* **Exclusion criteria** 1) Malign cervico-vaginal cytology 2) severe anemia 3) contraindications to current therapies 4) systemic diseases like hypertension, diabetes, thyroid diseases or coronary artery diseases 5) and history of previous medication for menorrhagia		assistance of trained research assistants before treatment and after 6 months. Statistical analysis Continuous data were shown as mean ± SD or median ± interquartile range. No ITT performed.	13.15±2.39 LNG-IUS: 13.60±2.39 Social domain Pretreatment NETA: 13.07±3.42 Tranexamic acid: 13.52±2.86 LNG-IUS: 14.60±2.85 Post-treatment NETA: 13.73±3.75 Tranexamic acid: 14.06±3.13 LNG-IUS: 13.87±2.68 Environmental domain Pretreatment NETA: 12.73±2.38 Tranexamic acid: 13.39±2.15	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				LNG-IUS: 13.08±2.09 Post-treatment NETA: 12.75±2.57 Tranexamic acid: 14.02±1.79 LNG-IUS: 12.95±1.71 Environmental domain-TR Pretreatment NETA: 13.00±2.24 Tranexamic acid: 13.49±2.00 LNG-IUS: 13.16±1.93 Post-treatment NETA: 13.00±2.42 Tranexamic acid: 13.86±1.82 LNG-IUS: 13.11±1.81	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				Outcome: Patient Satisfaction NETA: 14 (70%) Tranexamic acid: 14 (63.6%) LNG-IUS: 17 (77.2%)	
Full citation Kleijn, Jh, Engels, R, Bourdrez, P, Mol, Bw, Bongers, My, Five-year follow	**Sample size** **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Same trial as Bongers 2004. Included in NMA. Compares two 2nd generation ablation techniques,

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
up of a randomised controlled trial comparing NovaSure and ThermaChoice endometrial ablation, BJOG : an international journal of obstetrics and gynaecology, 115, 193-8, 2008 **Ref Id** 550241 **Country/ies where the study**					therefore, not included in the pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
was carried out **Study type** **Aim of the study** **Study dates** **Source of funding**					
Full citation Lethaby, Anne, Hussain, Munawar, Rishworth, Josephine R, Rees, Margaret C,	**Sample size** **Barrington 2003** N=50 randomised (n=25 LNG-IUS; n=25 ablation) **Busfield/Brown 2006 (TALIS trial)** N=83 randomised **Crosignani 1997**	**Interventions** **Barrington 2003** 1) Levonorgestrel-releasing intrauterine system (LNG IUS, Mirena) 2) Thermal balloon ablation after pre-operative endometrial thinning	**Details** **Barrington 2003** Design: RCT, Parallel group study in single centre Outcomes: PBAC score at 6 months, Improvement in bleeding, Requirement for further treatment (surgical) **Busfield/ Brown 2006**	**Results** **Comparison: LNG-IUS vs. any other medical treatment** Outcome: menstrual blood loss (AH method) **Kaunitz 2010*** Change from baseline at 3 months (mid study),	**Limitations** **Quality of Cochrane SR:** Systematic review assessed using AMSTAR checklist. Total score: 11/11 **Quality of**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Progesterone or progestogen-releasing intrauterine systems for heavy menstrual bleeding, Cochrane Database of Systematic Reviews, 2015 **Ref Id** 550298 **Country/ies where the study was carried out** **Study type**	N=70 randomised **De Souza 2010** N=58 randomised **Ergun 2012** N=58 randomised **Gupta 2015** N=571 randomised **Hurskainen 2001** N=236 randomised **Irvine 1998** N=44 randomised **Kaunitz 2010** N=165 randomised **Kittelsen 1998** N=60 randomised **Abdel Malak 2006** N=60 randomised	with gosarelin one month prior Duration: 6 months **Busfield 2006/ Brown 2006** 1) LNG IUS (Mirena) 2) Balloon ablation (Thermachoice I) **Crosignani 1997** 1) Levonorgestrel-releasing (20 ug/day) intrauterine contraceptive system inserted within seven days of menstruation 2) Endometrial resection in the early proliferative phase using a rollerball and a 90 degree loop. All the resections were	Design: RCT, single centre, parallel group Outcomes: PBAC score; Quality of life (SF36); Satisfaction rates at 3, 6, 12 and 24 months; 'Failure' r ates (expulsion/removal of LNG IUS or alternative therapy, initiation of medication or alternative surgery f or TBA); Amenorrhoea; Duration of bleeding; adverse events **Crosignani 1997** Design: RCT, Parallel group study in single centre Outcomes: Menstrual blood loss by PBAC at 6 and 12 months follow-up, Hb and serum Fe at 6 and 12 months, Participant satisfaction (very satisfied, satisfied, uncertain, dissatisfied), Quality of life (International Quality of Life Assessment Short Form 36 Italian version, release 1.6), Proportion of women with	mean (95% CI) IUS group: -108.3 (-125.4 to -91.2) Progestogen group: -21.2 (-38.1 to -4.3) Change from baseline at 6 months (end of study), mean (95% CI) IUS group: -114.7 (-144.2 to -85.1) Progestogen group: -39.0 (-68.2 to -9.8) **Shabaan 2011*** At baseline, mean±SD IUS group: 300.0±150.1 (n=56) COC group: 274.3±142.6 (n=56) At 12 months, mean ±SD IUS group: 44.4±34.9 (n=48)	**individual studies:** Risk of bias assessment taken from Cochrane SR (Cochrane risk of bias tool). **Barrington 2003** Random sequence generation: unclear Allocation concealment: unclear Blinding of participants and personnel: high risk Blinding of outcome assessors: high risk Incomplete outcome data: unclear

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Cochrane systematic review **Aim of the study** To determine the effectiveness, acceptability and safety of progesterone or progestogen-releasing intrauterine devices in achieving a reduction in heavy menstrual bleeding.	**Ozdegirmenci 2011** N=86 randomised **Reid 2005** N=51 randomised **Sayed 2011** N=58 randomised **Sesti 2012** N=72 randomised **Shabaan 2011** N=112 randomised **Shaw 2007** N=66 randomised **Soysal 2002** N=72 randomised **Tam 2006** N=44 randomised **Characteristics**	performed by the same surgeon Duration: 12 months. Follow-up assessments at 6 and 12 months **De Souza 2010** 1) Levonorgestrel-releasing IUS (Mirena) 2) Thermal balloon ablation (Thermachoice) under general anaesthesia Both procedures initiated during the first 15 days of a menstrual cycle **Ergun 2012** 1) LNG IUS inserted within first 15 days of menstrual cycle	amenorrhoea at 12 months, Proportion of women with side effects **De Souza 2010** Design: RCT, Parallel group study in single centre Outcomes: Menstrual blood loss (PBAC score), Other bleeding outcomes (amenorrhoea, decreased bleeding) , Hb levels, Quality of life (Psychological General Wellbeing Index), Failure of treatment, Satisfaction rates Assessed at 1, 6 and 12 months after the procedures and additionally at 5 years **Ergun 2012** Design: RCT, Parallel group study in single centre Outcomes: PBAC scores, Further surgical treatment, Failure of treatment, Amenorrhoea and hypomenorrhoea,	COC group: 118.2±75.0 (n=47) Outcome: PBAC score **Shabaan 2011*** At baseline, mean±SD IUS group: 306.7±131.8 (n=56) COC group: 323.8±97.3 (n=56) At 12 months, mean ±SD IUS group: 31.6±35.1 (n=48) COC group: 273.0±238.4 (n=47) Outcome: satisfaction NMA outcome Outcome: Quality of Life (SF-36) NMA outcome	Selective reporting: unclear other bias: high risk (Preoperative menstrual bleeding was significantly higher in the thermal balloon group compared to the LNG IUS group. Bias is likely as menstrual bleeding was measured postoperatively without adjustment for higher scores.) **Busfield 2006/Brown 2006** Random sequence generation: low risk Allocation concealment: low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study dates Search up to Janurary 2015. **Source of funding** • NHS Executive Anglia and Oxford Region R & D Programme, UK. • Health Research Council, Auckland, New Zealand.	**Of relevant studies:** **Barrington 2003** Population: 50 women with menorrhagia refractory to medical treatment referred by GPs to gynaecology clinic in district hospital Setting: UK **Busfield/Brown 2006** population: 83 women complaining of HMB (mean age 41-43) Setting: NZ **Crosignani 1997** Population: 70 women aged 38-53 years, all referred for a hysterectomy because of heavy menstrual bleeding Setting: Italy **De Souza 2010**	2) Rollerball endometrial ablation undertaken by obstetrics and gynaecology specialist Duration: 12 months **Gupta 2015** 1) Levonorgestrel-releasing IUS 2) Usual medical treatment (mefenamic acid, tranexamic acid, norethindrone, combined oestrogen-progestogen or progesterone-only oral contraceptive pill, medroxyprogesterone acetate injection, chosen by the physician and	Satisfaction, Hb levels **Gupta 2015** Design: RCT, parallel group, multicentre Outcomes: Patient reported score on the Menorrhagia Multi-Attribute Scale (MMAS), General health-related quality of life (measured on SF36, EQ-5D descriptive system and EQ-5D visual analogue scale, Sexual activity scale (Sexual Activity Questionnaire), Further requirement for surgery, Adverse events **Hurskainen 2001** Design: RCT, multicentre, parallel group Outcomes: Quality of life measured by EQ-5D, Quality of life measured by Rand 36, Anxiety scale, Becks depression scale, McCoy sex scale • Costs, Hospital services (operations,	Outcome: Quality of life (HRQoL-4) **Shabaan 2011*** Self-rated health very good or excellent Baseline IUS group: 3/56 COC group: 3/56 At 12 months IUS group: 15/56 (ITT) COC group: 13/56 (ITT) No. of days in the previous 30 days feeling physically unwell Baseline IUS group: 7.4±2.7 (n=56) COC group: 7.5±2.6 (n=56)	Blinding of participants and personnel: high risk Blinding of outcome assessors: high risk Incomplete outcome data: unclear (more loss to follow up in TBA group) Selective reporting: low risk other bias: low risk **Crosignani 1997** Random sequence generation: low risk Allocation concealment: low risk Blinding of

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	Population: 58 Women recruited between January 2005 and March 2007, with mean age 42 and 44 years and baseline PBAC 542 and 420 Setting: Brazil **Ergun 2012** Population: 58 women with abnormal uterine bleeding which had not responded to medical treatment Setting: Turkey **Gupta 2015** Population: 571 women Setting: UK **Hurskainen 2001** Population: 236 women, aged 35 to 49 (mean age 43) referred by GPs or gynaecologists to 5 university hospitals.	patient according to contraceptive needs and desire to avoid hormone therapy) Women are permitted to change treatments, as well as between groups or could discontinue treatment - to replicate usual practice Duration: 6 months, 2, 5 and 10 years **Hurskainen 2001** 1) LNG IUS 2) Hysterectomy (either abdominal, vaginal or laparoscopy) **Irvine 1998** 1) Levonorgestrel-releasing (20 ug/day) intrauterine	inpatient days, procedures, outpatient visits), Menstrual blood loss (measured by alkaline haematin method), Satisfaction, Adverse effects (urinary symptoms, bone mineral density, cardiovascular risk factors, ovarian cysts, lower abdominal pain, back pain) **Irvine 1998** Design: RCT, single centre parallel group Outcomes: Menstrual blood loss (alkaline haematin method) at 3 months follow-up, Hb and serum Fe at pretreatment and 3 months (or sooner if premature termination), Participant symptom/side effect questionnaire at pretreatment, 1 and 3 months, Participant satisfaction categorised as liking treatment very well, well, moderately, poorly, Women were asked how their periods interfered with their quality of life both before and after treatment.,	At 12 months IUS group: 3.7±2.0 (n=48) COC group: 4.7±2.7 (n=47) No. of days in the previous 30 days feeling mentally unwell Baseline IUS group: 5.9±2.8 (n=56) COC group: 6.2±3.1 (n=56) At 12 months IUS group: 6.7±3.1 (n=48) COC group: 4.4±1.7 (n=47) No. of los days in the previous 30 days	participants and personnel: high risk Blinding of outcome assessors: high risk Incomplete outcome data: low risk Selective reporting: low risk other bias: low risk **De Souza 2010** Random sequence generation: low risk Allocation concealment: unclear Blinding of participants and personnel: high risk Blinding of

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	Setting: Finland **Irvine 1998** Population: 44 women aged 18-45 years all referred to specialist clinic complaining of regular heavy menstrual bleeding Setting: UK **Kaunitz 2010** Population: 165 Women with mean age 38 or 39 years Setting: USA, Canada and Brazil **Kittelsen 1998** Population: 60 women Setting: Norway **Abdel Malak 2006** Population: 60 Women scheduled to undergo	contraceptive system inserted within seven days of menstruation 2) Norethisterone 5 mg three times daily taken on Day 5-26 of the menstrual cycle for three cycles Duration: 3 months **Kaunitz 2010** 1) LNG IUS (placed within 7 days of the onset of menstruation) (only 1 attempt at replacement could be made 2) Medroxyprogesterone acetate (MPA) 10mg once per day for 10 consecutive days of the cycle	Proportion of women with amenorrhoea, Proportion of women with specified side effects, Withdrawal from treatment because of adverse events relating to treatment, Acceptability of treatment (willingness to continue). **Kaunitz 2010** Design: RCT, multicentre, parallel group Outcomes: Primary: Absolute change in menstrual blood loss from baseline to end of study, Proportion of women in which the treatment was successful (defined as menstrual blood loss < 80 mL at end of study and >/= 50% reduction in HMB from baseline), Adverse events **Kittelsen 1998** Design: RCT, single centre, parallel group	Baseline IUS group: 6.8±2.6 (n=56) COC group: 7.0±2.7 (n=56) At 12 months IUS group: 1.6±2.4 (n=48) COC group: 6.7±2.2 (n=47) Outcome: Withdrawal due to adverse events NMA outcome Outcome: Infection (Vaginitis) **Kaunitz 2010** IUS group: 9/80 Control group: 3/82 Outcome: Infection (urinary tract)	outcome assessors: high risk Incomplete outcome data: unclear Selective reporting: unclear other bias: low risk **Ergun 2012** Random sequence generation: unclear Allocation concealment: unclear Blinding of participants and personnel: high risk Blinding of outcome assessors: high risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	hysterectomy for treatment of excessive uterine bleeding with or without dysmenorrhoea, with mean age 46 and 47 years Setting: Egypt **Ozdegirmenci 2011** Population: 86 Women with clinical suspicion of adenomyosis complaining of menorrhagia and/or dysmenorrhoea and with confirmed adenomyosis, with mean age 44 and 46 years Setting: Turkey **Reid 2005** Population: 51 women. Women were either referred by GPs or self referred after ads in the local press Setting: UK	starting on day Follow-up 3, 6 months **Kittelsen 1998** 1) Levonorgestrel-releasing intrauterine system (LNG IUS) (Mirena) inserted within 7 days of the start of menstruation. 2) Transcervical resection of the endometrium (TCRE) performed regardless of day of menstrual cycle. Duration: 20 months, 3 years. **Abdel Malak 2006** 1) LNG IUS inserted following menstruation	Outcomes: PBAC score 12, 24 and 36 months after treatment, Menstrual pain, Adverse events, Failure of treatment (further surgery or removal of IUS), Discontinuation from study **Abdel Malak 2006** Design: RCT, single centre, parallel group Outcomes: Women's decision to continue treatment (satisfaction), Menstrual blood loss - amenorrhoea or hypomenorrhoea, PBAC score at 12 months, Treatment success (defined as PBAC score < 75 at 12 months, Treatment failure (PBAC score > 75, removal of the LNG IUS in the LNG IUS group or resurgery for any reason in the ER group), Adverse events, Quality of life (EQ VAS score) **Ozdegirmenci 2011**	**Kaunitz 2010** IUS group: 6/80 Control group: 3/82 Outcome: Expulsion (partial or complete) **Kaunitz 2010*** IUS group: 4/80 Control group: N/A Outcome: Quality of life (Menorrhagia Multi-Attribut Scale, MMAS), summary score, mean±SD **Gupta 2015*** Baseline IUS group: 42.5±20.5 (n=280) Control group: 39.2±21.3 (n=269) At 6 months	Incomplete outcome data: high risk (substantial drop out with no reason given) Selective reporting: unclear other bias: unclear **Gupta 2015** Random sequence generation: low risk Allocation concealment: low risk Blinding of participants and personnel: high risk Blinding of outcome assessors: high risk Incomplete

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	Sayed 2011 Population: 58 Participants recruited from outpatient gynaecology clinics of Assiut University, mean age 37 years Setting: Egypt **Sesti 2012** Population: 72 women-Participants were women with HMB unresponsive to medical treatment with mean age 47 years Setting: Italy **Shabaan 2011** Population: 112 women recruited from gynaecology outpatient clinics of Assiut University Hospital, with mean age 39 years Setting: Egypt **Shaw 2007**	2) Endometrial resection (ER) under general anaesthesia **Ozdegirmenci 2011** 1) LNG IUS 2) Hysterectomy (abdominal) **Reid 2005** 1) Levonorgestrel-releasing intrauterine system 2) Mefenamic acid 500 mg 3 times daily for first 4 days of cycle. Duration: 3 cycles and 6 cycles **Shabaan 2011** 1) Levonorgestrel-releasing	Design: RCT, single centre, parallel group Outcomes: Quality of life (WHO Quality of Life - Short Form, Turkish Version (WHOQOL-BREF TR) at 12 months, Oligomenorrhoea, Side effects, Hb levels **Reid 2005** Design: RCT, single centre, parallel group Outcomes: HMB (measured by alkaline haematin method), Total menstrual fluid loss (TMFL), PBAC score. **Sayed 2011** Design: RCT, single centre, parallel group Outcomes: Reduction of HMB (%) (PBAC and alkaline haematin assessment) at 12 months, Hb and ferritin levels, Quality of life (HRQoL),	IUS group: 74.9±22.5 (n=222) Control group: 61.0±25.1 (n=212) At 12 months IUS group: 78.8±25.0 (n=218) Control group: 61.5±26.3 (n=216) At 2 years IUS group: 81.0±23.2 (n=225) Control group: 66.8±28.5 (n=208) At 5 years IUS group: 83.1 +24.4 (n=208) Control group: 87.1 +22.1 (n=216) **Comparison: IUS**	outcome data: low risk Selective reporting: low risk other bias: low risk **Hurskainen 2001** Random sequence generation: unclear Allocation concealment: low risk Blinding of participants and personnel: high risk Blinding of outcome assessors: high risk Incomplete outcome data: low risk Selective reporting:

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	Population: 66 Women with idiopathic menorrhagia in whom prior medical oral treatment had failed: mean age 42 or 43 years Setting: UK **Soysal 2002** Population: 72 Patients with mean age 44 years recruited from university medical centre. Setting: Turkey **Tam 2006** Population: 44 women with HMB , mean age 44-45 Setting: Hong Kong **Inclusion criteria** **Barrington 2003** NR in SR **Busfield/Brown 2006**	intrauterine system 2) Low-dose combined oral contraceptives 30 µg of ethinyl estradiol and 150 µg levonorgestrel **Shaw 2007** 1) LNG-IUS (Mirena) inserted in the uterine cavity just following menstruation 2) Thermal balloon ablation (Menotreat) - undertaken under general anaesthesia post menstruation without routine pretreatment **Soysal 2002** 1) LNG-IUS inserted in the uterine cavity within first seven	Treatment failure **Sesti 2012** Design: RCT, single centre, parallel-group Outcomes: PBAC, Qualiy of life (SF-36), Improvement in bleeding patterns, Intensity of postoperative pain (VAS scale 0 to 100 in categories), Early postoperative complications requiring readmission Follow-up at 3, 6, 12 and 24 months **Shabaan 2011** Design: RCT, single-centre, parallel group Outcomes: Reduction of HMB at 12 months (alkaline haematin and PBAC), Treatment failure, Hb and ferritin levels, Quality of life (HRQoL questionnaire) **Shaw 2007** Design: RCT, single centre, parallel group	**versus endometrial ablation** Outcome: PBAC NMA outcome Outcome: Satisfaction NMA outcome Outcome: Quality of Life (SF-36) NMA outcome Outcome: Infection (endometritis) **Kittelsen 1998** IUS group: 3/19 Ablation group: 0/22 Outcome: Infection (myometritis) **Kittelsen 1998** IUS group: 0/19 Ablation group: 1/22	low risk other bias: low risk **Irvine 1998** Random sequence generation: low risk Allocation concealment: low risk Blinding of participants and personnel: high risk Blinding of outcome assessors: high risk Incomplete outcome data: unclear risk Selective reporting: low risk other bias: low risk **Kaunitz 2010**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	completed family; age 25 to 50 years; regular cycle of menstruation, self described HMB **Crosignani 1997** > 80 mL/cycle loss (as measured by > 100 points on pictorial charts) . Negative smear within 12 months. Endometrial pathology excluded by transvaginal ultrasound, diagnostic hysteroscopy and endometrial biopsy. Uterine size less than 8 weeks. **De Souza 2010** clinical HMB refractory to medical treatment (OC, HT, NSAIDs), 3-month washout period, regular menstrual cycles, age > 35 years, menstrual blood loss > 80 mL (as measured by PBAC), negative pregnancy	days of menstruation 2) Thermal balloon ablation with 2 months of pre-treatment with GnRH analogues to thin the endometrium) **Tam 2006** 1) LNG-IUS inserted following diagnostic hysteroscopy 2) Thermal balloon endometrial ablation (Thermachoice) performed 6 weeks after thinning with GnRH analogue or oral danazol	Outcomes: PBAC scores at 12 months, PBAC scores at 3, 6 and 9 months, Changes in Hb and ferritin concentrations between baseline and 6 months, Patient satisfaction, Continuance of the method at 2 years, Hysterectomy rates at 2 years, Teatment failure (additional medical treatment required, expulsion or removal of LNG IUS or total abdominal hysterectomy) **Soysal 2002** Design: RCT, single-centre, parallel group Outcomes: Reduction in menstrual bleeding; increase in Hb, Quality of life (SF36, HADS; Side effects (including pain), Patient satisfaction. **Tam 2006** Design: RCT, single centre, parallel group	Outcome: Infection (vaginitis) **Abdel Malak 2006** IUS group: 4/30 Ablation group: 2/30 Outcome: Expulsion **Tam 2006*** IUS group: 2/18 TBA: N/A **Comparison: IUS versus hysterectomy** Outcome: PBAC NMA outcome Outcome: Quality of life NMA outcome Outcome: Quality of life at 10 years	Random sequence generation: low risk Allocation concealment: low risk Blinding of participants and personnel: high risk Blinding of outcome assessors: high risk Incomplete outcome data: low risk Selective reporting: low risk other bias: low risk **Kittelsen 1998** Random sequence generation: low risk Allocation

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	test, uterine volume < 200 mL (as measuredbytransvaginal sonogram), negative PAP smear within pastyear,nointracavity abnormalities, pelvic inflammatory disease, suspected endometrial pathology, abnormal endometrial histology, previous endometrial resection and ablation, or any other pathology for which hysterectomy would be appropriate. Women were also required to have completed their families **Ergun 2012** > 35 years of age, regular menstrual cycle, score of 100 on PBAC **Gupta 2015** aged between 25 and 50 years, presenting to primary care physicians with		Outcomes: Menstrual bleeding (amenorrhoea, hypomenorrhoea and normal rates of bleeding); Side effects; HB and iron status; Health status function (SF36)	**Hurskainen 2001 (data from Heliovaara-Peippo 2013)*** EQ-5D change from baseline to 10-year follow-up, mean (95% CI) (scale range 0-1) IUS group: -0.01 (-0.05 to 0.03) (n=110) Hysterectomy group: -0.01 (-0.05 to 0.03) (n=111) p=0.94 RAND-36 change from baseline to 10-year follow-up, mean (95% CI) (scale range 0-100) General health IUS group: -2.3 (-5.8 to 1.2) (n=110) Hysterectomy group: -4.5 (-8.3 to -0.8) (n=111)	concealment: low risk Blinding of participants and personnel: high risk Blinding of outcome assessors: high risk Incomplete outcome data: high risk (11/30 (36.7%) in LNG group had discontinued treatment by 36 months. 7/29 (24. 1%) in TCRE group discontinued (4 because of treatment failure) in the study by 36 months) Selective reporting: low risk other bias: low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	menorrhagia involving at least 3 consecutive menstrual cycles **Hurskainen 2001** menorrhagia, still menstruating, family completed, eligible for hysterectomy **Irvine 1998** >80mL/cycleloss(asmeasuredbyalkalinehaematinmethod),parous (1 or more children), normal pelvic examination, negative cervical cytology, regular menstrual cycle, good general health, uterine cavity sound length less than 10 cm. **Kaunitz 2010** parous women aged 18 yearsor more with idiopathic heavy menstrual bleeding (menstrual blood			p=0.39 Physical functioning IUS group: -3.4 (-7.5 to 0.8) (n=110) Hysterectomy group: -3.8 (-8.0 to 0.4) (n=111) p=0.88 Emotional well-being IUS group: 5.7 (1.3 to 10.1) (n=110) Hysterectomy group: 3.2 (-0.7 to 7.0) (n=111) p=0.40 Social functioning IUS group: 7.9 (2.3 to 13.4) (n=110) Hysterectomy group: 1.8 (-3.3 to 7.0) (n=111) p=0.12	**Abdel Malak 2006** Random sequence generation: unclear Allocation concealment: unclear Blinding of participants and personnel: high risk Blinding of outcome assessors: high risk Incomplete outcome data: unclear Selective reporting: low risk other bias: unclear (There was a significant difference in parity status between the

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	loss >/= 80 mL per cycle (assessed by alkaline haematin method) desiring intrauterine contraception and willing to use barrier contraception **Kittelsen 1998** premenopausal (FSH > 40 mLU/mL and 17B oestradiol < 0.2 nmol/ mL), score of > 100 on PBAC with a regular uterine cavity **Abdel Malak 2006** age between 40 and 50 years, regular uterine cavity < 10 cm in length as measured by ultrasound, no wish for further pregnancy **Ozdegirmenci 2011** not specifically reported- women with adenomyosis by sonogram and MRI **Reid 2005**			Energy IUS group: 6.0 (1.7 to 10.3) (n=110) Hysterectomy group: 5.3 (0.6 to 10.0) (n=111) p=0.83 Pain IUS group: 4.4 (-0.4 to 9.2) (n=110) Hysterectomy group: 4.0 (-2.1 to 10.0) (n=111) p=0.91 Physical role functioning IUS group: 8.2 (-0.53 to 16.9) (n=110) Hysterectomy group: 3.2 (-5.7 to 12.2) (n=111) p=0.40 Emotional role functioning	2 randomised groups) **Ozdegirmenci 2011** Random sequence generation: low risk Allocation concealment: unclear Blinding of participants and personnel: high risk Blinding of outcome assessors: high risk Incomplete outcome data: High risk (Substantial lost to follow-up from the hysterectomy group (26%) and none from the LNG

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	Aged 18 to 47 years; with good general health; regular ovulatory menstrual cycles 21-35 days and HMB measured by alkaline haematin method >/= 80mL. **Sayed 2011** heavy menstrual bleeding, requested contraception, regular cycle, between 20 and 50 years of age at initial assessment, lived sufficiently close to hospital for follow-up, fibroid(s) detected from pelvic ultrasound **Sesti 2012** presence of HMB, reproductive age 35 to 50 years, completed family, failedappropriate first line oral medical therapy, normal PAP smear, no pelvic pathology at			IUS group: 9.1 (-1.4 to 19.6) (n=110) Hysterectomy group: 4.9 (-5.1 to 14.1) (n=111) p=0.57 Outcome: Menstrual blood loss in ml (AH method) **Hurskainen 2001*** Baseline, mean (SD) IUS group: 130 (116) (n=119) Hysterectomy group: 128 (116) (n=117) At 1 year follow-up, mean (SD) IUS group: 13 (23.4) (n=25) Hysterectomy group: N/A Outcome: Urge urinary	IUS group) Selective reporting: low risk other bias: low risk **Reid 2005** Random sequence generation: low risk Allocation concealment: low risk Blinding of participants and personnel: high risk Blinding of outcome assessors: high risk Incomplete outcome data: low risk Selective reporting: low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	ultrasound, normal endometrial biopsy, PBAC >/= 100 (average of 2 consecutive cycles) **Shabaan 2011** self described HMB, requested contraception, 20 to 50 years old at initial assessment, regular cycle, living close to hospital for follow-up **Shaw 2007** previous LNG IUS, previous endometrial resection/ablation, abnormal uterine bleeding not fully investigated, other pathology where hysterectomy was indicated, submucosal fibroid identified on scan or hysteroscopy, uterine cavity < 7 cm or > 11 cm **Tam 2006**			incontinence **Hurskainen 2001** IUS group: 11/68 Hysterectomy group: 34/153 Outcome: stress urinary incontinence **Hurskainen 2001** IUS group: 23/68 Hysterectomy group: 74/153 Outcome: Wound infection **Hurskainen 2001** IUS group: 2/117 Hysterectomy group: 12/115 Outcome: Infected pelvic haematoma **Hurskainen 2001**	other bias: unclear (no table presented of baseline characteristics) **Sayed 2011** Random sequence generation: low risk Allocation concealment: low risk Blinding of participants and personnel: high risk Blinding of outcome assessors: high risk Incomplete outcome data: high risk (Substantial loss to follow-up and treatment failure- bleeding outcomes only

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	uterus >10 weeks gravid uterine size, presence of submucosal fibroids or endometrial polyps, any contraindications for progestogen use or an intrauterine device, evidence of cervical or endometrial malignancy **Exclusion criteria** **Barrington 2003** Cavity < 12 cm, subserous fibroids, malignant or pre-malignant pathology (from endometrial biopsy) **Busfield/Brown 2006** fibroids, polyps, FSH > 40, endometrial pathology, previous endometrial sx, bleeding, suggested endometriosis			IUS group: 9/117 Hysterectomy group: 6/115 Outcome: Peritonitis **Hurskainen 2001** IUS group: 0/117 Hysterectomy group: 1/115 Outcome: Bladder perforation **Hurskainen 2001** IUS group: 0/117 Hysterectomy group: 3/115 Outcome: Bowel perforation **Hurskainen 2001** IUS group: 0/117 Hysterectomy group:	measured in 20/58 (PBAC) and 22/58 (alkaline haematin)) Selective reporting: low risk other bias: low risk **Sesti 2012** Random sequence generation: low risk Allocation concealment: low risk Blinding of participants and personnel: high risk Blinding of outcome assessors: high risk Incomplete outcome data: low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	Crosignani 1997 Abnormal uterine cavity, fibroids greater than 3 cm, or atypical hyperplasia. Pregnancy, breast feeding or uncertainty about future fertility. Recent use of oestrogens or progestogens (within 3 months), GnRH (within 6 months), any medication affecting menstrual blood loss, concomitant illness, Hb < 10 g/dL **De Souza 2010** No additional reported **Ergun 2012** ongoing pregnancy, pelvic infection, abnormality in the uterus, uterine cavity and/or suspicious endometrial histology (screened by TVUS), abnormal cervical or endometrial histology,			1/115 Outcome: Thromboembolic disease **Hurskainen 2001** IUS group: 1/117 Hysterectomy group: 0/115 Outcome: Vesicovaginal fistula **Hurskainen 2001** IUS group: 0/117 Hysterectomy group: 1/115 Outcome: Ureter lesion **Hurskainen 2001** IUS group: 0/117 Hysterectomy group: 1/115	Selective reporting: low risk other bias: low risk **Shabaan 2011** Random sequence generation: low risk Allocation concealment: low risk Blinding of participants and personnel: high risk Blinding of outcome assessors: high risk Incomplete outcome data: high risk (Substantial loss to follow-up and bleeding outcomes measured in only

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	pathology that might require a hysterectomy, contraindication to administration of anaesthetic agents, desire to preserve fertility **Gupta 2015** intention to become pregnant over the next 5 years, taking hormone therapy or tamoxifen, intermenstrual bleeding, post coital bleeding, findings suggestive of fibroids or other disorders, contraindications to or a preference for either the LNG IUS or usual medical treatments, heavy irregular bleeding **Hurskainen 2001** submucosal fibroids; endometrial polyps; ovarian tumours or cysts; cervical disease; urinary or bowel symptoms or pain due to			*Data extracted from original paper by the NGA technical team.	64/112 at 12 months (because of treatment failure)) Selective reporting: low risk other bias: low risk **Shaw 2007** Random sequence generation: low risk Allocation concealment: low risk Blinding of participants and personnel: high risk Blinding of outcome assessors: high risk Incomplete outcome data: high risk (Substantial

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	fibroids; lack of indication for hysterectomy; history of cancer; menopause; severe depression; metrorrhagiaas main complaint; previous treatment failure with LNG IUS; severeacne; uterine malformation **Irvine 1998** abnormal pelvic examination, recent use of oestrogens, progestogens or anticoagulants (within 3 months), injectable hormones for contraception (within 12 months) **Kaunitz 2010** changes in menstrual irregularity, hot flushes, sleeping disorders, changes in mood within the 3 months before the study, breastfeeding, congenital or acquired uterine abnormality, including fibroids if they distorted the				attrition from trial by 12 months) Selective reporting: low risk other bias: low risk **Soysal 2002** Random sequence generation: low risk Allocation concealment: low risk Blinding of participants and personnel: high risk Blinding of outcome assessors: high risk Incomplete outcome data: low risk Selective reporting:

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	uterine cavity or cervical canal, history of organic causes of abnormal uterine bleeding, use of LNG IUS or a copper IUS during the 30 days before the study, history of vascular or coagulation disorders, concomitant use ofmedication or presenceofanunderlying disease/condition knowntoaffectthemetabolism orpharmacokineticsofthestudy medication, bodymass index > 35k g/m2 **Kittelsen 1998** hormone treatment in past 3 months, previous history of DVT, thromboembolism or liver disease, uncertain about future wish for pregnancy, pregnancy or breastfeeding, fibroids, endometrial pathology, congenital or acquired				low risk other bias: low risk **Tam 2006** Random sequence generation: low risk Allocation concealment: low risk Blinding of participants and personnel: high risk Blinding of outcome assessors: high risk Incomplete outcome data: high risk Selective reporting: unclear other bias: low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	uterine anomaly, current infection or PID within last 6 months, endometriosis or adenomyosis **Abdel Malak 2006** one fibroid > 3cm in diameter or > 3 uterine fibroids as assessed by ultrasonography, history or current clinical evidence or suspicion of malignancy or current liver disease, adnexal tumours or cysts or pelvic inflammatory disease within the previous 12 months **Ozdegirmenci 2011** endometrial pathology, submucosal fibroids, intramural or subserous fibroids > 2 cm, postmenopausal status, pelvic inflammatory disease, malignancy or suspicion of malignancy, thromboembolism, desire to				**Other information** 2 studies in SR not relevant to review question: Cameron 1987 not relevant to review due to short follow-up time and unlicensed (old) IUS; Kilic 2009 not relevant population (Women taking anticoagulant therapy after cardiac valve replacement);

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	become pregnant, cardiac or hepatic disease, use of oral progestogen during previous 3 months, contraindications to MRI **Reid 2005** Undiagnosed abnormal bleeding; anovulatory; submucosal fibroids or fibroids>5cm3intotalvolume (US);uterinesound >10cm;abnormal cervical cytology; untreated hypertension; abnormal thyroid or liver function tests; asthma; IUCD in situ; previous treatment for menorrhagia; hormonal contraceptives in previous 4 months **Sayed 2011** pregnancy, history of ectopic pregnancy, puerperal sepsis, pelvic inflammatory disease, evidence of defective				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	coagulation, abnormalities on ultrasound (including submucosal fibroids of any size distorting the cavity of the uterus or intramural or subserous fibroids > 5 cm in diameter), history of malignancy or evidence of hyperplasiaintheendometrial biopsy, incidental adnexal abnormality onultrasound, previous endometrial ablation/resection, uninvestigated postcoital bleeding, untreated abnormal cervical cytology, contraindication to COCs **Sesti 2012** previous endometrial resection/ablation, previous insertion of LNG IUS, any uterine pathology on scan or hysteroscopy, any pathology where hysterectomy was indicated, not fully investigated abnormal				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	uterine bleeding, postmenopausal bleeding **Shabaan 2011** pregnancy, history of ectopic pregnancy, puerperal sepsis, pelvic inflammatory disease, evidenceof defective coagulation, history or evidence of malignancy or hyperplasia in the endometrial biopsy, incidental adnexal abnormality on ultrasound, contraindications to COC, previous endometrial ablation/resection, uninvestigated postcoital bleeding, untreated abnormal cervical cytology, fibroids of any size **Shaw 2007** previous LNG IUS, previous endometrial resection/ablation, abnormal uterine bleeding				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	not fully investigated, other pathology where hysterectomy was indicated, submucosal fibroid identified on scan or hysteroscopy, uterine cavity < 7 cm or > 11 cm **Soysal 2002** congenital and acquired uterine abnormalities; PID, breast cancer; pre malignant or malignant uterine disease; concomitant uterine disorders except iron deficiency anaemia; uterine volume > 8 weeks pregnancy or > 190 mL; pathologies (intramural or subserous fibroids > 2 cm); abnormalities on hysteroscopy **Tam 2006** uterus >10 weeks gravid uterine size, presence of submucosal fibroids or				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	endometrial polyps, any contraindications for progestogen use or an intrauterine device, evidence of cervical or endometrial malignancy				
Full citation Lethaby, Anne, Irvine, Gill A, Cameron, Iain T, Cyclical progestogens for heavy menstrual bleeding, Cochrane Database of Systematic Reviews,	**Sample size** **Irvine 1998** N= 44 **Characteristics** **Irvine 1998** Population: 44 Patients aged 30 to 45 years with a complaint of heavy regular pe r iods recruited from gynaecology outpatient clinics in the UK **Inclusion criteria** **Irvine 1998** parous, aged 18 to 45	**Interventions** **Irvine 1998** 1) Norethisterone (NET) 5mg daily from day 5 to 26 of the cycle. 2) Levonorgestrel intrauterine system (Mirena) fitted into the uterus within 7 days of the onset of a menstrual period. Duration: 3 menstrual cycles.	**Details** **Irvine 1998** Design: RCT, single centre, parallel-group Outcomes: MBL (alkaline haematin method); proportion with no improvement in qual ity of life; proportion who found the treatment unacceptable; Adverse events	**Results** **Comparison: Progestagen therapy vs. LNG-IUS** Outcome: Menstrual blood loss (A-H method) NMA outcome	**Limitations** **Quality of Cochrane SR:** Assessed using AMSTAR checklist. Total score: 11/11 **Quality of individual studies:** Risk of bias assessment taken from Cochrane SR (Cochrane risk of bias tool). **Bonduelle 1991**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
2008 **Ref Id** 550299 **Country/ies where the study was carried out** **Study type** Cochrane review **Aim of the study** The primary objective of this review was to investigate the effectivene	years, in good health, regular menstrual cycle, normal pelvic exam and uterine measurement <10 cm, negative cervical cytology and MBL>80 ml. **Exclusion criteria** **Irvine 1998** treatment with steroid hormones or anticoagulants in the previous 3 months, treatment with injectable hormones for contraception in the previous 12 months				Random sequence generation: unclear Allocation concealment: unclear Blinding: high risk Incomplete outcome data: unclear (no intention-to-treat analysis) Selective reporting: unclear Other bias: low risk **Higham 1993** Random sequence generation: high risk (sequential order) Allocation concealment: low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
ss of oral progestogen therapy taken either during the luteal phase or for a longer course of 21 days in achieving a reduction in menstrual blood loss in women of reproductive years with heavy menstrual bleeding (HMB). **Study dates**					Blinding: high risk Incomplete outcome data: low risk (intention-to-treat analysis) Selective reporting: unclear Other bias: low risk **Irvine 1998** Random sequence generation: low risk Allocation concealment: low risk Blinding: high risk Incomplete outcome data: low risk (intention-to-treat analysis) Selective reporting: unclear

