NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of uterine artery embolisation for treating adenomyosis

Treating adenomyosis by blocking the blood supply to affected parts of the uterus

Adenomyosis is a condition where some of the lining tissue of the womb grows into its outer muscular layer: this can cause heavy and painful menstrual periods.

Uterine artery embolisation involves injecting small particles into the blood vessels that take blood to the uterus, via arteries in the groin. The aim is to block the blood supply to the adenomyosis so that it shrinks, which may then relieve the symptoms.

Introduction

The National Institute for Health and Care Excellence (NICE) has prepared this overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in April 2013.

Procedure name

- Uterine artery embolisation for treating adenomyosis

Specialist societies

- British Society of Interventional Radiology
- Royal College of Obstetricians and Gynaecologists
- Royal College of Radiologists

Description

Indications and current treatment

Adenomyosis is a benign condition characterised by presence of ectopic endometrial glands and stroma within the myometrium. Adenomyosis frequently occurs coincidentally with fibroids. Adenomyosis may cause no symptoms but some women with adenomyosis experience heavy, prolonged menstrual bleeding with severe cramps, pelvic pain and discomfort.

Treatment for symptomatic adenomyosis includes anti-inflammatory medications, hormone therapy or endometrial ablation. For severe symptoms that do not respond adequately, hysterectomy has been the conventional surgical treatment. Uterine artery embolisation may be an alternative option for patients who do not wish to have hysterectomy and/or who wish to preserve their fertility.

What the procedure involves

The aim of uterine artery embolisation for treating adenomyosis is to block the blood supply to the adenomyosis causing it to shrink. The intended benefits of the procedure are that it offers a less invasive alternative to hysterectomy and fertility may be preserved.

With the patient under sedation and local anaesthesia, a catheter is inserted into the femoral artery (bilateral catheters are sometimes used). Fluoroscopic guidance is used to manipulate the catheter into the uterine artery. Small embolisation particles are injected through the catheter into both uterine arteries until cessation of blood flow is achieved.

Various embolisation agents can be used for this procedure.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to uterine artery embolisation for treating adenomyosis. Searches were conducted of the following databases, covering the period from their commencement to 25 April 2013: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with adenomyosis.
Intervention/test	Uterine artery embolisation.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on 234 patients from 7[1-6] case series and 2 case reports[7-9].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on uterine artery embolisation for treating adenomyosis

Abbreviations used: HRQoL, health-related quality of life; NS, not significant; PVA, polyvinyl alcohol; QoL, quality of life; UAE, uterine artery embolisation; UFS, uterine fibroid symptom.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Kim MD (2007)[1]
Case series
Korea
Recruitment period: 1998-2000
Study population: patients with symptomatic adenomyosis without fibroids. Presenting symptoms: bulk-related symptoms – 43% (23/54); number of patients presenting with menorrhagia -78% (42/54)

n=54
Age: mean 40 years; range 29 to 49 years

Patient selection criteria: Eligibility not restricted by age or by whether adenomyosis was of the focal or diffuse type. Women who wanted to become pregnant were not excluded but were informed on uncertain effects of UAE on fertility.

Technique: embolisation with varying sizes (250-500 µm) of PVA particles (Contour, Boston Scientific) was carried until there was complete</td>
<td>Number of patients analysed: varied by outcome
Resolution of menorrhagia
At ‘short- term’: 92.9% (39/42)
<table>
<tr><td>At ‘long-term’ follow-up</td><td>% (n/39)</td></tr>
<tr><td>additional resolution</td><td>25.6 (10)</td></tr>
<tr><td>no change</td><td>43.6 (17)</td></tr>
</table>
Resolution of bulk-related symptoms (n=23)
<table>
<tr><td></td><td>% (n)</td></tr>
<tr><td>complete resolution</td><td>34.8 (8)</td></tr>
<tr><td>marked resolution</td><td>47.8 (11)</td></tr>
<tr><td>no change</td><td>17.4 (4)</td></tr>
</table>
Number of patients with improvement (complete and marked resolution): 82.6%(19) was significant (p<0.001).
Improvement of symptoms (mean symptom scores)
<table>
<tr><td></td><td>Before the procedure</td><td>At long-term follow-up</td><td>Difference in score[a]</td></tr>
<tr><td>menorrhagia</td><td>10</td><td>4.7</td><td>5.3</td></tr>
<tr><td>dysmenorrhoea</td><td>10</td><td>4.9</td><td>5.1</td></tr>
</table>
[a]the change in scores was statistically significant (p<0.001)
Symptom recurrence - 38% (19/50) at long-term follow-up; 5 patients underwent hysterectomy because of symptom recurrence. No further details reported for the remaining patients. Time between UAE and recurrence ranged from 4 to 48 months.
Treatment failure (defined as unsuccessful embolisation or no resolution of symptoms after UAE)
• 7.4% (4/54) patients had ‘immediate’ treatment failure. At short-term follow-up, 2 patients were regarded as having treatment failure because of lack of resolution of</td>
<td>Amenorrhoea
Amenorrhoea was reported in 3.7% (2/54) of patients (aged 41 and 44 years) immediately after UAE.
Menopause was reported in 9 patients at long-term follow-up (mean age 48.3 years). Mean time to menopause after UAE was 2.9 years.