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Search up to April 2007 **Source of funding** Internal sources • Department of Obstetrics and Gynaecology, University of Auckland, Auckland, New Zealand. External sources • Health Research					Other bias: low risk **Other information** 4 studies excluded due to short treatment times (Cameron 1987, Cameron 1990, Preston 1995, Pinion 1994). Buyru 1995 excluded as Turkish language. Bonduelle 1991 and Higham 1993 relevant to NMA only (Danazol)

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Council, Auckland, New Zealand.					
Full citation Lethaby,Anne, Penninx,Josien, Hickey,Martha, Garry,Ray, Marjoribanks,Jane, Endometrial resection and ablation techniques for heavy menstrual bleeding, Cochrane	**Sample size** **Meyer 1998** N=275 randomised **van Zon-Raebelink 2003** N=139 randomised **Duleba 2003** N=279 randomised **Characteristics** **Meyer 1998** Population: 275 women aged 29 to 50 years recruited from 12	**Interventions** **Meyer 1998** 1) Rollerball ablation 2) Balloon ablation (Thermachoice) Duration: 12 months follow up **van Zon-Rabelink 2003** 1) RBE hysteroscopic rollerball electrocoagulation (n=62) 2) UBT non-hysteroscopic uterine balloon	**Details** **Meyer 1998** Design: RCT, multicentre, parallel group Outcomes: Satisfaction rate; Improvement in dysmenorrhoea symptoms; Proportion with PMS after treatment; Inability to work; PBAC score; Complication rate; Duration of surgery **van Zon-Rabelink 2003** Design: RCT, single centre, parallel group Outcomes: Technical safety aspects; reduction in menstrual bleeding; success rate (PBAC<185); satisfaction	**Results** **Comparison: 1st generation vs. 2nd generation ablation** Outcome: PBAC NMA outcome Outcome: PBAC score ≤75 at 12 months follow-up **Duleba 2003*** Cryoablation group: 132/156 Rollerball group: 64/72 Outcome: Satisfaction NMA outcome	**Limitations** **Quality of the SR:** Assessed using AMSTAR checklist. Total score: 11/11. **Quality of individual studies:** Extracted from the Cochrane SR (Cochrane risk of bias tool). **Abbott 2003** Random sequence generation: low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Database of Systematic Reviews, -, 2013 **Ref Id** 327783 **Country/ies where the study was carried out** **Study type** Cochrane Systematic Review **Aim of the study** To compare the efficacy,	investigative centres setting: US and Canada **van Zon-Raebelink 2003** Population: 139 women with unreported ages recruited from a teaching hospital Setting: Netherlands **Duleba 2003** Population: 279 women aged 30-50 years Setting: university and private medical centres in the USA **Inclusion criteria** **Meyer 1998** 30 years or more and premenopausal; normal Pap smears; normal endometrial biopsies within last 6 months; history of 3 months of excessive uterine	thermal ablation ThermachoiceTM (n=77) **Duleba 2003** 1) Endometrial cryoablation (n=193) 2) Rollerball electroablation (n=86)	**Duleba 2003** Design: RCT, multicentre, parallel group Outcomes: Menstrual diaries 1 cycle before and 12months after; PBAC, bleeding, pain,mood, PMS; QOL - Dartmouth COOP assessment questionnaire, anaesthesia, adverse outcomes, satisfaction; those randomised to cryoablation had significantly worse menorrhagia	Outcome: endometritis **Meyer 1998** Balloon group: 3/125 Rollerball group: 1/114 **Corson 2001*** Hydrotherm endometrial ablation group: 2/184 Rollerball group: 1/85 Outcome: Infection **Duleba 2003*** Cryoablation group: 0/193 Rollerball group: 1/86 Outcome: UTI **Meyer 1998**	Allocation concealment: low risk Blinding: low risk Incomplete outcome data: low risk Selective reporting: low risk Other bias: unclear (medical equipment company provided funding) **Bhattacharya 1997** Random sequence generation: low risk Allocation concealment: low risk Blinding: high risk Incomplete

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
safety and acceptability of of endometrial destruction techniques to reduce heavy menstrual bleeding (HMB) in premenopausal women. **Study dates** Searches complete up to June 2013 **Source of funding** External	bleeding (PBAC score >/= 150); ineffective medical therapy; uterine cavity normal (by either hysterosalpingography, hysteroscopy or TSS) and with a r ange between 4 and 10 cm; no desire for future fertility; willing to continue current contraception **van Zon-Rabelink 2003** menstrual blood loss score = 185 pt in 2 periods due to dysfunctional uterine bleeding according to ultrasound and diagnostic hysteroscopy **Duleba 2003** menorrhagia due to benign causes, good general health, documented history of excessive uterine bleeding for at least 3 months, failed traditional therapy, did			Balloon group: 0/125 Rollerball group: 1/114 **Corson 2001*** Hydrotherm endometrial ablation group: 5/184 Rollerball group: 2/85 **Duleba 2003*** Cryoablation group: 0/193 Rollerball group: 1/86 Outcome: Cervical laceration **Corson 2001*** Hydrotherm endometrial ablation group: 0/184 Rollerball group: 2/85 Outcome: Uterine perforation **Duleba 2003***	outcome data: high risk (different numbers of participants provided data for different outcomes) Selective reporting: low risk Other bias: unclear (recruitment occurred over 2 different time periods- 2 groups differed in baseline characteristics) **Bongers 2004** Random sequence generation: low risk Allocation concealment: low risk Blinding: low risk Incomplete outcome data: low

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
sources • UK NHS, Not specified. The update in 2009 was funded by Dept of Health (England) Incentive Scheme 2008	not desire future fertility, PBAC>150 **Exclusion criteria** **Meyer 1998** Exclusion criteria: submucosal fibroids; suspected genital tract infection or malignancy; previous endometrial ablation **van Zon-Rabelink 2003** not reported **Duleba 2003** uterine volume greater than 300 ml, uterine cavity sounding more than 10 cm, clotting deficit or bleeding disorders, active pelvic inflammatory disease, abnormal cervical cytology within 1 year; history of			Cryoablation group: 0/193 Rollerball group: 1/86 *Data extracted from the original paper by the NGA technical team.	risk Selective reporting: low risk Other bias: unclear (medical equipment company provided funding) **Brun 2006** Random sequence generation: low risk Allocation concealment: low risk Blinding: high risk Incomplete outcome data: high risk (withdrawals unbalanced between groups) Selective reporting: low risk Other bias: high

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	gynaecologic malignancy within 5 years, intramural myomas>2 cm, submucosal myomas or endometrial polyps; septate uterus; previous endometrial ablation or other surgery in which thinning of uterine wall may occur; malignant pathology or hyperplasia; pregnancy				risk (differences in baseline menstrual blood loss between groups) **Clark 2011** Random sequence generation: low risk Allocation concealment: low risk Blinding: unclear risk (women not told of allocation but unclear how it was maintained) Incomplete outcome data: high risk Selective reporting: low risk Other bias: low risk **Cooper 1999**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
					Random sequence generation: low risk Allocation concealment: low risk Blinding: high risk Incomplete outcome data: low risk Selective reporting: low risk Other bias: unclear (medical equipment company provided funding) **Cooper 2002** Random sequence generation: low risk Allocation concealment: unclear Blinding: high risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
					Incomplete outcome data: unclear risk Selective reporting: low risk Other bias: unclear (medical equipment company provided funding) **Cooper 2004** Random sequence generation: low risk Allocation concealment: unclear Blinding: high risk Incomplete outcome data: low risk Selective reporting: low risk Other bias: unclear

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
					(authors employed by medical equipment company) **Corson 2000** Random sequence generation: low risk Allocation concealment: low risk Blinding: high risk Incomplete outcome data: unclear (reasons for loss of follow up not given) Selective reporting: low risk Other bias: unclear (medical equipment company provided funding) **Corson 2001**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
					Random sequence generation: low risk Allocation concealment: unclear Blinding: high risk Incomplete outcome data: unclear (loss of follow up uneven between groups) Selective reporting: low risk Other bias: unclear (medical equipment company provided funding) **Duleba 2003** Random sequence generation: unclear Allocation concealment:

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
					unclear Blinding: high risk Incomplete outcome data: unclear (reasons for loss of follow up not given) Selective reporting: low risk Other bias: unclear (differences in PBAC scores at baseline) **Hawe 2003** Random sequence generation: low risk Allocation concealment: low risk Blinding: low risk Incomplete outcome data: low

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
					risk Selective reporting: low risk Other bias: unclear (medical equipment company provided funding) **McClure 1992** Random sequence generation: unclear Allocation concealment: unclear Blinding: high risk Incomplete outcome data: low risk Selective reporting: low risk Other bias: low risk **Meyer 1998**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
					Random sequence generation: low risk Allocation concealment: unclear Blinding: high risk Incomplete outcome data: low risk Selective reporting: low risk Other bias: unclear risk (funding provided by medical company) **Pellicano 2002** Random sequence generation: low risk Allocation concealment: unclear Blinding: high risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
					Incomplete outcome data: unclear Selective reporting: low risk Other bias: unclear risk (funding provided by medical company) **Penninx 2010** Random sequence generation: low risk Allocation concealment: low risk Blinding: Unclear risk (patients blinded; surgeons not blinded.) Incomplete outcome data: low risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
					Selective reporting: unclear Other bias: low risk **Perino 2004** Random sequence generation: low risk Allocation concealment: unclear Blinding: high risk Incomplete outcome data: low risk Selective reporting: low risk Other bias: low risk **Sambrook 2009** Random sequence generation: low risk Allocation

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
					concealment: low risk Blinding: Unclear risk (patients blinded; investigators not blinded.) Incomplete outcome data: low risk Selective reporting: low risk Other bias: low risk **van Zon-Rabelink 2003** Random sequence generation: unclear Allocation concealment: unclear Blinding: high risk Incomplete

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
					outcome data: low risk Selective reporting: low risk Other bias: unclear (numbers in randomized groups differed) **Vercellini 1999** Random sequence generation: low risk Allocation concealment: low risk Blinding: high risk Incomplete outcome data: low risk Selective reporting: low risk Other bias: unclear (numbers in

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
					randomized groups differed) **Other information** Studies outside protocol: Onoglu 2007 (quasi-experimental); Romer 1998 (German language); Thabet 2010 (2 types of curettes compared); Boujida 2002 (no outcomes for NMA); Soysal 2001 (no relevant outcomes) Studies relevant to NMA only (comparison or intervention not of interest to review): Abbott 2003, Bhattacharya 1997, Bongers 2004, Brun 2006, Clark 2011, Cooper

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
					1999, Cooper 2002, Cooper 2004, Corson 2000, Corson 2001, Hawe 2003, McClure 1992, Pellicano 2002, Penninx 2010, Perino 2004, Sambrook 2009, Vercellini 1999
Full citation Marjoribanks, Jane, Lethaby, Anne, Farquhar, Cindy, Surgery versus medical therapy for heavy menstrual	**Sample size** For **Barrington 2003, Crosignani 1997, de Souza 2010, Ergun 2012, Hurskainen 2001, Malak 2006, Sesti 2012, Shaw 2007, Soysal 2002** please see Lethaby 2015 Cochrane systematic review. **Ghazizadeh 2014** N=110 randomised	**Interventions** **Ghazizadeh 2014** 1) hysteroscopic endometrial resection. Endometrial resection was done by monopolar loop resection with a depth of 3 mm to 5 mm, and rollerball resection with superficial	**Details** **Ghazizadeh 2014** Design: RCT Outcomes: Treatment success (according to decreased blood loss and less interaction between bleeding and normal activity) - measure unclear, data not used in analysis, Complications (data not used as totals unclear), Resurgery, Satisfaction	**Results** **Comparison: Surgery versus oral medication** Outcome: HRQoL SF-36 **Cooper 1997** Physical function: Surgical mean change vs Medical mean change 4 months: + 10.16 (SD 16. 51) vs + 4.84 (SD 16.72) - P value < 0.05	**Limitations** **Quality of SR:** Assessed using AMSTAR checklist. Total score: 11/11 **Quality of individual studies:** Risk of bias taken from the Cochrane

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
bleeding, Cochrane Database of Systematic Reviews, 2016 **Ref Id** 447030 **Country/ies where the study was carried out** **Study type** Cochrane systematic review **Aim of the study** To compare	**Istre 1998** N=60 randomised **Kupperman 2004** N=63 randomised **Cooper 1997** N=187 randomised **Characteristics** **Barrington 2003, Crosignani 1997, de Souza 2010, Ergun 2012, Hurskainen 2001, Malak 2006, Sesti 2012, Shaw 2007, Soysal 2002** See Lethaby 2015 **Ghazizadeh 2014** Population: 110 women 35-45 **Istre 1998** Population: 60 premenopausal women	cauterisation was applied to the cornual region (n = 32) 2) bipolar electrocauterisation (NovaSure) endometrial ablation (n = 30) Medical arm: Mirena (n = 48) Actual treatment received: appears to be as above **Istre 1998** 1) endometrial resection with diathermy loop (regardless of day of menstr ual	**Istre 1998** Design: RCT Outcomes: Primary outcome: treatment success (defined as a PBAC subjective bleeding score ≤ 75 at 12 months, no re-surgery in TCRE group, no removal of device in LNG-IUS group) menorrhoea/oligomenorrhoea rates (bleeding diary) Genital he alth: defined by the trialist as an “overall feeling of lower abdominal health”) Quality of life on a VAS : hot flushes, sweating, sleeping problems, dyspareunia (pain on intercourse), vaginal dryness, urinary frequency, nervousness, depression, oedema, libido Additional treatment received Adverse effects	2 years: + 5.00 (SD 18.97) vs + 3.73 (SD 17.19) - P value = 0.65 5 years: + 7.75 (SD 16.39) vs + 1.06 (SD 23.81) - P value = 0.10 Social function: Surgical mean change vs Medical mean change 4 months: + 17.44 (SD 16. 51) vs + 7.57 (SD 26.26) - P value < 0.05 2 years: + 10.59 (SD 26. 52) vs + 3.94 (SD 25.26) - P value = 0.10 5 years: + 10.24 (SD 24. 49) vs + 2.96 (SD 27.22) - P value = 0.10 Physical role: Surgical mean change vs Medical mean change 4 months: + 32.26 (SD 38. 23) vs + 15.32 (SD 46. 78) - P value < 0.01 2 years: + 18.60 (SD 45. 73) vs + 12.95 (SD 44.	systematic review (Cochrane risk of bias tool). **Ghazizadeh 2014** Random sequence generation: unclear Allocation concealment: unclear Blinding: high risk Incomplete outcome data: low risk Selective reporting: unclear (adverse events not reported adequately) Other bias: high risk (study reports contradictory statements about menorrhagia) **Istre 1998**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
the effectiveness, safety and acceptability of surgery versus medical therapy for heavy menstrual bleeding. **Study dates** Search up to January 2016 **Source of funding** Internal sources • University of	aged 30 to 49 years who had sought medical attention for heavy menstrual bleeding, referred by general practitioner for surgery to gynaecological outpatient clinic in Oslo specialising in operative hysteroscopy **Kupperman 2004** Population: 63 women who failed on cyclical MPA Setting: USA **Cooper 1997** Population: 187 women referred to gynaecologists at Aberdeen Royal Infirmary, Scotland for treatment of clinically diagnosed dysfunctional uterine bleeding (i.e. uterus < 10 weeks' pregnancy size and normal endometrial pathology)	cycle) under spinal block or general anaesthesia 2) levonorgestrel-releasing intrauterine device inserted within 7 days of star t of menstruation **Kupperman 2004** 1) Abdominal or vaginal hysterectomy as decided by gynaecologist. Prophyl actic oophorec- tomy discouraged. 2) As decided by participating	**Kupperman 2004** Design: Multicentre RCT Outcomes: Health-related quality of life, measured by a range of instruments, the primary one being the mental component summary of SF-36 but also including (among others) 12 items from the MOS mental health inventory, 2 from a health distress scale and complete sleep problems, 4-item body attitudes questionnaire, 5 sexual functioning scales SF-36 phy sical component summary	58) - P value = 0.42 5 years + 31.62 (SD 33. 15) vs + 15.14 (SD 39. 77) - P value = 0.06 Emotional role: Surgical mean change vs Medical mean change 4 months: + 31.54 (SD 45. 94) vs + 8.96 (SD 49.93) - P value < 0.01 2 years: + 22.48 (SD 50. 47) vs + 11.25 (SD 45. 17) - P value = 0.13 5 years: + 33.81 (SD 34. 11) vs + 14.35 (SD 40. 61) - P value = 0.02 Mental health: Surgical mean change vs Medical mean change 4 months: + 15.01 (SD 19. 00) vs + 4.78 (SD 16.69) - P value < 0.01 2 years: + 9.98 (SD 19.14) vs + 7.17 (SD 19.20) - P value = 0.35	Random sequence generation: low risk Allocation concealment: low risk Blinding: high risk Incomplete outcome data: high risk (large number of withdrawals in LNG-IUS group) Selective reporting: low risk Other bias: unclear **Kupperman 2004** Random sequence generation: low risk Allocation concealment: low risk Blinding: high risk

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Auckland, New Zealand	**Inclusion criteria** **Ghazizadeh 2014** consecutive women with menorrhagia. Patients were candidates for hysterectomy. They had all been treated with hormonal therapy for at least 6 months and had shown no response to this therapy **Istre 1998** Required to have a PBAC score > 75 for 2 months before randomisation. Family complete Regular uterine cavity ≤ 10 cm in length **Kupperman 2004** Premenopausal women aged 31 to 49 with abnormal uterine bleeding (> 7 days of flow each	gynaecologist, who was told that "preferred" treatment was a combination of low-dose oral contraceptives with 21 active days and 7 placebo days **Cooper 1997** 1) injection of gonadotrophin-releasing hormone analogue followed 5 weeks later by transcervical resection of endometrium using rollerball coagulation to fundus and cornua plus loop resection of cavity walls.	Overall health, measured by EuroQol VAS and single-item global health question Single-item ratings of symptom resolution and symptom satisfaction Symptom resolution Satisfaction Resource use over 2-year f ollow-up (inpatient and outpatient services, including all diagnostic and therapeutic procedures), using Diagnosis-Related Groups, relative value units associated with Current Procedural Terminology codes: the se assign relative weights and values to services, based on estimated average resource use **Cooper 1997**	5 years: + 13.26 (SD 16. 94) vs + 3.62 (SD 18.21) - P value = 0.01 Energy/fatigue:Surgical mean change vs Medical mean change 4 months: + 20.53 (SD 20. 76) vs + 7.07 (SD 20.23) - P value < 0.01 2 years: + 14.58 (SD 21. 96) vs + 10.06 (SD 19. 57) - P value = 0.17 5 years: + 17.31 (22.35) vs + 10.62 (SD 18. 79) - P value = 0.07 Pain: Surgical mean change vs Medical mean change 4 months: + 21.62 (SD 31. 33) vs + 8.84 (SD 26.39) - P value < 0.01 2 years: + 12.34 (SD 27. 20) vs + 11.38 (SD 28. 51) - P value = 0.82 5 years: + 14.81 (SD 25.	Incomplete outcome data: Low risk Selective reporting: low risk Other bias: low risk **Cooper 1997** Random sequence generation (selection bias): Low risk (Computer randomisation) Allocation concealment (selection bias): Low risk (Allocation by serially numbered, opaque envelopes) Blinding

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	month or heavy flow with haematocrit < 32%), recruited in clinical centres at Alabama or Tennessee Universities, USA , who were dissatisfied with medical treatment including a course of cyclic MPA for at le ast 3 months **Cooper 1997** Dysfunctional uterine bleeding (i.e. uterus < 10 weeks' pregnancy size and normal endometrial pathology) **Exclusion criteria** **Ghazizadeh 2014** Patients who were pregnant or who were null-gravid or primiparous, and those who had	2) 3 cycles of medical treatment not previously used by patient, as selected by senior gynaecologist Actual treatment received: 33% (31 women) received progestogens (prescribed only to women with heavy and irregular periods; days 12 to 25, or 5 to 25 if there was also dysmenorrhoea) 26% (24 women) received combined pill (second-generation with 30 µg of estradiol) 23% (22 women) received tranexamic acid (1 g 4 times daily for first 5 days	Design: RCT Primary outcome: treatment satisfaction (direct question) Other outcomes: subjective relief of menstrual symptoms, bleeding score (1 to 5), pain score (1 to 5), anxiety and depression score (HADS) Health-related quality of life: SF-36, premenstrual symptoms Treatment acceptability (direct question and semantic differential technique)	35) vs + 11.98 (SD 23. 66) - P value = 0.6 General health: Surgical mean change vs Medical mean change 4 months: + 10.49 (SD 20. 85) vs -0.25(SD15.99) - P value = <0.01 2 years: + 1.69 (SD 18.83) vs - 0.67 (SD 13.90) - P value = 0.36 5 years: + 6.97 (SD 23.10) vs -3.88 (SD 20.13) - P value = 0.01 Outcome: Patient Satisfaction **Cooper 1997*** Totally or generally satisfied with treatment: Medical (n= 93) vs TCRE (n=93), 95% CI for difference in proportion (%) 4 months: 25 (27%) vs 70	(performance bias and detection bias) All outcomes: High risk (Blinding not feasible. Our primary review outcomes are subjective and therefore susceptible to bias related to lack of blinding) Incomplete outcome data (attrition bias): Primary outcomes: High risk (143/187 analysed at 5 years. Reasons for withdrawal/dropout given in 11 cases) Selective reporting (reporting bias): Low risk (All expected outcomes reported)

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	had an abnormal Pap smear, genital infection, hormonal disorder, hormonal treatment, anomalous uterus, any intra-cavity disorder, coagulative disorder, or an abnormal en- dometrial biopsy were excluded. With regard to myomas, they only excluded those sub- mucosal myomas that were > 2 cm and intramural myomas that moved the endometrial layer. A uterine cavity > 11 cm was also classified as an exclusion criterion **Istre 1998**	of period in women with regular periods, plus mefenamic acid 500 mg 3 times a day if there was associated dysmenorrhoea) 16% (15 women) received danazol (200 mg daily for 90 days) 2%(2 women) received hormone replacement therapywith anon-steroidal anti-inflammatory drug All women could request further and/or different treatment at 4-month follow-u		(76%), 95% CI -61 to -36, p-value = <0.001 2 years: 48 (57%) vs 68 (79%), 95% CI -36 to -9, p-value = 0.002 5 years: 49 (71%) vs 55 (76%), 95% CI non calculable Cure or acceptable improvement in symptoms: Medical (n= 93) vs TCRE (n=93), 95% CI for difference in proportion (%) 4 months: 29 (32%) vs 77 (76%), 95% CI -64 to -40, p-value <0.001 2 years: 53 (61%) vs 69 (81%), 95% CI -31 TO -4, p-value = 0.017 5 years: 52 (75%) vs 61 (86%), 95% CI -23 to 2, p-value = 0.26 Treatment	Other bias: Low risk (No other potential bias identified) **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	Breast feeding Current pregnancy Sub serous myoma > 40 mm diameter Use of hormonal medication within past 3 months History of thrombo-embolic disease or liver disease Any abnormal intrauterine pathology Pelvic inflammatory disease within past 6 months or current infection Participants were initially prepared to undergo hysterectomy. 40% had unsuccessfully tried medical therapy. The rest h ad either refused conservative surgery or had had no			acceptable: Medical (n= 93) vs TCRE (n=93), 95% CI for difference in proportion (%) 4 months: 33 (35) vs 85 (91), 95% CI -67 to -45, p-value = <0.001 2 years: 65 (77%) vs 79 (93%), 95% CI -26 to -4, p-value = 0.004 5 years: 64 (91%) vs 65 (93%), 95% CI - 10 to 7, p-value = 0.75 Prepared to have same treatment again: Medical (n= 93) vs TCRE (n=93), 95% CI for difference in proportion (%) 4 months: 29 (31%) vs 86 (92%), 95% CI -72 to -51, p-value= <0.001 2 years: no details provided 5 years: no details	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	previous treatment **Kupperman 2004** Other causes of anaemia, FSH > 30, pregnancy, desire to maintain fertility, endocrinopa- thy, coagulation problems, treatment for abnormal blee ding with depo-MPA or GnRH antagonist within the past 6 months, oral contraceptive or intrauterine device use within the past 3 months, contraindications to study medications, potential problems with sub- ject compliance, participation in another trial,			provided Would recommend the treatment: Medical (n= 93) vs TCRE (n=93), 95% CI for difference in proportion (%) 4 months: 38 (41) vs 84 (90%), 95% CI -61 to -38, p-value= <0.001 2 years: results non calculable 5 years: 14 (20%) vs 57 (72%), 95% CI -73 to -45, p-value = <0.001 *Extracted from Cooper 1997 (4 month data), 1999 (2 year data), and 2001 (5 year data) **Comparison: Surgery versus LNG-IUS** Outcome: PBAC	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	evidence of pelvic pathology for which hysterectomy or other specific directed therapy was indicated (e.g. neoplasia, cancer, hyperplasia, intrauterine polyps, submucosal myomas) Recruitment strategy: mass mailing, medical records review, advertisements in local mass media, physician referrals **Cooper 1997** Women referred specifically for surgery.			NMA outcome Outcome: Satisfaction NMA outcome Outcome: Change in EQ5D score at 1 year **Hurskainen 2001** Sx group: mean (SD)= 0.1 (0.21), n=112 Medical group: mean (SD)= 0.1 (0.21), n=116 Outcome: Change in EQ5D score at 5 years **Hurskainen 2001** Sx group: mean (SD)= 0.1 (0.27), n=115 Medical group: mean (SD)= 0.08 (0.27), n=117 Outcome: Change in EQ5D score at 10 years **Hurskainen 2001**	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				Sx group: mean (SD)= -0.01 (0.22), n=111 Medical group: mean (SD)= -0.01 (0.21), n= 110 Outcome: Final PGWBI score **De souza 2010** Sx group: mean (SD)= 90.1 (20.19), n=11 Medical group: mean (SD)= 100.4 (23.19), n=17 Outcome: SF-36 score NMA outcome Outcome: Operative complications (reported by study) **Hurskainen 2001** 3 bladder perforation, 1 bowel perforation in	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				Hysterectomy group **Kupperman 2004** 1 bowel injury in hysterectomy group Outcome: LNG-IUS adverse events (reported by study) **Istre 1998** Sx arm: 1/29 vaginitis in first year IUS arm: None reported in first year **Abdel Malak 2006** 2/30 vaginitis in LNG-IUS arm **Shaw 2007** 2/33 expulsion of LNG-IUS **Soysal 2002** 1/36 expulsion of LNG-	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				IUS	
Full citation Ozdegirmenci, O., Kayikcioglu, F., Akgul, M. A., Kaplan, M., Karcaaltincaba, M., Haberal, A., Akyol, M., Comparison of levonorgestrel intrauterine system versus hysterectomy on efficacy	**Sample size** No of women randomised: 86 No of women analysed: 75 (11 lost to follow-up from hysterectomy group) Power calculation for sample size: total of 72 participants for 90% power and d = 0.70 effect size. 20% more patients enrolled to allow for loss to follow-up Analysis not by ITT **Characteristics** Mean age 44-46 years old All women had Menorrhagia **Inclusion criteria**	**Interventions** 1) LNG IUS 2) Hysterectomy (abdominal)	**Details** Sample size calculation Power calculation for sample size: total of 72 participants for 90% power and d = 0.70 effect size. 20% more patients enrolled to allow for loss to follow-up. Follow-up Health-related quality of life was assessed at baseline and at 1-year follow-up with the WHO Quality of Life Short Form, Turkish Version (WHOQOL-BREF TR). The WHOQOL-BREF TR has 4 domains: physical health, psychological health, social relationships, and environment. Each facet of the WHOQOL-BREF TR is measured using a 5-point Likert scale about how the respondent felt in the last 2 weeks, and the	**Results** Outcome: Quality of life [WHO Quality of Life - Short Form, Turkish version (WHOQOL-BREF TR)] at 12 months LNG IUS: n = 43 Physical domain - median = 68, IQR 59-77 Psychological domain - median = 58, IQR 51-66 Social domain - median = 67, IQR 59-75 Environmental TR - mean = 62, SD 15 Hysterectomy: n = 32	**Limitations** **Cochrane Risk of Bias Tool** Selection bias Random sequence generation: Low risk, "computer generated codes Allocation concealment: Unclear risk, not reported Performance bias Blinding of participants and personnel: Unclear risk, not blinded Detection bias Blinding of

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
and quality of life in patients with adenomyosis, Fertility & Sterility, 95, 497-502, 2011 **Ref Id** 338533 **Country/ies where the study was carried out** Turkey **Study type** Single centre RCT	Women with clinical suspicion of adenomyosis complaining of menorrhagia and/or dysmenorrhoea and with confirmed adenomyosis. Inclusion criteria: not specifically reported - women with adenomyosis by sonogram and MRI **Exclusion criteria** Endometrial pathology, submucosal fibroids, intramural or subserousfibroids > 2cm, postmenopausal status, pelvic inflammatory disease, malignancy or suspicion of malignancy, thromboembolism, desire to become pregnant, cardiac or hepatic disease, use of oral progestogen during previous 3 months,		range of scores is between 1 and 100, with higher scores indicating better quality of life. Statistical analysis Analysis not by ITT. Descriptive data were expressed as mean + SD. Skewed data were shown as median and interquartile range (IQR).	Physical domain - median = 72, IQR 57-84 Psychological domain - median = 62, IQR 50-75 Social domain - median = 67, IQR 55-78 Environmental TR - mean = 68, SD 13 Mann Whitney U test, no difference between groups. Student's T test, no difference between groups Outcome: Wound Infection LNG IUS: 0/43 Hysterectomy: 1/32	outcome assessment: High risk, not blinded Attrition bias Incomplete outcome data: High risk, substantial loss to follow-up from the hysterectomy group (26%) and none from the LNG IUS group, ITT analysis not done Reporting bias Selective reporting: Low risk, outcomes were clearly specified and reported Other bias: Groups appeared comparable at baseline and no other potential bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study To prospectively compare levonorgestrel intrauterine system versus hysterectomy in patients with adenomyosis and to study the effects of both treatments on QOL in a randomised clinical trial **Study**	contradictions to MRI.				**Other information** Postoperative pathology findings confirmaed the presence of adenomyosis in 21 (65.6%), myomas in six (18.8%), adenomyosis with coexisting myoma in three (9.4%), and normal uterus in two (6.2%) women.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
dates April 2007-February 2009 **Source of funding** None reported					
Full citation Penninx, Jpm, Herman, Mc, Kruitwagen, Rfpm, Ter, Haar Ajf, Mol, Bw, Bongers, My, Bipolar versus	**Sample size** **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Included in the NMA. Compares two 2nd generation ablation techniques, therefore, not included in the pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
balloon endometrial ablation in the office: A randomized controlled trial, European Journal of Obstetrics Gynecology and Reproductive Biology, 196, 52-6, 2016 **Ref Id** 550470 **Country/ies where the study was carried out**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study type **Aim of the study** **Study dates** **Source of funding**					
Full citation Penninx, Jp, Herman, Mc, Mol, Bw, Bongers, My, Five-year follow-up after comparing bipolar	**Sample size** **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Included in the NMA. Compares two 2nd generation ablation techniques, therefore, not included in the pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
endometrial ablation with hydrothermablation for menorrhagia, Obstetrics and Gynecology, 118, 1287-92, 2011 **Ref Id** 550471 **Country/ies where the study was carried out** **Study type** **Aim of the**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
study **Study dates** **Source of funding**					
Full citation Penninx, Jp, Mol, Bw, Engels, R, Rumste, Mm, Kleijn, C, Koks, Ca, Kruitwagen, Rf, Bongers, My, Bipolar radiofrequency endometrial ablation	**Sample size** **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Included in the NMA. Compares two 2nd generation ablation techniques, therefore, not included in the pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
compared with hydrothermablation for dysfunctional uterine bleeding: a randomized controlled trial, Obstetrics and Gynecology, 116, 819-26, 2010 **Ref Id** 550473 **Country/ies where the study was carried out**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study type **Aim of the study** **Study dates** **Source of funding**					
Full citation Ruuskanen, A., Hippelainen, M., Sipola, P., Manninen, H., Uterine artery embolisation versus hysterectomy for	**Sample size** Please see Gupta 2014 Cochrane systematic review **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
leiomyomas: primary and 2-year follow-up results of a randomised prospective clinical trial, European Radiology, 20, 2010 **Ref Id** 511881 **Country/ies where the study was carried out** **Study type** **Aim of the study**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study dates **Source of funding**					
Full citation Sambrook, Am, Elders, A, Cooper, Kg, Microwave endometrial ablation versus thermal balloon endometrial ablation (MEATBall): 5-year follow up of a randomise	**Sample size** **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Included in the NMA. Microwave ablation not an intervention of interest according to protocol, therefore, not included in the pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
d controlled trial, Bjog, 121, 748-54, 2014 **Ref Id** 550557 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Sambrook, A.M., Bain,C., Parkin,D.E., Cooper,K.G., A randomised comparison of microwave endometrial ablation with transcervical resection of the endometrium: follow up at a minimum of 10 years,	**Sample size** **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Included in the NMA. Microwave ablation not an intervention of interest according to protocol, therefore, not included in the pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
BJOG: An International Journal of Obstetrics and Gynaecology, 116, 1033-1037, 2009 **Ref Id** 99696 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
dates **Source of funding**					
Full citation Sayed, Gh, Zakherah, Ms, El-Nashar, Sa, Shaaban, Mm, A randomized clinical trial of a levonorgestrel-releasing intrauterine system and a low-dose combined	**Sample size** N=58 (LNG-IUS n=29; COC n=29) **Characteristics** **Baseline characteritics** Age in years, mean±SD LNG-IUS: 37.0±4.9 COC: 37.2±5.2 BMI, mean±SD LNG-IUS: 30.0±6.1 COC: 30.2±5.1	**Interventions** 1) LNG-IUS LNG-IUS was inserted according to the manufacturer's instructions. 2) COC Women in the COC group received their monthly number of pills in a sealed package at each clinic visit. the pills contained 30 µg of ethinyl estradiol and 150 µg of levonorgestrel. The women were	**Details** Sample size calculation Using the 2-sided X^2 test and assuming an attrition rate of 15%, it was calculated that 58 partiicpants (29 in each group) were needed for the study to attain 90% powerat a level of significance of 0.05. Reduction of menstrual blood loss was the primary outcome. Randomisation and allocation concealment Computer-generated table of ranomd numbers were written on pieces of paper. The pieces of papers were then inserted into envelopes that were immediately sealed. When the participant	**Results** Outcome: PBAC score PBAC score at baseline, mean±SD LNG-IUS: 303.1±99.9 (n=29) COC: 345.4±99.7 (n=29) PBAC score at 12 months, mean±SD LNG-IUS: 33.7±43.5 (n=29) COC: 153.9±156.1 (n=29) Outcome: Menstrual blood loss (AH method)	**Limitations** **Cochrane risk of bias tool** Selection bias Random sequence generation: Low risk Allocation concealment: Low risk Performance bias Blinding of participants and personnel: Unclear risk, blinding was not possible due to the nature of the interventions,

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
oral contraceptive for fibroid-related menorrhagia, International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics, 112, 126-30, 2011 **Ref Id** 550569	Education years, mean±SD LNG-IUS: 6.0±6.3 COC: 8.3±5.6 Dysmenorrhea, % LNG-IUS: 45 COC: 55 **Inclusion criteria** -heavy menstrual bleeding -regular cycle -20-50 years of age at the initial assessment -living sufficiently close to the hospital to make follow-up possible -fibroids detected in ultrasound (see exclusion criteria) **Exclusion criteria**	instructed on how to use them. Compliance was assessed at each visit.	was enrolled, the first envelope on the pile was opened and her allocation was made. Blinding Not possible due to the nature of the interventions Follow-up All participants were requested to come for a clinic visit at 3, 6, 9, and 12 months at the outpatient gynaecology clinic of the study. Menstrual blood loss was assessed by pictorial blood loss assessment chart (PBAC) at baseline, at 6 months, and 12 months. The participants were explained how to fill the PBAC and all completed 1 menstrual cycle during the screening phase of the study to increase the reliability of the measurement. Sanitary pads (Always Ultra) were provided to the participants.	Menstrual blood loss in ml (Alkaline heamtin method) at baseline, mean±SD LNG-IUS: 240.1±118.6 (n=29) COC: 202.9±95.1 (n=29) Menstrual blood loss in ml (Alkaline heamtin method) at 12 months, mean±SD LNG-IUS: 19.4±36.5 (n=29) COC: 193.0±36.2 (n=29) Outcome: Health-related quality of life (assessed with HRQoL-4 questionnaire) Self-rated health good or excellent at baseline LNG-IUS: 0/29	however, not clear if it can introduce performance bias. Detection bias Blinding of outcome assessment: High risk, blinding not possible due to the nature of the interventions, therefore, there is a high risk of bias on subjective outcomes (quality of life) and possibly for assessment of blood loss because the methods are not perfectly objective. Attrition bias Incomplete outcome data: High risk, 6/29 and 8/29 lost to follow in