Worsening of symptoms
30.8% (12/39) reported worse symptoms of menorrhagia at long-term follow-up.</td>
<td>Follow-up issues:
• 12patients lost to follow-up (not related to procedure).
Study design issues:
• Retrospective review of prospective collected database.
• Of 66 patients eligible, patients with follow-up period of 3 years or longer were enrolled in the study.
• Symptom status scored on a scale ranging from 0 (defined as little bleeding or no pain during menstrual period) to 10 (initial symptoms of menorrhagia or pain). Baseline symptom score was not assessed; the score was set as 10.
• Bulk-related symptoms assessed on a 5 category scale: complete resolution, marked improvement, slight improvement, no change or worse condition.
• Presence of recurrence: based on an operational definition, considered presence of recurrent symptoms after initial improvement after UAE with a >4 change in score between long-term and short-term follow-up symptom score or the patient felt they had a recurrence regardless of the difference in symptom score.

Study population issues:
• Diagnosis of adenomyosis established by MRI.</td>
</tr>
</table>

Abbreviations used: HRQoL, health-related quality of life; NS, not significant; PVA, polyvinyl alcohol; QoL, quality of life; UAE, uterine artery embolisation; UFS, uterine fibroid symptom.			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
cessation of blood flow in the ascending uterine artery with residual flow in the lower uterine segment. Secondary supplemental embolisation with gelatin sponge pledgets was performed in all cases. Follow-up: **mean 5 years** Short-term: 3.5 months Conflict of interest/source of funding: not reported	symptoms. • 38% (19/50) patients had relapses at long-term follow-up. • There were no technical failures resulting from inability to catheterise the uterine artery. **Pregnancy** Of 5 patients who achieved uneventful intrauterine pregnancies- 3 patients elected to carry to full term and had uneventful deliveries (2 patients opted for termination as unwanted pregnancies). There was no evidence of uteroplacental vascular insufficiency or abnormal uterine contraction during labour or post-partum. **Patient satisfaction** (at long-term follow-up) 70% (35/50) of patients were satisfied at long-term follow-up (64.8% if treatment failures were included). 37% (7/19) of patients with recurrences were satisfied for the following reasons: less severe symptoms, pregnancy, long symptom-free period, and delay of hysterectomy.		Other issues: • Embolisation effects according to different size of PVA particles (250-355µm; 500-710µm; 355-500 µm) were also reported. A significant difference was reported in abnormal bleeding (symptom score) at short-term follow-up.

Abbreviations used: HRQoL, health-related quality of life; NS, not significant; PVA, polyvinyl alcohol; QoL, quality of life; UAE, uterine artery embolisation; UFS, uterine fibroid symptom.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Smeets AJ (2012)[2]
Case series
Netherlands
Recruitment period: 1999-2006
Study population: patients with adenomyosis with or without associated fibroids. Presenting symptoms were: abnormal bleeding- 95% (38/40); pain-63%(25/40); and pressure-33%(13/40)
n=40 (18 with pure adenomyosis)
Age: mean 44 years; range 31 to 51 years

Patient selection criteria: Treatment offered to patients who wished to preserve the uterus.

Technique: UAE was performed after selective catheterisation of both uterine arteries. Different sizes (500-700µm ;700-900 µm of embospheres (Biosphere Medical) were used, with smaller sizes preferred in women with pure adenomyosis.
Follow-up: mean 65 months
Conflict of interest/source of funding: none</td>
<td>Number of patients analysed: 40
Improvement in symptoms (assessed by standardised questionnaire at mean 65 months)
<table>
<tr><th>Symptoms</th><th>Pure adenomyosis %(n) (n=18)</th><th>Adenomyosis and fibroids; %(n) (n=22)</th></tr>
<tr><td>Bleeding</td><td>82 (14/17)</td><td>76 (16/21)</td></tr>
<tr><td>Pain</td><td>100 (9/9)</td><td>73 (16/22)</td></tr>
<tr><td>Bulk-related symptoms</td><td>73(11/15)</td><td>69 (11/16)</td></tr>
</table>
No change in symptoms:
• In patient with pure adenomyosis, symptoms were unchanged in 17% (3/17) of patients who presented with bleeding and 27% (4/15) of patients who presented with bulk-related symptoms.
• In patients with adenomyosis and fibroids, symptoms were unchanged in 24% (5/21) of patients who presented with bleeding , 27% (6/22) of patients who had pain and 31%
(5/16) patients who presented with bulk-related symptoms.
Additional therapy (because of insufficient symptom relief): 20% (8/40)
• Hysterectomy: 7 patients (3 with pure adenomyosis). 5 of these hysterectomies occurred within 18 months after UAE; 2 occurred after >5 years after UAE.
• Second UAE : in 1 patient with adenomyosis and fibroids (timing unclear).
UFS-QoL (in n=33 patients during follow-up). Baseline scores not reported.
Overall QoL: mean 90 (SD 13); symptom severity: mean 14(SD 20).
• 29 patients had symptom severity scores <20 in combination with overall health-related QoL scores >80,</td>
<td>Complications (timing unclear):
• Transient increased vaginal discharge was reported in 7.5% (3/40) patients.
• Transient amenorrhoea was reported in 1 patient (age 38 years)
• Permanent amenorrhoea was reported in 5%(2/40) of patients (age 40 and 44 years).

There were no procedural complications.</td>
<td>Study design issues:
• Retrospective review of prospectively collected data; consecutively enrolled patients
• The UFS-QOL is a disease-specific questionnaire that assesses symptom severity and HRQL in patients with uterine fibroids. It consists of an 8-item symptom severity scale and 29 HRQoL items comprising 6 domains: Concern, Activities, Energy/Mood, Control, Self-consciousness, and Sexual Function. Each question asks how much distress is experienced from each symptom during the previous 3 months All items are scored on a 5-point Likert scale, ranging from "not at all" to "a very great deal" for symptom severity items and "none of the time" to "all of the time" for the HRQoL items. Symptom severity and HRQoL subscale scores are summed and transformed into a 0–100 point scale. The Symptom Severity scale and HRQoL subscale scores are inversely related with higher Symptom Severity scores indicating greater symptoms while higher HRQoL subscale scores indicate better QoL.

Study population issues:
• Diagnosis of adenomyosis established by history, clinical examination, and MRI.</td>
</tr>
</table>

Abbreviations used: HRQoL, health-related quality of life; NS, not significant; PVA, polyvinyl alcohol; QoL, quality of life; UAE, uterine artery embolisation; UFS, uterine fibroid symptom.			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
	indicating they were asymptomatic. • 4 patients had symptom severity scores of 50-85 and overall QoL scores of 60-66, indicating substantial clinical symptoms.		• All patients had insufficient clinical response to progestogens, haemostatic agents or gonadotrophin releasing hormone agonists. **Other issues:** • Number of patients presenting with pain was 25; results presented for 31 patients.

Abbreviations used: HRQoL, health-related quality of life; NS, not significant; PVA, polyvinyl alcohol; QoL, quality of life; UAE, uterine artery embolisation; UFS, uterine fibroid symptom.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Froeling V (2012)[3]
Case series
Germany
Recruitment period: 2001-9
Study population: patients with adenomyosis with or without uterine leiomyomata
n=40
Age: median 46 years; range 39 to 56 years
Patient selection criteria: Premenopausal woman with dominant menorrhagia, dysmenorrhoea with or without bulk symptoms, confirmed diagnosis of isolated uterine adenomyosis or coexisting with uterine leiomyomata, not desiring to become pregnant. Patients with active pelvic inflammatory disease, undiagnosed pelvic mass, pregnant, or renal insufficiency were excluded.