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Country/ies where the study was carried out Egypt **Study type** RCT **Aim of the study** To compare the efficacy of a levonorgestrel-releasing intrauterine system (LNG-IUS) with that of a low-dose	-pregnancy -history of ectopic pregnancy -puerperal sepsis -pelvic inflammatory disease -evidence of defective coagulation -abnormalities on ultrasound (**including submucosal fibroids of any size distorting the cavity of the uterus or intramural or subserous fibroids > 5 cm in diameter**) -history of malignancy or evidence of hyperplasia in the endometrial biopsy -incidental adnexal abnormality on ultrasound -previous endometrial		A direct measurement of menstrual blood loss was also performed by the alkaline hematin method at baseline and at 12 months. Health-related quality of life -4 (HRQL-4) questionnaire was administered at baseline, at 6 months, and 12 months to assess quality of life in the previous 30 days. The questionnaire includes the following 4 questions: health as self-assessed, number of days feeling physically unhealthy, number of days feeling mentally unhealthy, and "lost days" (defined as days when work or other daily activities were not possible). Statistical analysis All analysis ITT. Independent t test, Wilcoxon rank sum test, X^2 test, and Fisher exact test were used, as appropriate. Mean and SD were reported for normally	COC: 0/29 Self-rated health good or excellent at 12 months LNG-IUS: 9/29 COC: 7/29 No. of days feeling physically unwell at baseline, mean±SD LNG-IUS: 9.2±3.2 (n=29) COC: 9.2±3.2 (n=29) No. of days feeling physically unwell at 12 months, mean±SD LNG-IUS: 3.7±3.2 (n=29) COC: 6.4±3.0 (n=29) No. of days feeling mentally unwell at baseline, mean±SD LNG-IUS: 9.0±3.0 (n=29) COC: 8.5±2.9 (n=29)	treatment arms at 12 months follow up. Reporting bias Selective reporting: Low risk Other bias Other sources of bias: - **Other information** Also included in Cochrane systematic review by Lethaby et al. 2015.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
combined oral contraceptive (COC) in reducing fibroid-related menorrhagia. **Study dates** Recruitment between May 1, 2003 and March 31, 2004. **Source of funding** Bayer Schering Pharma (Berlin Germany); the sanitary	ablation/resection -uninvestigated postcoital bleeding -untreated abnormal cervical cytology -contraindication to COCs		distributed variables and median and IQR for skewed variables.	No. of days feeling mentally unwell at 12 months, mean±SD LNG-IUS: 6.6±3.7 (n=29) COC: 8.7±3.6 (n=29) No. of lost days (no regular activity) at baseline, mean±SD LNG-IUS: 8.2±3.3 (n=29) COC: 8.3±3.2 (n=29) No. of lost days (no regular activity) at 12 months, mean±SD LNG-IUS: 1.3±1.5 (n=29) COC: 6.3±3.3 (n=29)	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
pads were supplied by Proctor & Gamble (Cairo, Egypt); funding for laboratory work was provided by Assiut University, Egypt.					
Full citation Sesti, F, Piancatelli, R, Pietropolli, A, Ruggeri, V, Piccione, E, Levonorge	**Sample size** Please see Lethaby 2015 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
strel-releasing intrauterine system versus laparoscopic supracervical hysterectomy for the treatment of heavy menstrual bleeding: a randomized study, Journal of women's health (2002), 21, 851-7, 2012 **Ref Id** 550586 **Country/ies where**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
the study was carried out **Study type** **Aim of the study** **Study dates** **Source of funding**					
Full citation Sesti, F., Ruggeri, V., Pietropolli, A., Piancatelli, R., Piccione,	**Sample size** Please see Fergusson 2013 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
E., Thermal balloon ablation versus laparoscopic supracervical hysterectomy for the surgical treatment of heavy menstrual bleeding: a randomized study, Journal of Obstetrics & Gynaecology Research, 37, 1650-7, 2011 **Ref Id**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
454628 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**					
Full citation Shaw, Rw, Symonds, Im, Tamizian,	**Sample size** Please see Lethaby 2015 Cochrane Systematic Review and Marjoribanks 2016 Cochrane Systematic Review.	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
O, Chaplain, J, Mukhopadhyay, S, Randomised comparative trial of thermal balloon ablation and levonorgestrel intrauterine system in patients with idiopathic menorrhagia, The Australian & New Zealand journal of obstetrics & gynaecolo	**Characteristics** **Inclusion criteria** **Exclusion criteria**				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
gy, 47, 335-40, 2007 **Ref Id** 550598 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**					
Full citation	**Sample size**	**Interventions**	**Details**	**Results**	**Limitations**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Silva-Filho, AI, Pereira, Fde A, Souza, Ss, Loures, Lf, Rocha, Ap, Valadares, Cn, Carneiro, Mm, Tavares, RI, Camargos, Af, Five-year follow-up of levonorgestrel-releasing intrauterine system versus thermal balloon ablation for the treatment	Randomised N=58 (LNG-IUS: 30, Thermal balloon ablation(TBA): 28) Analysed N=52 (LNG-IUS: 27, Thermal balloon ablation(TBA): 25) **Characteristics** **Baseline characteristics** Age LNG-IUS: 42±0.7 TBA: 43.4±0.7 Parity LNG-IUS: 2.4±0.2 TBA: 2.6±0.4 Education (years of schooling) LNG-IUS: 7.5±0.7	All procedures were initiated during the first 15 days of a menstrual cycle and were performed by one of the investigators. Insertion of the LNG-IUS was performed according to the manufacturer's instructions in the outpatient department. All subjects received meloxicam 15 mg 1h prior to the device insertion. TBA was performed with the uterine balloon therapy system under general anesthesia in the operating room according to the manufacturer's instructions. The	Sample size calculation Sample size was calculated based on an expected PBAC score of 156.6 after 3 months of cyclical progestogens therapy Randomisation and allocation concealment With the use of a computer-generated randomization list, the patients were then randomly allocated to one of two groups: the LNG-IUS group (30 women) or the TBA group (28 women) Blinding The treatment was revealed to the patient because of the different nature of treatments. Blinding of the outcome assessors not reported Follow-up Hemoglobin levels; patient well-being, evaluated (PGWBI) ; and uterine bleeding patterns were	Outcome: PGWBI (mean± SD) Baseline LNG-IUS: 88.5±3.8 TBA: 85.9±6.9 After 5 years LNG-IUS: 100.4±5.8 TBA: 90.1±6.1 Outcome: Patient satisfaction To the statement “I feel much better after treatment,” the answers “Definitely agree” and “Somewhat agree” were reported by 100% in the LNG-IUS group vs. 72% in the TBA group To the statement “I am very satisfied with the	**Cochrane risk of bias tool** Selection bias Random sequence generation: Low risk Allocation concealment: Unclear risk Use of a computer-generated randomization list and the patients were then randomly allocated to one of two groups Performance bias Blinding of participants and personnel: Unclear risk Blinding was not

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
of heavy menstrual bleeding: a randomized controlled trial, Contraception, 87, 409-15, 2013 **Ref Id** 550607 **Country/ies where the study was carried out** Brazil **Study type** Randomised	TBA: 8.2±0.7 Income (number of minimum salaries) LNG-IUS: 3.3±0.4 TBA: 3.4±0.3 Hemoglobin level LNG-IUS: 12.5±0.3 TBA: 12.3±0.4 PBAC LNG-IUS: 522.1±90.3 TBA: 492.2±56.8 Psychological general well-being index (PGWBI)	thermal balloon was placed in the uterine cavity and then inflated with 5% dextrose solution until intrauterine pressure stabilized between 160 and 180 mmHg. The fluid inside the thermal balloon was heated to 87°C and maintained at this temperature for 8 min. At the end of this procedure, the balloon was deflated and removed. The entire procedure lasted between 10 and 20 min. Treatment was considered to have failed when blood loss increased or when there was no improvement in	evaluated prior to treatment and at 5 years post-treatment. PGWBI for quality of life was calculated by applying a questionnaire. PBAC was evaluated only at the beginning as one of the inclusion criteria. The uterine bleeding patterns were classified in accordance with the menstrual and inter-menstrual blood loss criteria. Treatment was considered to have failed when blood loss increased or when there was no improvement in hemoglobin levels. In these cases, patients were offered a hysterectomy as definitive treatment. The hysterectomy rates, patient acceptability, perceived clinical improvement and overall satisfaction of the groups were also analyzed. Three patients were lost to follow-up in each group. At the end of the 5th year of follow-up, in order to avoid misinterpretation of data due to menopause transition, all	treatment," the answers "Definitely agree" and "Somewhat agree" were reported by 100% in the LNGIUS group vs. 80% in the TBA group To the statement "If I had a choice, I would do the same treatment," the answer "Definitely agree" was reported by 100% in the LNG-IUS group vs. 56% in the TBA group To the statement "I noticed great improvements in my physical well-being after treatment," the answers "Definitely agree" and "Somewhat agree" were reported by 100% in the LNG-IUS group vs. 68% in the TBA group To the statement "I noticed great improvements in my emotional well-being after	possible due to the nature of the interventions, however, not clear if it can introduce performance bias Detection bias Blinding of outcome assessment: High risk Blinding of outcome assessors not reported and most probably not done Attrition bias Incomplete outcome data: High risk Outcome reported based on participant completing the trial

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
controlled trial **Aim of the study** To compare results of women submitted to LNG-IUS or TBA (thermal ablation balloon) for the treatment of HMB after 5-year follow-up using as end points hemoglobin levels, bleeding patterns,	LNG-IUS: 88.5±3.8 TBA: 85.9±6.9 **Inclusion criteria** 1) Clinical HMB refractory to medical treatment (i.e., oral contraceptive pills, estrogen– progestin preparations, nonsteroidal anti-inflammatory drugs) 2) a 3-month washout period, regular menstrual cycles, age ≥35 years 3) menstrual blood loss >80 mL as measured by the Pictorial Bleeding Assessment Chart (PBAC) 4) a negative pregnancy test, uterine volume <200 mL as measured by transvaginal sonogram (the uterine volume was calculated as length×width×height×0.45)	hemoglobin levels. In these cases, patients were offered a hysterectomy as definitive treatment. At the end of the 5th year of follow-up, in order to avoid misinterpretation of data due to menopause transition, all patients with amenorrhea were evaluated by measuring serum follicle-stimulating hormone (FSH) levels and for the presence of hypoestrogenism symptoms. Patients with serum FSH > 40 and climacteric symptoms were considered to be postmenopausal	patients with amenorrhea were evaluated by measuring serum follicle-stimulating hormone (FSH) levels and for the presence of hypoestrogenism symptoms. Patients with serum FSH > 40 and climacteric symptoms were considered to be postmenopausal and withdrawn from analyses of hemoglobin levels, PGWBI scores and bleeding pattern. PBAC was evaluated only at the beginning as one of the inclusion criteria. PGWBI which measured quality of life was calculated by applying a questionnaire. Satisfaction rates were reported with questionnaire. Statistical analysis The variables are described as means with their respective ranges and standard error of the mean. Comparison between the two groups was performed using the $\chi 2$ and unpaired Student's t test, and comparison before and	treatment," the answers "Definitely agree" and "Somewhat agree" were reported by 88.9% in the LNG-IUS group vs. 56% in the TBA group	and no adjustment mae in final analysis for drop outs Reporting bias Selective reporting: High risk PBAC score was only reported at baseline and no explanation for not reporting in follow up analysis Other bias Other sources of bias: **Other information** Included in the NMA. This publication did not report on outcomes relevant for the pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
patient quality of life and satisfactio n rates **Study dates** January 2005 - March 2007 **Source of funding** Bayer pharmace utical partially funded this study through the donation of the Gynecare Thermach oice	5) a negative Pap smear within the last year **Exclusion criteria** Intracavitary abnormalities, pelvic inflammatory disease, suspected endometrial pathology, abnormal endometrial histology, abnormal cervical cytology, previous endometrial resection and ablation, and any other abnormality such as uterine prolapse, large myomas or any ovarian disease for which hysterectomy would be more appropriate	and withdrawn from analyses of hemoglobin levels, PGWBI scores and bleeding pattern. PGWBI was a masure of patient quality of life	after the treatment was performed using the paired Student's t test. Significance level was established as p>.05.		

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Uterine Balloon Therapy System and Mirena™					
Full citation Tosun, Ak, Tosun, I, Suer, N, Comparison of levonorgestrel-releasing intrauterine device with oral progestins in heavy menstrual bleeding (HMB) cases with	**Sample size** Total N=60 LNG-IUD n=30; NETA n=30 **Characteristics** Age range 33-45 years in the total sample Mean age in years LNG-IUD group: 39.15 ±2.79 NETA group: 38.91 ±3.46 Mean parity LNG-IUD group: 2.6 ±1.1	**Interventions** Levonorgestrel-releasing intrauterine device (LNG-IUD) versus oral progesterone norethisterone acetate (NETA). LNG-IUD LNG-IUD was applied in the first 10 days of the menstrual cycle. NETA The participants were given oral	**Details** Randomisation Random-sequence methods were used. Randomisation was undertaken using computational random-number generators. Allocation concealment Not reported. Blinding Open-label study (no blinding) due to the nature of the trial. Follow up The assessment of the menstrual blood loss was done	**Results** Outcome: PBAC score At baseline, mean±SD LNG-IUS: 518.0±120.35 (n=30) NETA: 414.33±112.94 (n=30) At 6 months of treatment, mean±SD LNG-IUD: 77.41±106.15 (n=30) NETA: 169.44±166.106 (n=30)	**Limitations** **Cochrane risk of bias tool** Selection bias Random sequence generation: Low risk Allocation concealment: Unclear risk, not reported. Performance bias Blinding of participants and personnel: Unclear risk, blindin

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
uterine leiomyoma (LNG-IUD and oral progestin usage in myoma uteri), Pakistan Journal of Medical Sciences, 30, 2014 **Ref Id** 550668 **Country/ies where the study was carried out** Turkey **Study type**	NETA group: 2.4 ±1.1 Locations of fibroids LNG-IUD group: 9% submucosal, 72% intramural, 19% subserosal NETA group: 25% submucosal, 60% intramural, 15% subserosal 100% of women had heavy menstrual bleeding at enrollment. **Inclusion criteria** Women with myoma uteri with bleeding. Otherwise not clearly reported. **Exclusion criteria** Women with pelvic inflammatory disease, malignancy,	NETA 10 mg (5 mg twice daily) during the cycle of 5-25 days.	by using the pictorial assessment developed by Highham et al. (1990). Scores of 1, 5, 20 have been given for sanitary pads and tampons considering the degree of dirtiness as minimum, middle and heavy. The participants were asked to write down their menstrual period. To minimise subjectivity the participants were advised to use the same brand sanitary pads. Further details not reported. Statistical analysis Student t, Mann Whitney U, Paired Samples t, Ki-Kare and Fisher's Exact KiKare tests have been used. The significance value is $p < 0.05$. The results are taken from all the patients who continued to participate in the study.		g was not possible due to the nature of the interventions, however, not clear if it can introduce performance bias. Detection bias Blinding of outcome assessment: High risk, blinding not possible due to the nature of the interventions, therefore, there is a high risk of bias on because blood loss was assessed using PBAC which is not absolutely objective. Attrition bias Incomplete outcome data: Unclear risk, number of

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
RCT **Aim of the study** To compare the effectiveness and acceptability of levonorgestrel-releasing intrauterine device (LNG-IUD) with oral progesterone (norethisterone acetate: NETA) in achieving a reduction in volume of the	thromboembolism, pregnancy, submucosal fibroid having component indise the cavity over 50%, and fibroids bigger than 5 cm.				participants with outcome data not reported. Reporting bias Selective reporting: Low risk Other bias Other sources of bias: Paper is poorly written with limited details on methods provided. **Other information** The study used the pictorial blood loss assessment (PBAC) technique developed by Higham et al. (1990) to assess blood loss, however, the publication does

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
myomas, hemoglobin levels, satisfaction of the women. **Study dates** January 1st 2010 to March 1st 2011 **Source of funding** None. "No financial or commercial interests from any drug company or others were taken and there is no relationshi					not call is PBAC but calls in visual bleeding score (VBS) instead. Also, the cut-off for VBS they reportedly used was 185, instead of the more commonly seen 100 for PBAC.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
p of authors that may pose conflict of interest."					
Full citation van der Kooij, S. M., Hehenkamp, W. J., Volkers, N. A., Birnie, E., Ankum, W. M., Reekers, J. A., Uterine artery embolization vs hysterectomy in the	**Sample size** Please see Gupta 2014 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
treatment of symptomatic uterine fibroids: 5-year outcome from the randomized EMMY trial, American Journal of Obstetrics & GynecologyAm J Obstet Gynecol, 203, 105.e1-13, 2010 **Ref Id** 550686 **Country/ies where the study**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
was carried out **Study type** **Aim of the study** **Study dates** **Source of funding**					
Full citation Volkers, Na, Hehenkamp, Wj, Birnie, E, Ankum, Wm, Reekers, Ja, Uterine	**Sample size** Please see Gupta 2014 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
artery embolization versus hysterectomy in the treatment of symptomatic uterine fibroids: 2 years' outcome from the randomized EMMY trial, American journal of obstetrics and gynecology, 196, 519.e1-11, 2007 **Ref Id** 550704 **Country/ie**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
s where the study was carried out **Study type** **Aim of the study** **Study dates** **Source of funding**					
Full citation Moss, J. G., Cooper, K. G., Khaund, A., Murray, L. S.,	**Sample size** Please see Gupta 2014 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Murray, G. D., Wu, O., Craig, L. E., Lumsden, M. A., Randomised comparison of uterine artery embolisation (UAE) with surgical treatment in patients with symptomatic uterine fibroids (REST trial): 5-year results, BJOG: An International Journal					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
of Obstetrics & Gynaecology, 118, 936-44, 2011 **Ref Id** 566867 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Edwards, R. D., Moss, J. G., Lumsden, M. A., Wu, O., Murray, L. S., Twaddle, S., Murray, G. D., Committee of the Randomized Trial of Embolization versus Surgical Treatment for, Fibroids, Uterine-	**Sample size** Please see Gupta 2014 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
artery embolization versus surgery for symptomatic uterine fibroids, N Engl J Med, 356, 360-70, 2007 **Ref Id** 587971 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
dates **Source of funding**					
Full citation Jun, F., Yamin, L., Xinli, X., Zhe, L., Min, Z., Bo, Z., Wenli, G., Uterine artery embolization versus surgery for symptomatic uterine fibroids: a randomized controlled trial and a	**Sample size** Please see Gupta 2014 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
meta-analysis of the literature, Arch Gynecol Obstet, 285, 1407-13, 2012 **Ref Id** 587972 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
funding					
Full citation Manyonda, I. T., Bratby, M., Horst, J. S., Banu, N., Gorti, M., Belli, A. M., Uterine artery embolization versus myomectomy: impact on quality of life--results of the FUME (Fibroids of the Uterus: Myomecto	**Sample size** Please see Gupta 2014 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
my versus Embolization) Trial, Cardiovascular and interventional radiology, 35, 530-6, 2012 **Ref Id** 428767 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Source of funding					
Full citation Mara,M., Maskova,J., Fucikova,Z., Kuzel,D., Belsan,T., Sosna,O., Midterm clinical and first reproductive results of a randomized controlled trial comparing uterine fibroid	**Sample size** Please see Gupta 2014 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
embolization and myomectomy, CardioVascular and Interventional Radiology, 31, 73-85, 2008 **Ref Id** 107531 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
dates **Source of funding**					
Full citation Nieman,L. K., Blocker,W., Nansel,T., Mahoney, S., Reynolds,J., Blithe,D., Wesley,R., Armstrong, A., Efficacy and tolerability of CDB-2914 treatment for	**Sample size** Randomised N=42 (n=14 placebo; n=14 ulipristal acetate 10 mg; n=14 ulipristal acetate 20 mg) Analysed N=38 (n=12 placebo; n=13 ulipristal acetate 10 mg; n=13 ulipristal acetate 20 mg) **Characteristics** Baseline characteristics of 38 women who completed treatment 1 (N=38) Race/ethnicity - black/Hispanic/white/mixed, n	**Interventions** Placebo; or ulipristal acetate 10 mg or 20 mg For treatment 1, after a negative pregnancy test, subjects were randomized and began treatment on menstrual cycle day 1 or 2. Treatment administration continued for three menstrual cycles (90–102 days in amenorrheic women). Women received	**Details** Randomisation and allocation concealment The Pharmaceutical Development Service assured allocation concealment and randomized participants to receive CDB-2914 10 mg (ulipristal acetate 10 mg) or 20 mg (ulipristal acetate 20 mg), or a placebo using computer-generated blocks of six. Blinding Laboratoire HRA-Pharma provided 10-mg CDB-2914 tablets and a lookalike inert placebo. Follow up	**Results** Outcome: Health-related quality of life at the end of 3 cycles of treatment Change in scores from baseline, mean±SD SF-36 - Role physical score Ulipristal acetate: 4.2±1.2 (n=26) Placebo: -1.5±2.0 (n=12) p=0.019 SF-36 - Role mental component Ulipristal acetate: 4.1±1.5 (n=26)	**Limitations** **Cochrane risk of bias tool** Selection bias Random sequence generation: Low risk Allocation concealment: Unclear risk, reported in the supplemental material that "The Pharmaceutical Development Service assured allocation concealment", however, methods

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
symptomatic uterine fibroids: a randomized, double-blind, placebo-controlled, phase IIb study, Fertility and Sterility, 95, 767-772, 2011 **Ref Id** 130552 **Country/ies where the study was carried out** United States	Placebo: 9/0/2/1 Ulipristal acetate 10 mg: 11/0/2/0 Ulipristal acetate 20 mg: 12/1/0/0 Age in years, mean±SD Placebo: 43.1±6.0 Ulipristal acetate 10 mg: 42.5±4.3 Ulipristal acetate 20 mg: 41.3±5.0 BMI, mean±SD Placebo: 28.3±4.6 Ulipristal acetate 10 mg: 27.3±4.9 Ulipristal acetate 20 mg: 27.8±3.2	two bottles and were instructed to swallow one tablet from each bottle every morning before eating.	After initial treatment, women could elect hysterectomy, myomectomy, or 3 months of treatment with CDB-2914 (termed treatment 2, TX2). Surgery occurred after ovulation in the third month, in the follicular phase of the fourth month, or after 90-102 days of treatment. In TX2, women received their earlier CDB dose or were randomized to 10 or 20 mg if they had received placebo. Study procedures were identical to TX1. Women who did not undergo surgery or underwent myomectomy were invited to continue under an “extension” study during which they underwent pelvic MRI and health-related quality-of-life (HRQL) questionnaires at 3, 6, and 12 months after stopping taking the	Placebo: -2.2±2.4 (n=12) p=0.037 UFS - Symptom severerity score Ulipristal acetate: -28.3±4.2 (n=26) Placebo: -4.2±6.5 (n=12) p=0.004 UFS - Overall HRQL Ulipristal acetate: 27.8±3.6 (n=26) Placebo: 8.6±5.6 (n=12) p=0.008 UFS - Concern subscore Ulipristal acetate: 46.1±4.5 (n=26) Placebo: 12.1±6.9 (n=12) p<0.001	or details not explained. Performance bias Blinding of participants and personnel: Low risk Detection bias Blinding of outcome assessment: Low risk Attrition bias Incomplete outcome data: Unclear risk, number of women completing the HRQL questionnaires not reported, however, the paper reports that "SF-36 and UFS data were available for nearly

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study type A randomised double-blind, placebo-controlled clinical trial **Aim of the study** To evaluate the efficacy and tolerability of the P receptor modulator CDB-2914 (Ulipristal, CDB). **Study dates**	Gravidity, mean±SD Placebo: 2.3±2.1 Ulipristal acetate 10 mg: 2.1±1.8 Ulipristal acetate 20 mg: 1.8±2.3 Parity, mean±SD Placebo: 1.1±2.0 Ulipristal acetate 10 mg: 1.0±1.4 Ulipristal acetate 20 mg: 0.6±1.0 Total fibroid volume cm³, mean±SD Placebo: 149.1±120.6 Ulipristal acetate 10 mg:		study drug. (However, the publication only reports results after phase 1.) The short form-36 evaluates components of health-related quality-of-life (HRQL): physical and social functioning, role limitations due to physical or emotional health, bodily pain, general health, vitality, and mental health. These domains form a physical component scale and a mental component scale. The uterine fibroid symptom quality-of-life (UFS-QOL) is a disease-specific questionnaire that assesses symptom severity and HRQL. The HRQL domains (concern, activities, energy/mood, control, selfconsciousness, and sexual function) are collapsed into an overall HRQL score.	UFS - Energy/mood subscore Ulipristal acetate: 19.2±3.7 (n=26) Placebo: 3.7±5.8 (n=12) p=0.037 UFS - Control subscore Ulipristal acetate: 20.3±4.3 (n=26) Placebo: 9.1±6.8 (n=12) p=0.18 UFS - Self-conscious subscore Ulipristal acetate: 19.0±4.7 (n=26) Placebo: 15.8±7.5 (n=12) p=0.72 UFS - Sexual function subscore	all women". Reporting bias Selective reporting: Unclear risk, HRQL was only reported after phase 1 even though according to the paper data was also collected at 6 months and 12 months post-treatment, however, it is a secondary outcome and the paper narratively reports that "These scores were similar at the end of 3 and 6 months of treatment in those who received CDB." Other bias Other sources of bias: -

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Not reported **Source of funding** Supported by in part by the Intramural Program in Reproductive and Adult Endocrinology, Eunice Kennedy Shriver National Institute of Child Health and Human Development, and by the National Institutes	231.1±192.8 Ulipristal acetate 20 mg: 259.5±147.2 **Inclusion criteria** Women with symptomatic (anemia, pelvic pressure, chronic lower abdominal pain, bladder pressure with increased urinary frequency, or menorrhagia) uterine fibroids more than 2 cm in diameter with the following additional inclusion criteria: -age 25–50 years, -ovulatory menstrual cycles of 24–35 days, -a hemoglobin of >10 g/dL, -creatinine of <1.3 mg/dL, -liver function tests within 130% of the upper normal range,		Statistical analysis Change from baseline was evaluated using univariate ANOVA on the difference between pretreatment and treatment scores. Results from the two CDB dose groups did not differ. They were combined into a single group and compared with the placebo group. Sample size calculation A formal power calculation was not performed. The sample size was derived from the assumption that CDB–2914 has a similar potency to mifepristone in reduction of fibroid size and previous data (Stratton P, Hartog B, Hajizadeh N, Piquion J, Sutherland D, Merino M, Lee YJ, Nieman LK. A single midfollicular dose of CDB-2914, a new antiprogestin, inhibits	Ulipristal acetate: 25.7±5.5 (n=26) Placebo: 18.7±8.5 (n=12) p=0.50 UFS - Activities subscore Ulipristal acetate: 83.9±4.4 (n=26) Placebo: 56.1±7.0 (n=12) p=0.002 UFS - Composite bleeding score Ulipristal acetate: 2.1±0.2 (n=26) Placebo: 0.43±0.3 (n=12) p<0.001	**Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
of Health Clinical Center, National Institutes of Health, Bethesda, MD. Under a Cooperative Research and Development Agreement, Laboratoire HRA-Pharma, Paris, France, provided study drug and placebo as well as salary support for	-and a body mass index (BMI) <35 kg/m2. **Exclusion criteria** -use of glucocorticoids or megesterol within 1 year, -cervical dysplasia, -adnexal mass, -previous malignancy, -inability to complete study requirements, -serum FSH >20 U/L, -anovulation, -rapidly growing leiomyoma, -unexplained vaginal bleeding, -pregnancy, -lactation, -use of hormonal		folliculogenesis and endometrial differentiation in normally cycling women. Hum Reprod 2000;15:1092–9) showing its effects in groups of 10–12 women receiving CDB–2914.		

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
one member of the research team. The research team analyzed the data and drafted the manuscript, and Laboratoire HRAPharma agreed to the final submission, NCT00290251.	compounds within 8 weeks of start of study, or -therapy affecting ovarian or hepatic function.				
Full citation	**Sample size** Please see Lethaby 2015	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Tam WH; Yuen PM; Shan Ng DP; Leung PL; Lok IH; Rogers MS. , Health status function after treatment with thermal balloon endometrial ablation and levonorgestrel intrauterine system for idiopathic menorrhagia: a randomized study. ,	Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Tam WH; Yuen PM; Shan Ng DP; Leung PL; Lok IH; Rogers MS., 62, 84-8, 2006 **Ref Id** 587977 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation A randomised trial of endometrial ablation versus hysterectomy for the treatment of dysfunctional uterine bleeding: outcome at four years. Aberdeen Endometrial Ablation Trials Group, Br J Obstet Gynaecol, 106, 360-	**Sample size** N=204 **Characteristics** Endometrial ablation group: N= 105 Mean age (SD): 40.1 (5) Dysmenorrhea: 75% Hysterectomy: N= 99 Mean age (SD): 40.3 (5.2) Dysmenorrhea: 69% **Inclusion criteria** -under 50 years of age;	**Interventions** 1) Endometrial ablation The gonadotrophin releasing hormone agonist analogue goserelin was given to women having hystero-scopic surgery five weeks pre-operatively to prepare the endometrium. 2) Hysterectomy Abdominal hysterectomy was performed in 85/95 cases (six of whom had bilateral oophorectomy and one a sub-total hysterectomy) and	**Details** Follow-up A postal questionnaire was sent to all women four years after their initial trial management, assessing gynaecological symptoms, satisfaction, anxiety, depression, and sexual activity. The women had completed a similar questionnaire at recruitment and at six, 12 and 24 months post-operatively. Anxiety and depression were measured using the Hospital Anxiety and Depression Scale" the higher the score the more depressed or anxious the women. At four years, overall satisfaction with treatment was measured using a seven point Likert scale which ranged from totally satisfied to totally dissatisfied; sexual activity questions were adapted from the Psychological	**Results** Outcome: Patient Satisfaction Endometrial ablation: 61/76* reported being totally or generally satisfied Hysterectomy: 64/72* reported being totally or generally satisfied * N responding to 4-year follow-up questionnaire	**Limitations** **Cochrane risk of bias tool** Selection bias random sequence generation: unclear Allocation concealment: unclear Performance bias Blinding: unclear risk, blinding not possible but unclear how it might affect performance bias Detection bias Blinding: high risk, blinding not

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
6, 1999 **Ref Id** 549650 **Country/ies where the study was carried out** UK **Study type** RCT **Aim of the study** To assess the long term impact of initial management by endometri	-weighed under 100 kg -clinical diagnosis of dysfunctional uterine bleeding (uterine size less than 10 weeks); -would have otherwise undergone hysterectomy **Exclusion criteria** Not reported	vaginal hysterectomy was performed in 10/95.	Adjustment to Illness Scale". Initial non-responders were sent one reminder; if a woman still did not respond, her general practitioner was contacted and the address checked. If it was known that the woman was no longer resident at the address recorded in the trial documents, the Primary Care Record Department at Grampian Health Board was contacted for the woman's new address, if available. A review of all casenotes was conducted during May 1996 (at least four years after initial trial management) to identify re-treatments, other surgical procedures and investigations. The time from a woman's initial surgical management to any re-treatment was recorded to the nearest month.		possible, high risk of bias for subjective outcomes Attrition bias Low risk, outcome data complete Reporting bias Low risk, outcomes stated in the objective were reported **Other information** Same study as Pinion 1994, Bhattacharya 1996. Included in the NMA. This publication did not report on outcomes relevant for the pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
al ablation for women with dysfunctional uterine bleeding who would otherwise have had a hysterectomy. **Study dates** These women received their initial trial management between October 1990 and April 1992 **Source of funding**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Grant support was provided by the Chief Scientist Office of the Scottish Office Department of Health, which also funds the Health Services Research Unit.					
Full citation Barrington, J. W., Arunkalaiv	**Sample size** N=50 (LNG-IUS= 25, endometrial balloon therapy= 25)	**Interventions** Twenty-five women had a LNG-IUS (Mirena, Schering Healthcare) inserted	**Details** Follow-up A pictorial menstrual chart was completed pre-operatively and again at 6 months post-	**Results** Outcome: Discontinuation due to AE LNG-IUS: 2/25	**Limitations** **Cochrane risk of bias tool** Selection bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
anan, A. S., Abdel-Fattah, M., Comparison between the levonorgestrel intrauterine system (LNG-IUS) and thermal balloon ablation in the treatment of menorrhagia, Eur J Obstet Gynecol Reprod Biol, 108, 72-4, 2003 **Ref Id** 549675	**Characteristics** Not reported **Inclusion criteria** -no malignant or pre-malignant pathology -menorrhagia refractory to medical therapy **Exclusion criteria** Any woman with a cavity length of >12 cm or subserous fibroids were excluded from the study.	aseptically in the out-patient department. The remaining 25 women underwent endometrial balloon therapy (Thermochoice, Gynecare) under a total intravenous anaesthetic in the day surgery unit. Pre-operative endometrial thinning was undertaken using Goseralin 3.6 mg (Zoladex, AstraZeneca) 1 month beforehand.	operatively. Statistical analysis Non-parametric tests (Mann-Whitney) were used.	TBA: NA Outcome: Mean Menstrual Blood Loss (PBAC) Baseline, mean (SD) LNG-IUS: 107 (95) TBA: 122 (74) Post-treatment, mean (SD) LNG-IUS: 31 (31) TBA: 61 (99)	Random sequence generation: unclear Allocation concealment: unclear Performance bias Blinding: unclear risk, blinding not possible but unclear how it might affect performance bias Detection bias Blinding: high risk, blinding not possible, high risk of bias for subjective outcomes Attrition bias Low risk, outcome data complete

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Country/ies where the study was carried out UK **Study type** RCT **Aim of the study** To compare the effectiveness of endometrial thermal ablation and the levonorgestrel intrauterin					Reporting bias Low risk, outcomes were not stated in objectives **Other information** Short report; limited data. Baseline characteristics of women not reported. Included in the NMA. This publication did not report on outcomes relevant for the pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
e system (LNG-IUS) in the managem ent of menorrhag ia. **Study dates** Not reported **Source of funding** Not reported					
Full citation Bhattachar ya, S., Cameron, I. M., Parkin, D.	**Sample size** **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Included in the NMA. This publication did not report on outcomes relevant for the

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
E., Abramovich, D. R., Mollison, J., Pinion, S. B., Alexander, D. A., Grant, A., Kitchener, H. C., A pragmatic randomised comparison of transcervical resection of the endometrium with endometrial laser ablation for the treatment of menorrhag					pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
ia, Br J Obstet Gynaecol, 104, 601-7, 1997 **Ref Id** 549651 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Bongers,M.Y., Bourdrez, P., Heintz,A.P., Brolmann, H.A., Mol,B.W., Bipolar radio frequency endometrial ablation compared with balloon endometrial ablation in dysfunctional uterine bleeding: impact on patients'	**Sample size** N= 115 **Characteristics** Bipolar group: N=75 mean age (SD): 42.2 (5.3) Dysmenorrhea: 49/75 Balloon group: N= 40 mean age (SD): 43.3 (3.9) Dysmenorrhea: 27/40 **Inclusion criteria** -Women with menorrhagia documented by a pictorial chart with a Higham score of 150 points or more were eligible for the trial	**Interventions** Women were treated with either bipolar radio frequency endometrial ablation (NovaSure, Novacept, Palo Alto, CA) or balloon endometrial ablation (ThermaChoice I, Gynecare, Johnson and Johnson, Somerville, NJ). Details on both procedures have been provided previously. We used the ThermaChoice I systema because systems by ThermaChoice were not available in Europe.	**Details** Follow-up Quality of Life Assessment: All patients were asked to complete quality of life questionnaires. The medical outcomes study Short-Form 36 (SF-36), the Rotterdam Symptom Checklist (RSCL), the Selfrating Depression Scale (SDS), the State-Trait Anxiety Inventory (STAI), and the structured clinical history questionnaire for menorrhagia were selected to evaluate quality of life. The SF-36 has been used as an indicator of healthrelated quality of life, and its reliability and validity are well documented. This questionnaire has proven to have the ability to measure the effcts of treatment on quality of life in women suffering from menorrhagia.	**Results** Outcome: Health-related quality of life (SF-36) SF-36: Physical functioning, mean (SD) At baseline Bipolar group: 82 (19) Balloon group: 83 (16) At 1 year Bipolar group: 91 (18) Balloon group: 88 (21) SF-36: Role physical At baseline Bipolar group: 79 (30) Balloon group: 73 (27) At 1 year Bipolar group: 94 (28) Balloon group: 89 (24) SF-36: Role emotional	**Limitations** **Cochrane risk of bias tool** Selection bias Random sequence generation: computer generated Allocation concealment: opaque sealed envelopes Performance bias Blinding: patients blinded to surgical technique used Detection bias Blinding: investigating doctors unaware of randomization Attrition bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
health-related quality of life, Fertility and Sterility, 83, 724-734, 2005 **Ref Id** 98526 **Country/ies where the study was carried out** The Netherlands **Study type** RCT **Aim of the**	-Saline infusion sonography or diagnostic hysteroscopy were required to confirm a normal uterine cavity with histological benign endometrium and a uterine depth between 6 and 11 cm **Exclusion criteria** Women who had intracavitary abnormalities were not included in the study.			At baseline Bipolar group: 85 (26) Balloon group: 80 (26) At 1 year Bipolar group: 99 (5) Balloon group: 95 (15) SF-36: Social functioning At baseline Bipolar group: 76 (19) Balloon group: 76 (21) At 1 year Bipolar group: 89 (16) Balloon group: 86 (21) SF-36: Mental health At baseline Bipolar group: 72 (18) Balloon group: 72 (18)	Low risk, outcome data complete Reporting bias Low risk, outcomes stated in the objective were reported **Other information** Participating women were those choosing endometrial ablation after being counselled on many options (medical and surgical) for menorrhagia. Included in the NMA. This publication did not report on outcomes relevant for the

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
study To compare health-related quality of life (HRQoL) after bipolar radio frequency ablation and thermal balloon ablation in women with dysfunctional uterine bleeding. **Study dates** November				At 1 year Bipolar group: 80 (18) Balloon group: 80 (18) SF-36: Energy At baseline Bipolar group: 56 (19) Balloon group: 54 (20) At 1 year Bipolar group: 73 (1) Balloon group: 64 (21) SF-36: Pain At baseline Bipolar group: 62 (20) Balloon group: 63 (22) At 1 year Bipolar group: 76 (24) Balloon group: 77 (25)	pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
1999 until June 2001 **Source of funding** Not reported				SF-36: General health At baseline Bipolar group: 76 (19) Balloon group: 76 (21) At 1 year Bipolar group: 81 (18) Balloon group: 75 (23)	
Full citation Cooper,K. G., Bain,C., Lawrie,L., Parkin,D.E., A randomised comparison of microwave	**Sample size** **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Included in the NMA. This publication did not report on outcomes relevant for the pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
endometrial ablation with transcervical resection of the endometrium; follow up at a minimum of five years, BJOG: An International Journal of Obstetrics and Gynaecology, 112, 470-475, 2005 **Ref Id** 98676 **Country/ies where**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
the study was carried out **Study type** **Aim of the study** **Study dates** **Source of funding**					
Full citation Goldrath,M.H., Evaluation of HydroThermAblator and rollerball	**Sample size** N= 276 (Rollerball= 89, Hydrotherm Ablator= 187) **Characteristics** Pretreatment PBAC scores (range 173–2370, median 490), age (range 30–50 yrs,	**Interventions** Participants received a single injection of depot leuprolide acetate 7.5 mg on day 21 ± 2 of their cycle. Treatment was scheduled between 19 and 27 days	**Details** The primary end point of the study at 12 months after treatment was reduction of PBAC scores to 75 or less (established by the FDA) between HTA treatment group and the control group (rollerball). Aquality of life questionnaire4 was administered for	**Results** Outcome: Surgical Complication: Cervical Lacerations Rollerball group: 2/ 89 Hydrotherm Ablation group: 0/ 187	**Limitations** **Cochrane risk of bias tool** Selection bias Random sequence generation: computer permuted blocks

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
endometrial ablation for menorrhagia 3 Years after treatment, Journal of the American Association of Gynecologic Laparoscopists, 10, 505-511, 2003 **Ref Id** 98968 **Country/ies where the study was carried out**	median 40 yrs), and bodymass index (range 17–45.8 kg/m2, median 29 kg/m2). **Inclusion criteria** -age 30 to 50 years, -childbearing completed, -history of at least 3 months of excessive bleeding documented by a pictorial bleeding assessment chart (PBAC), -uterine cavity measuring between 4 and 10.5 cm, -and failed, not tolerated, or refused medical therapy **Exclusion criteria** -active or symptomatic pelvic inflammatory disease, -intramural myomas greater that 4 cm,	later, provided menses had ensued. HTA Intervention After the cervix is dilated to accept the insulated hysteroscopic sheath (7.8 mm outer diameter; Figure 2), which accommodates hysteroscope telescopes 3 mm or smaller, flow of room-temperature saline is started to allow visualization of the cervical canal and uterine cavity. As a safety feature, the HTA system is calibrated to detect loss of as little as 10 ml of saline from closed-loop circulation, so care	pretreatment and posttreatment secondary analyses. Patients visited the treating physician for follow-up 2 weeks and 3, 6, and 12 months after treatment. Further follow-up was done at 2 and 3 years after treatment through interviews if patients were not examined.	Outcome: Post-op Infection: Endometritis or UTI Rollerball group: 3/89 HTA group: 7/187 Outcome: PBAC <100 at 12 months Rollerball group: 71/83 HTA group: 137/ 167 Outcome: PBAC <100 at 24 months Rollerball group: 68//74 HTA group: 139/ 151 Outcome: PBAC <100 at 36 months Rollerball group: 62/68	Allocation concealment: unclear Performance bias Blinding: unclear Detection bias Blinding: unclear Attrition bias Low risk, outcome data complete Reporting bias Low risk, outcomes stated in the objective were reported **Other information** At 1 year, 12 patients who had received complete

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
USA **Study type** RCT **Aim of the study** To compare the safety and efficacy of endometrial ablation using HydroThermAblator (HTA) and rollerball (RB) for treatment of menorrhagia. **Study**	-submucosal myomas or polyps, -fully septate uterus	is taken to not overdilate the cervix to ensure a good seal. Diagnostic hysteroscopy is performed with the HTA sheath to ensure absence of unrecognized pathology, and to identify the tubal ostia as landmarks indicating that the sheath has not been placed in a false passage. Only then is heating of circulating saline begun, with a therapy cycle of 10 minutes. On completion of the therapy cycle, the operator is prompted to wait for the 1-minute cooling cycle to finish, followed by a prompt that the		HTA group: 127/ 135 Outcome: Patient Satisfaction at 36 months Rollerball: 97% HTA: 98%	treatment were lost to follow-up, 10 (5.6%) from the HTAgroup, including 2 accidental deaths unrelated to surgery, and 2 (2.4%) from the rollerball group. Two patients in the HTA group had hysterectomies during the first year, which provided a per protocol population of 250 patients (167 HTA, 83 rollerball) at 12 months. At 2 years, the per protocol population was 220 patients (151 HTA, 74 rollerball), and overall, 203 (77%) of the original 262 patients treated per protocol (135 HTA,

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
dates Not reported **Source of funding** Supported by BEI Medical Systems, a Boston Scientific Company, Natick, Massachusetts. The author has a financial interest in the HydroThermAblator.		sheath may be removed from the patient. Hysteroscopic visualization is maintained throughout the procedure, allowing full appreciation of blanching caused throughout the cavity, even in the presence of cavity asymmetry. Rollerball Not described.			68 rollerball) were available for evaluation of clinical efficacy data at 3 years.
Full citation	**Sample size** Please see Loffer 2002.	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Grainger, D. A., Tjaden, B. L., Rowland, C., Meyer, W. R., Thermal balloon and rollerball ablation to treat menorrhagia: two-year results of a multicenter, prospective, randomized, clinical trial, J Am Assoc Gynecol Laparosc, 7, 175-9,	**Characteristics** **Inclusion criteria** **Exclusion criteria**				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
2000 **Ref Id** 549702 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**					
Full citation Hehenkam	**Sample size** N= 177 UAE= 88, Hysterectomy=	**Interventions** UAE Patients were	**Details** Randomization After written informed consent	**Results** Outcome: Surgical blood loss	**Limitations** **Cochrane risk of bias tool**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
p, W. J., Volkers, N. A., Donderwinkel, P. F., de Blok, S., Birnie, E., Ankum, W. M., Reekers, J. A., Uterine artery embolization versus hysterectomy in the treatment of symptomatic uterine fibroids (EMMY trial): peri- and postprocedural results from a randomize	89 **Characteristics** UAE Group Mean age (SD): 44.6 (4.8) Mean BMI (SD): 26.7 (5.6) Previous treatment: none 12.5%, surgical 19.3%, hormonal 67%, NSAID/TXA 51.1% % with menorrhagia: 100% % with dysmenorrhea: 53.4% Median # fibroids (range)= 2 (1-20) Median uterine volume (range)= 321 cm3 (31-3005) Median fibroid volume (range)= 59 cm3 (1-673)	advised to discontinue any GnRH analogues treatment at least 1 month before the UAE. UAE was performed in all participating hospitals. The first 2 to 3 procedures were supervised by an interventional radiologist (J.R.) with ample experience in UAE. All radiologists were experienced in intervention radiology, including various embolization techniques in general. At the start of the study UAE was not a routine procedure for all radiologists. Seven radiologists were considered	had been obtained the attending gynecologist contacted the trial bureau by telephone, where the patient was registered and randomly assigned (1:1) to UAE or hysterectomy, using a computer-based minimization scheme (‘balancing procedure’), and stratified for study center. The randomization result was recorded electronically. Follow-up Complications were classified as ‘‘major’’ when the events were potentially life-threatening, could lead to permanent sequelae, or required surgical intervention. Other complications were listed as ‘‘minor.’’ Nausea, pain, and fever were considered ‘‘general’’ complications. Whenever a definite cause of fever was identified (eg, urinary tract infection), this was listed under minor or major complications, using the criteria described above.	UAE group: Mean (SD): 30.9 mL (23.8) Hysterectomy group: Mean (SD): 436.1 mL (474.5) Outcome: Anemia requiring transfusion UAE: 0/81 Hyst: 10/75 Outcome: Pulmonary Embolism or Thrombosis UAE: 1/81 Hyst: 1/75 Outcome: Return to theatre at 6 weeks UAE: 1/81 (due to fibroid expulsion requiring re-intervention) Hyst: 0/75	Selection bias Random sequence generation: computer-based minimization scheme Allocation concealment: by centralized trial bureau Performance bias Blinding: unclear but unlikely due to obvious difference between treatments Detection bias Blinding: unclear but unlikely due to obvious difference between treatments Attrition bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
d controlled trial, Am J Obstet Gynecol, 193, 1618-29, 2005 **Ref Id** 549631 **Country/ies where the study was carried out** The Netherlands **Study type** RCT **Aim of the study**	Hysterectomy Group Mean age (SD): 45.4 (4.2) Mean BMI (SD): 25.4 (4.0) Previous treatment: none 16.9%, surgical 12.4%, hormonal 66.3%, NSAID/TXA 46.1% % with menorrhagia: 100% % with dysmenorrhea: 56.2% Median # fibroids (range)= 2 (1-9) Median uterine volume (range)= 313 cm3 (58-3617) Median fibroid volume (range)= 87 cm3 (4-1641) **Inclusion criteria** 1) the clinical diagnosis of	experienced in UAE group having performed >10 UAE procedures) and 19 interventional radiologists had less experience in UAE (having performed less than 10 UAE procedures). Patients received an intravenous line and a Foley catheter before UAE. UAE was performed under local or epidural/ spinal anesthesia. The use of analgesics and antibiotics was not standardized. Femoral artery access could be unilateral or bilateral. A 4-F or 5-F catheter was introduced into the femoral artery and advanced over the	All UAE patients were routinely telephoned by the gynecologist 1 week after discharge to inquire about their health status. At the first routine visit (6 weeks after the procedure), complications after discharge, unscheduled visits, readmissions, and reinterventions were recorded. Statistics Study outcomes were analyzed according to original treatment assignment (intention to treat). Differences in baseline characteristics were tested with multiple logistic regression analysis. Differences in complications between groups were expressed in absolute numbers, rates, and relative risks (RR) with 95% CI. Differences in hospital stay were tested with the Mann-Whitney U test. Differences in categorical data were compared with c2-tests or Fisher exact tests if appropriate. We also	Outcome: Infection at 6 weeks (endometritis or UTI) UAE: 7/81 Hyst: 2/75	Low risk, outcome date complete Reporting bias Low risk, outcomes stated in the objective were reported **Other information** All women were to be scheduled for hysterectomy. N type of hysterectomy performed in hysterectomy group: Open: 63 Vaginal: 9 Laparoscopic: 2 Laparoscopic

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
This was a randomized controlled trial to evaluate the safety of uterine artery embolization (UAE) compared with hysterectomy. **Study dates** Patients were enrolled between March 2002 and February 2004. **Source of**	uterine fibroids had been confirmed by ultrasonography; 2) menorrhagia (subjectively reported by the patient as increased or prolonged menstrual blood loss which causes dysfunction in daily life) was their predominant complaint, among other possibly fibroid-related signs and symptoms; 3) they were premenopausal; 4) they were to be scheduled for a hysterectomy. Whenever other treatment options were still available, women were not asked to participate, but were treated otherwise.	aortic bifurcation to the contralateral internal iliac artery to identify the origin of the uterine artery. In case of spasm, the policy was to wait, but a microcatheter and/or spasmolytics could be used within the study protocol. When catheters were placed correctly, the actual embolization was carried out. Polyvinyl alcohol particles (PVA, Contour, Boston Scientific, Beek, The Netherlands) with a size of 355 to 500 mm, were used. Only if an anastomosis with the ovarian artery was observed were	investigated the effect of experience of the radiologist and hospitals perfoming UAE on technical failure, complications, and readmission. A P-value of <0.05 was considered statistically significant.		assisted vaginal: 1

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
funding The Emmy study is funded by ZonMw 'Netherlands Organisation for Health Research and Development' (grant application number 945-01-017), and supported by Boston Scientific Corporation, The Netherlands.	**Exclusion criteria** 1) preservation of the uterus was warranted for future pregnancy; 2) renal failure (creatinine O150 mmol/L), active pelvic infection, or clotting disorders were clinically established; 3) they were allergic to contrast material; 4) uterine malignancy was suspected; 5) submucosal fibroids with 50% of their diameter within the uterine cavity or dominant pedunculated serosal fibroids were present	500 to 700 mm particles used. PVA, mixed with contrast medium and saline, was injected into each uterine artery until parenchyma filling of the fibroids had stopped (target embolization), or until the main uterine artery was blocked with stasis of contrast (selective embolization). After the procedure, groin pressure was applied for 10 to 15 minutes. Hysterectomy The type of hysterectomy and the route of access were left at the discretion of the attending			

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
		gynecologist in order to keep as close to daily practice as possible. The following procedures were allowed: abdominal hysterectomy, either by median or a pfannenstiel incision, vaginal hysterectomy, laparoscopically assisted vaginal hysterectomy (LAVH), and laparoscopic hysterectomy. Both supravaginal and total hysterectomies were allowed. We used no guidelines for: antibiotic prophylaxis; type of anesthesia; removal or ablation of endocervical tissue in the supravaginal hysterectomy group;			

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
		concomitant adnexal surgery; wound closure; evaluation and treatment of fever; or hospital discharge criteria.			
Full citation Loffer, F. D., Three-year comparison of thermal balloon and rollerball ablation in treatment of menorrhagia, J Am	**Sample size** Please see Loffer 2002 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Assoc Gynecol Laparosc, 8, 48-54, 2001 **Ref Id** 549704 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of funding**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Loffer, F. D., Grainger, D., Five-year follow-up of patients participating in a randomized trial of uterine balloon therapy versus rollerball ablation for treatment of menorrhagia, J Am Assoc Gynecol Laparosc, 9, 429-35,	**Sample size** N= 255 Followed for 3 years: 214* (147 available to be interviewed at 5 years of follow-up). **Characteristics** Demographics of each group similar for all characteristics.* **Inclusion criteria** -menorrhagic -premenopausal -no evidence of cervical or uterine malignancy -no uterine anatomic abnormalities -desired no further fertility **Exclusion criteria**	**Interventions** No medical pre-treatment. Suction curettage performed for both procedures.* Rollerball Endometrial Ablation: Rollerball was performed by experienced hysteroscopists using standard hysteroscopic instruments and a low-viscosity distention medium.** Thermal Balloon Ablation (Thermachoice): Balloon catheter	**Details** Follow-up One, two, three and five years follow-up. Patients kept record of menstrual blood loss through pictorial diary (PBAC method). Women were also required to complete a questionnaire regarding impact on life, dysmenorrhea, and satisfaction with treatment. 5-year follow-up was not originally planned. 12 of 14 centres agreed to participate. Each participant received an introductory letter from her physician explaining the purpose of the follow-up study. A questionnaire regarding menstrual status, dysmenorrhea, pelvic pain, satisfaction, and additional gynecologic treatments or conditions was administered.	**Results** Outcome: Cervical Laceration* UBT: 0/ 131 RB: 1/124 Outcome: Uterine Perforation* UBT: 0/ 131 RB: 1/124 Outcome: Post-op infection: Endometritis or UTI* UBT: 4/131 RB: 1/124 Outcome: Menstrual Blood Loss at 1 year** UBT: 85.5% decrease in PBAC	**Limitations** **Cochrane risk of bias tool** Selection bias Random sequence generation: unclear Allocation concealment: unclear Performance bias Blinding: unclear risk, blinding not possible but unclear how it might affect performance bias Detection bias Blinding: high risk, blinding not possible, high risk of bias for

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
2002 **Ref Id** 549705 **Country/ies where the study was carried out** USA and Canada **Study type** RCT **Aim of the study** To collect long-term follow-up information from women who	-malignancy -genital tract infection -those who had undergone previous ablation -submucosal myomas*	inserted into the uterine cavity and filled with sterile 5% dextrose in water. The heating element of the balloon was heated to 87 degrees Celsius. An 8-minute cycle at 87 degrees ablated endometrial tissue. At completion of the heat cycle, the fluid inside the balloon was withdrawn and the balloon catheter was removed from the uterus.*		RB: 97.1% decrease in PBAC Outcome: Patient Satisfaction at 1-year** Participants reporting satisfied or very satisfied with the procedure at 2 years. UBT: 96% Rollerball: 99.1% Outcome: Patient Satisfaction at 2-years** Participants reporting satisfied or very satisfied with the procedure at 2 years. UBT: 95.9% Rollerball: 98.1%	subjective outcomes Attrition bias Low risk, outcome data complete Reporting bias Low risk, outcomes stated in the objective were reported **Other information** Same trial as Meyer 1998, Grainger 2000, Loffer 2001 3-year, 5-year bleeding was self-reported not validated measure.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
participated in a randomized trial comparing uterine balloon therapy or rollerball ablation. **Study dates** January and September 1996** **Source of funding** Supported in part by Gynecare (division of Ethicon).				Outcome: Patient Satisfaction at 3-years* Participants reporting satisfaction with the procedure at 3 years. UBT: 109/114 Rollerball: 97/100 Outcome: Patient Satisfaction at 5 years Participants reporting satisfaction with the procedure at 5 years. UBT: 57/61 Rollerball: 61/61 *data extracted from Loffer 2001*	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				data extracted from Grainger 2000	
Full citation Pinto, I., Chimeno, P., Romo, A., Paul, L., Haya, J., de la Cal, M. A., Bajo, J., Uterine fibroids: uterine artery embolization versus abdominal hysterectomy for treatment--a	**Sample size** Please see Gupta 2014 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
prospective, randomized, and controlled clinical trial, Radiology, 226, 425-31, 2003 **Ref Id** 549760 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Source of funding					
Full citation van Zon-Rabelink, I. A., Vleugels, M. P., Merkus, H. M., de Graaf, R., Endometrial ablation by rollerball electrocoagulation compared to uterine balloon thermal ablation. Technical	**Sample size** N= 139 (Roller ball n=62; thermal balloon ablation n=77) **Characteristics** Both groups were comparable regarding age and length of the uterine cavity. Baseline characteristics of participants NR. **Inclusion criteria** -Patients with menorrhagia without sufficient relief by medical therapy prescribed by the general practitioner	**Interventions** All patients were pre-treated with goserelin acetate (Zoladex) 6 and 2 weeks prior to the rollerball endometrial ablation to reduce endometrial thickness, uterine volume and vascularity. All patients were hospitalised 1 day to standardise both procedures and to observe them during 24 h. To prevent uterine cramping premedication of 100 mg diclofenac	**Details** Statistics Within each of both treatment groups relations between operative characteristics have been studies by using Spearman's rank correlation analyses. Comparing both groups with respect to operative complications, technical complications, post-operative complaints and medication needed, has been done by Fisher's exact tests for a 2x2 table. Comparison of both groups with respect to the operation time was carried out by the two-sample Student t-test and checked by means of Satterthwaite's approximation for the degrees of freedom. Subsequently for examining	**Results** Outcome: Surgical Complication: perforation of uterus Rollerball group: 3/62 Thermal balloon ablation group: 0/77 Outcome: Post-Op Infection Rollerball group: 1/62 Thermal balloon ablation group: 0/77	**Limitations** **Cochrane risk of bias tool** Selection bias Random sequence generation: unclear Allocation concealment: sealed envelope technique Performance bias Blinding: unclear Detection bias Blinding: unclear Attrition bias Low risk, outcome

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
and safety aspects, Eur J Obstet Gynecol Reprod Biol, 110, 220-3, 2003 **Ref Id** 549677 **Country/ies where the study was carried out** The Netherlands **Study type** RCT **Aim of the**	-PBAC score was 185 points or more in two periods. -The blood loss was due to dysfunctional uterine bleeding according to ultrasound and diagnostic hysteroscopy **Exclusion criteria** Not reported.	(Voltaren) suppository was given. All procedures were done by one hysteroscopically skilled gynecologist (Michel P.H. Vleugels) and using general anaesthesia. The endometrial ablation by the rollerball was performed with a 9 mm hysteroscope and 75 Wof electrocoagulation. The Thermachoice uterine balloon therapy catheter had a 4.5 mm diameter and a latex balloon with a heating element at its distal end. Before insertion into the uterine cavity the balloon was	more carefully a difference in operation time an analysis of covariance was applied including cavity length and an indicator variable for the presence of operative or technical complications, as covariables. Allowing heterogeneity of slope also an interaction between treatment group and cavity length was incorporated in this model.		data complete Reporting bias Low risk, outcomes stated in the objective were reported; other outcomes reported elsewhere **Other information** Same trial as van Zon-Rabelink 2004.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
study To compare two methods of endometrial ablation, hysteroscopic rollerball electrocoagulation (RBE) and non-hysteroscopic uterine balloon thermal (UBT) ablation regarding intra- and post-operative technical complications and safety		checked for leakage. After intrauterine insertion the balloon was filled with 5% dextrose water up to the mean starting pressure of 167±8 mm Hg. After pre-heating the fluid temperature to 87±5C, the treatment cycle of 8 min commenced. For safety, the device automatically deactivated when pressure fell below 45 mm Hg or reached above 200 mm Hg.			

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
aspects. **Study dates** Not reported. **Source of funding** Not reported.					
Full citation Vihko, K. K., Raitala, R., Taina, E., Endometrial thermoablation for treatment of menorrhag	**Sample size** **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information** Included in the NMA. This study compared two types of thermal balloon ablation techniques, therefore, not included in the pairwise analysis.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
ia: comparison of two methods in outpatient setting, Acta Obstet Gynecol Scand, 82, 269-74, 2003 **Ref Id** 549625 **Country/ies where the study was carried out** **Study type** **Aim of the study**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study dates **Source of funding**					
Full citation Zupi, E., Zullo, F., Marconi, D., Sbracia, M., Pellicano, M., Solima, E., Sorrenti, G., Hysteroscopic endometrial resection versus laparoscop	**Sample size** N= 181 **Characteristics** Endometrial resection group: N=89 Mean age (SD): 43.2 (3.5) Mean BMI (SD): 35.6 (1.4) Mean uterine volume (SD): 315 cm3 (43) Dysmenorrhea: 37% Hysterectomy group:	**Interventions** Endometrial resection Patients randomized were treated by a depot formulation of a gonadotropin-releasing hormone antagonist (GnRH-a), 3.75 mg, 1 month before surgery. HER was performed by means of a rigid resectoscope equipped with a 12-degree fore-oblique telescope and a	**Details** Follow-up The follow-up visits were at 3 months and 1 and 2 years, when patients were checked for hemoglobin levels and queried about pain and bleeding patterns. The patients completed the SF-36 on quality-of-life issues, administered by a nurse blinded to the assigned treatment, before treatment and after 1 year of follow-up. No specific assessment for premenstrual syndrome or pelvic pain was done. Statistics The statistical analysis was	**Results** Outcome: Patients requiring blood transfusion post-op Endometrial resection: 0/89 Hysterectomy: 2/92 Outcome: Hospital stay (days) Endometrial resection: Mean (SD): 1.3 (1.1) Hysterectomy: Mean (SD): 1.6 (1.5)	**Limitations** **Cochrane risk of bias tool** Selection bias Random sequence generation: computer-generated randomization sequence Allocation concealment: unclear Performance bias Blinding: unclear risk, blinding not

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
ic supracervical hysterectomy for menorrhagia: a prospective randomized trial, Am J Obstet Gynecol, 188, 7-12, 2003 **Ref Id** 549635 **Country/ies where the study was carried out** Italy **Study**	N=92 Mean age (SD): 42.6 (4.4) Mean BMI (SD): 34.5 (1.9) Mean uterine volume (SD): 295 cm3 (58) Dysmenorrhea: 41.3% **Inclusion criteria** -The patients had to be younger than the age of 50 years -weigh less than 100 kg -not be seeking conception -normal endometrial histology -a Papanicolaou (Pap) smear documented within the previous 12 months. **Exclusion criteria**	loop electrode introduced into the uterine cavity after a dilatation up to Hegar probe No. 9. The cavity was distended with a nonconductive hypo-osmolar solution of 2.7% sorbitol and 0.54% mannitol instilled under manometric control, with a pressure of 100 to 120 mm Hg generated by a pneumatic cuff and a vacuum of 30 mm Hg to 0 was applied for suction. After careful inspection of the cavity, the endometrium was resected with a cutting waveform unipolar current. The mucosa of the cornual areas was	performed with the use of a commercial software program STATISTICA for Windows (Statsoft, Inc, Tulsa, Okla). Differences in age, parity, and body mass index (BMI) between groups were compared with the use of the two-tailed Student t-test for unpaired data. Preoperative basal values were compared with the postoperative value in each group with a Student t test for paired data. Postoperative complications were compared using the Chi2 test. A repeated measures analysis of variance (ANOVA) was performed to detect differences in the postoperative pain score and satisfaction profile between the two groups. Operative time differences, estimated blood loss, duration of symptoms, and mean discharge time were compared with the use of the Wilcoxon rank sum test. P-value of <0.05 was defined as statistically significant.	Outcome: Post-op urinary infection Endometrial resection: 1/89 Hysterectomy: 1/92 Outcome: Quality of Life: SF-36 General health Endometrial resection (baseline/post-tx): 51.9 (12.7)/ 59.6 (13.7) Hysterectomy (baseline/post-tx): 52.1 (12.1)/69.4 (14.3) Physical functioning Endometrial resection (baseline/post-tx): 62.6 (14.4)/ 66.4 (15.1)	possible, unclear how it might affect performance bias Detection bias Blinding: high risk, blinding not possible for participants, high risk of bias for subjective outcomes, however, nurse administrating follow-up blinded to treatment group Attrition bias Low risk, outcome date complete Reporting bias Low risk, outcomes stated in the objective were reported

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
type RCT **Aim of the study** This study was undertaken to compare the relative efficacy and safety of hysteroscopic endometrial resection and laparoscopic supracervical hysterectomy in the treatment of	-size of the uterus more than 12 weeks of pregnancy size -without submucosal fibroids, adnexal masses, or endometriosis.	then treated in a radial fashion with a ball electrode starting from the tubal ostia and withdrawing the electrode toward the surgeon slowly. Vaporization was then completed on the fundus and the remaining cavity down the isthmus. Hysterectomy= Laparoscopic Supracervical LSH was performed under a pneumoperitoneum ranging from 12 to 15 mm Hg, using a 10-mm, 0-degree umbilical scope, an adequate uterine manipulator, two lateral ancillary 5-mm ports, and a 12-		Hysterectomy (baseline/post-tx): 62.8 (10.9)/67.6 (13.2) Role functioning (phys) Endometrial resection (baseline/post-tx): 58.3 (13.0)/ 61.3 (14.8) Hysterectomy (baseline/post-tx): 59.2 (15.4)/62.1 (13.9) Role functioning (emo) Endometrial resection (baseline/post-tx): 60.8 (12.0)/ 64.2 (14.4) Hysterectomy (baseline/post-tx): 60.3 (11.9)/68.1 (15.2) Mental health Endometrial resection (baseline/post-tx): 58.1 (12.3)/ 60.5 (14.8) Hysterectomy	**Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
abnormal uterine bleeding. **Study dates** Not reported **Source of funding** Not reported		mm suprapubic trocar. After careful inspection of the pelvis and upper abdomen, all associated lesions (adhesions, endometriosis, and ovarian cysts) were removed. Bipolar forceps and scissors were used for round ligaments and either uteroadnexal pedicle or infundibulopelvic ligament, depending on the clinical choice for adnexectomy or not. The uterovesical fold was incised and dissected and the uterine vessels clearly exposed before bipolar excision at the level of the bifurcation		(baseline/post-tx): 59.8 (12.9)/63.2 (13.6) Social functioning Endometrial resection (baseline/post-tx): 56.4 (11.0)/ 67.3 (12.7) Hysterectomy (baseline/post-tx): 53.6 (9.7)/88.5 (11.5) Vitality Endometrial resection (baseline/post-tx): 56.7 (11.0)/ 61.0 (12.8) Hysterectomy (baseline/post-tx): 55.4 (10.3)/72.3 (11.3) Pain Endometrial resection (baseline/post-tx): 57.1 (19.2)/ 58.6 (17.0) Hysterectomy (baseline/post-tx): 56.4	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
		between ascending and cervical branches. The uterus was then transversally cut by scissors or a unipolar flat electrode. A Vicryl (Ethicon, Somerville, NJ) 1 loop was applied at the time of uterine probe extraction and the uterus was removed by means of an automatic morcellator (ranging from 12- to 20-mm diameter). After the cavity was washed, hemostasis was achieved with bipolar forceps on the cervical stump.		(18.5)/60.1 (14.0)	
Full citation	**Sample size**	**Interventions**	**Details**	**Results**	**Limitations**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Cooper, K. G., Parkin, D. E., Garratt, A. M., Grant, A. M., A randomised comparison of medical and hysteroscopic management in women consulting a gynaecologist for treatment of heavy menstrual loss, British Journal of Obstetrics	Total randomised N= 187 (Medication=94, TCRE=93) At 4 month follow up N=186 (Medication= 93, TCRE=93) **Characteristics** Mean Age Medical: 41.4 (5.2) TCRE: 41.7 (5.2) Almost 80% in each group were employed with about 30% requiring time off work because of menstrual symptoms. Similar numbers had heavy menstrual flow for more than one year (78% and 84%, respectively) while 24/82 women (29%) in the medical arm and 22/85 (26%) in the surgical arm had haemoglobin levels of	Women are randomly allocated to either group on 1:1 basis. Women allocated surgery received an injection of the gonadotrophin releasing hormone analogue, goserelin 3.6 mg. Five weeks later they were admitted under the care of one of the three participating gynaecologists who performed hysteroscopic surgery. Transcervical resection of the endometrium was performed under general anaesthesia using rollerball coagulation to the fundus and cornua	Sample size calculation Based on expected satisfaction rates of approximately 80% at four to six months after transcervical resection of the endometrium, it was calculated that a minimum of 180 women would be required to have 80% power to detect an absolute difference of 20% at the 5% level of significance Randomisation and allocation concealment Women were randomly allocated to either ‘transcervical resection’ or ‘medical treatment’ by opening sealed, serially numbered, opaque envelopes; the order was determined by computer generated random numbers within balanced blocks of twenty. The actual choice of medical treatment, which should not have been used by the patient before as treatment for heavy menstrual loss was	See NMA.	**Cochrane risk of bias tool** Selection bias Random sequence generation: Low risk Allocation concealment: Low risk Performance bias Blinding of participants and personnel: Unclear risk blinding was not possible due to the nature of the interventions, however, not clear if it can introduce performance bias. Detection bias Blinding of outcome

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
& GynaecologyBr J Obstet Gynaecol, 104, 1360-6, 1997 **Ref Id** 590837 **Country/ies where the study was carried out** United Kingdom **Study type** Randomised controlled trial **Aim of the**	less than 12 g/dL. 22% of women had received no previous medical treatment, 56% one, and 22% two different treatments, from their general practitioner. 60% of women in both arms reported self treatment with analgesics perimenstrually. Overall, baseline anxiety scores were elevated (8.96 and 8.85) whereas depression scores were in the normal range (5.62 and 5.32) **Inclusion criteria** 1) if consulting a gynaecologist for the first time with a complaint of heavy menstrual loss 2) their family was complete 3) they had a clinical	with resection of the cavity walls using a 90°, 7 mm diameter loop, with 1.5% glycine solution as the distending medium For women receiving medical treatment, Progestogens were prescribed from day 12-25, or 5-25 if there was also dysmenorrhoea. The combined oral contraceptive pill preparations recommended were second generation containing 30 pg oestradiol. Tranexamic acid was prescribed at a dose of 1 g four times a day for the first five days of the period in women	selected by the senior gynaecologist responsible for the clinic and continued for at least three cycles Blinding The treatment was revealed to the patient because of the different nature of treatments. Blinding of outcome assessor not reported Follow-up All women but one were assessed at follow up at an average of nineteen weeks following TCRE or starting medication Outcome measure The main outcomes were Treatment satisfaction and acceptability, relief of symptoms, change in haemoglobin, and improvement in health related quality of life, all after four months.		assessment: High Riskisk Blinding of outcome assessors not reported and most probably not done Attrition bias Incomplete outcome data: Low risk Only 1 patient was loss to follow up after 4 months in whole trial. Intention to treat used. Reporting bias Selective reporting: Low risk All outcomes reported Other bias Other sources of

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
study To compare medical with hysteroscopic management in women referred to a gynaecologist complaining of heavy menstrual loss **Study dates** October 1994 - September 1995 **Source of funding**	diagnosis of dysfunctional uterine bleeding (uterus less than ten weeks pregnancy size and normal endometrial pathology) and had not been referred specifically for surgery 4) They also had to be willing to be randomised to either medical or hysteroscopic management. **Exclusion criteria** Not reported	with regular periods, with mefenemic acid 500 mg three times a day added if there was associated dysmenorrhoea. Danazol was prescribed at a dose of 200 mg per day continuously for 90 days	Statistical analysis Analysis was by intention-to-treat. Independent and paired t tests were used for continuous variables (independent and related) with a normal distribution and the Mann-Whitney U test for ordinal or non parametric continuous variables. The x2 test was used for independent nominal data and McNemars test for paired data describing dichotomous variables. Secondary analyses were stratified according to the number of medical treatments used prior to gynaecological referral.		bias: - **Other information** Please see Marjoribanks 2016 Cochrane systematic review. Included in NMA, this publication only reported on outcomes relevant for the NMA.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
This trial was undertaken as part of a research training fellowship awarded by the Scottish Office Department Health.					
Full citation Dwyer, N., Hutton, J., Stirrat, G. M., Randomised controlled trial	**Sample size** Please see Fergusson 2013 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
comparing endometrial resection with abdominal hysterectomy for the surgical treatment of menorrhagia, British Journal of Obstetrics & GynaecologyBr J Obstet Gynaecol, 100, 237-43, 1993 **Ref Id** 590838 **Country/ies where the study**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
was carried out **Study type** **Aim of the study** **Study dates** **Source of funding**					
Full citation Sculpher, M. J., Dwyer, N., Byford, S., Stirrat, G. M., Randomised trial comparing	**Sample size** Same trial as Dwyer 1993. Please see Fergusson 2013 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
hysterectomy and transcervical endometrial resection: effect on health related quality of life and costs two years after surgery, British Journal of Obstetrics & GynaecologyBr J Obstet Gynaecol, 103, 142-9, 1996 **Ref Id** 590841					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Country/ies where the study was carried out **Study type** **Aim of the study** **Study dates** **Source of funding**					
Full citation O'Connor, H., Broadbent, J. A., Magos, A. L.,	**Sample size** Tandomised: N=202, n=68 hysterectomy; n=134 TCRE Received allocated treatment: n=57 hysterectomy; n=119 TCRE	**Interventions** Patients were randomly assigned hysterectomy or TCRE at the time of recruitment in the clinic, in most cases several	**Details** Randomisation and allocation concealment Individuals were assigned TCRE and hysterectomy in a ratio of two to one because little information was available about	**Results** Outcome: Patient satisfaction with treatment NMA outcome	**Limitations** **Cochrane risk of bias tool** Selection bias Random sequence generation: Low

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
McPherson, K., Medical Research Council randomised trial of endometrial resection versus hysterectomy in management of menorrhagia, Lancet, 349, 897-901, 1997 **Ref Id** 594099 **Country/ies where the study was carried out**	Followed-up at 3 months: n=56 hysterectomy; n=116 TCRE Followed-up at 1 year: n=46 hysterectomy; n=104 TCRE Followed-up at 2 years: n=38 hysterectomy; n=86 TCRE Followed-up at 3 years: n=28 hysterectomy; n=54 TCRE **Characteristics** Age in years, mean (SD) Hysterectomy: 39.4 (4.8) TCRE: 40.1 (4.7) Parous, n (%) Hysterectomy: 52 (92.9) TCRE: 113 (97.4)	weeks before their planned surgery. Both types of surgery were done by staff proficient in TCRE or hysterectomy techniques. In the case of TCRE, operators were required to have at least 20 successful procedures; hysterectomy had to be done by or be supervised by an experienced surgeon. Individual clinicians were permitted to decide whether to use pharmacological agents to thin the endometrium before resection. TCRE involved resection	the hysteroscopic procedure and this protocol was felt to assist recruitment.A computer-generated random-number sequence was used, the code for which was kept at the Royal Free Hospital, London. When making appointments for surgery, the recruiting physician telephoned the coordinating centre and patients were given the next treatment on the randomisation schedule. Blinding Not feasible due to the nature of the interventions. Follow-up Patients were reviewed 3 months after surgery in the local outpatient clinic by the surgical team and then by a structured, multiple-choice-type postal questionnaire at 12, 24, and 36	Outcome: Uterine perforation Hysterectomy: N/A TCRE: 3/116 Outcome: Blood transfusion Hysterectomy: 4/56 TCRE: 1/116 Outcome: Length of hospital stay in days, mean (SD) Hysterectomy: 6.3 (1.9) TCRE: 1.3 (1.2) Outcome: Sepsis before discharge Hysterectomy: 2/56	risk Allocation concealment: Low risk Performance bias Blinding of participants and personnel: Unclear risk, blinding not feasible due to the nature of the interventions, however, unclear how that might affect performance bias. Detection bias Blinding of outcome assessment: High risk, blinding was not feasible due to the nature of the interventions, high risk of bias in the

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
UK **Study type** RCT **Aim of the study** To test the hypothesis that the proportion of patients dissatisfied and requiring further gynaecological surgery within 3 years of endoscopic management would be no	Duration of symptoms in years, mean (SD) Hysterectomy: 7.3 (6.3) TCRE: 6.2 (5.8) Previous treatment, n (%) Hysterectomy: 49 (83.9) TCRE: 108 (93.1) **Inclusion criteria** Women who had symptomatic menorrhagia that required hysterectomy and who fulfiled the entry criteria for the study were invited to participate. Eligible women were aged 30–50; had decided to have no more children; had regular menstrual cycles of between 21 and 35 days,	or rollerballing of the uterine fundus and tubal ostia, followed by resection of the remainder of the uterine cavity to the endocervical canal with a modified urological resectoscope. In some units, women were offered the option of TCRE with local anaesthesia.20 Hysterectomy was done according to standard surgical techniques. The decision as to whether the patient was given abdominal or vaginal hysterectomy was made by the operating clinican	months. The primary endpoints were patient satisfaction with the results of treatment and the avoidance of further gynaecological surgery. Patient satisfaction with the results of treatment was scored on a scale of 0–4 (0=very satisfied, 1=satisfied, 2=not sure, 3-dissatisfied, 4=very dissatisfied). Secondary outcome measures included operative and postoperative complications, duration of hospital stay, time taken to return to normal activities and work, time to resume sexual intercourse, unrelated gynaecological and other symptoms, and use of primary-health-care services. Psychiatric and social assessments by the three questionnaires were repeated	TCRE: 0/116 Outcome: Sepsis after discharge (unclear how long after) Hysterectomy: 16/56 TCRE: 9/116 Outcome: Unplanned additional surgery before discharge Hysterectomy: 3/56 TCRE: 0/116 Outcome: Cervical tear Hysterectomy: 0/56 TCRE: 2/116	subjective outcomes (patient satisfaction). Attrition bias Incomplete outcome data: Low to high risk depending on the time of follow-up Low loss of follow-up for outcomes assessed soon after procedure but high loss to follow-up (50% or more) for outcome assessed at 3 years. Reporting bias Selective reporting: Low risk Other bias Other sources of bias: -

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
more than 15% greater than the proportion after hysterectomy. **Study dates** Not reported. **Source of funding** The study was funded by a project grant from the Medical Research Council, UK.	with each period lasting for less than 50% of the cycle; and had documented evidence of normal endometrial histology within the previous 12 months and normal cervical smear within the previous 3 years. **Exclusion criteria** Serious intercurrent illness; intermenstrual or postcoital bleeding; uterine size corresponding to pregnancy of more than 12 weeks' gestation; submucosal fibroids more than 5 cm in diameter; adnexal tenderness that is suggestive of pelvic inflammatory disease or endometriosis; major uterovaginal prolapse or severe urinary symptoms; and severe premenstrual	based on clinical factors and personal preference and was not influenced by patient preference.	at the same times. Statistics Analysis was done by intention to treat. Sample size calculation 200 women were planned to recruit to the study based on the expectations that about 5% of patients undergoing hysterectomy would need further gynaecological surgery;16 20% of those undergoing TCRE would be dissatisfied and need further surgery; the probability of a type 1 statistical error (two-sided) was less than 0·05; the probability of a type 2 statistical error was less than 0·1;21 and the drop-out rate after randomisation would be 10%.		**Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	syndrome or menopausal symptoms.				
Full citation Cooper, K. G., Jack, S. A., Parkin, D. E., Grant, A. M., Five-year follow up of women randomised to medical management or transcervical resection of the endometrium for heavy	**Sample size** Please see Marjoribanks 2016 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
menstrual loss: clinical and quality of life outcomes, BJOG, 108, 1222-8, 2001 **Ref Id** 594100 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates** **Source of**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
funding					
Full citation Cooper, K. G., Parkin, D. E., Garratt, A. M., Grant, A. M., Two-year follow up of women randomised to medical management or transcervical resection of the endometrium for heavy menstrual	**Sample size** Please see Marjoribanks 2016 Cochrane systematic review. **Characteristics** **Inclusion criteria** **Exclusion criteria**	**Interventions**	**Details**	**Results**	**Limitations** **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
loss: clinical and quality of life outcomes, Br J Obstet Gynaecol, 106, 258-65, 1999 **Ref Id** 594101 **Country/ies where the study was carried out** **Study type** **Aim of the study** **Study dates**					

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Source of funding					

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