Technique: Under local anaesthesia, bilateral UAE with tris-acryl gelatin (Embosphere, Biosphere Medical), PVA (Contour, Boston Scientific/Medi-Tech) or acryl-amido PVA microspheres (BeadBlock, Biocompatibles) were carried out ; access was via common</td>
<td>Number of patients analysed: 40
Clinical failure (defined as no improvement in all categories of symptom severity or needing second invasive therapy)
27.5% (11/40) of patients (5 with pure adenomyosis) clinically failed to respond to therapy resulting in unchanged, worsened, markedly worsened symptoms, or resulting in the need for surgical reintervention (hysterectomy, n=10; dilatation and curettage, n=1). Timing of follow-up to second intervention: median 23 months (range 5 to 69).
Residual symptom severity and HRQoL scores (assessed using UFS-QoL; median 40 months)
<table>
<tr><th>Adenomyosis type (n)</th><th>Symptom severity score</th><th>HRQoL</th></tr>
<tr><td>Pure adenomyosis (11)</td><td>3.1(0 to 28.1)</td><td>94.8 (71.6 to 100)</td></tr>
<tr><td>Adenomyosis dominant (19)</td><td>0 (0 to 6.3)</td><td>99.1 (94 to 100)</td></tr>
<tr><td>Leiomyoma dominant (9)</td><td>0 (0 to 9.4)</td><td>100 (95.3 to 100)</td></tr>
</table>
Data reported as median (25th to 75th percentile).
Change in symptoms
<table>
<tr><th>Symptoms: before the procedure %(n)</th><th>After the procedure %(n)</th></tr>
<tr><td>Menorrhagia: 90%(36/40)</td><td>77.7% (28/36) resolved; 11.1% (4) improved markedly; 2.7% (1) improved; 8.8% (3) clinical failure.</td></tr>
<tr><td>Dysmenorrhoea: 85%(34/40)</td><td>67.6% (23/34) resolved [this was reported as 73.5%]; 17.6% (6) markedly improved; 5.9% (2) improved; 8.8%(3) no improvement.</td></tr>
<tr><td>Bulk symptoms: 75% (30/40)</td><td>73.3 %(22/30) resolved;13.3%(4) marked improvement; 6.7% (2) improvement; 6.6% (2) failed to respond; 3.3%(1) no improvement.</td></tr>
</table>
</td>
<td>No complications occurred during treatment or hospital stay.</td>
<td>Study design issues:
• Retrospective review of prospectively collected database.
• QoL assessed using UFS-QoL: a 37 item questionnaire (29 on HRQoL and 8 on type and residual severity of symptoms) assessing distress associated with each symptom during previous 3 months; scores range from 0-100, with higher scores indicating greater symptom severity. Clinical follow-up symptom severity score was assessed by a questionnaire on the following options for each symptom category: resolved, markedly improved, improved, unchanged, worsened, markedly worsened.
• No baseline evaluation of HRQoL
• Presence of clinical symptoms at baseline assessed on a yes/no basis.

Study population issues:
• Pure adenomyosis (defined as adenomyosis in the absence of uterine leiomyomata) was identified in 11 patients. If leiomyomata was present and <5 cm it was defined as dominant adenomyosis (n=19) or if >4 cm leiomyoma dominant (n=9). 1 patient was not classifiable to one of the subgroups.
• Diagnosis of adenomyosis established with MRI.
Other issues:
• 30 patients presented with bulk symptoms at baseline; result</td>
</tr>
</table>

<table>
<tr><td colspan="4">Abbreviations used: HRQoL, health-related quality of life; NS, not significant; PVA, polyvinyl alcohol; QoL, quality of life; UAE, uterine artery embolisation; UFS, uterine fibroid symptom.</td></tr>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr><td>femoral artery.

Follow-up: median 40 months

Conflict of interest/source of funding: none</td><td>Mean cumulative survival free from reintervention and time to second intervention<table><tr><td>Adenomyosis type</td><td>Mean cumulative survival free from reintervention %(SD)</td><td>Time to second intervention (months) Mean (range)</td></tr><tr><td>Pure adenomyosis</td><td>48(17)</td><td>80 (65 to 95)</td></tr><tr><td>Adenomyosis dominant</td><td>58 (14)</td><td>68 (48 to 88)</td></tr></table>None of the patients with uterine leiomyomata predominance had a clinical failure.</td><td></td><td>presented for 31 patients</td></tr>
</table>

Abbreviations used: HRQoL, health-related quality of life; NS, not significant; PVA, polyvinyl alcohol; QoL, quality of life; UAE, uterine artery embolisation; UFS, uterine fibroid symptom.

<table>
<tr>
<th>Study details</th>
<th>Key efficacy findings</th>
<th>Key safety findings</th>
<th>Comments</th>
</tr>
<tr>
<td>Bratby MJ (2009)[4]
Case series
UK
Recruitment period: 1998-2004
Study population: patients with symptomatic adenomyosis
n=27 (14 with associated fibroids)
Age: mean 46 years; range 39 to 56 years

Patient selection criteria: included patients for whom the only alternative treatment offered was hysterectomy and wished to preserve their uterus if possible.

Technique: UAE using non-spherical PVA (Contour, Boston Scientific) was injected until flow in the uterine artery ceased. All patients treated with 355-500 µm PVA particles.

Follow-up: 3 years

Conflict of interest/source of funding: not reported</td>
<td>Number of patients analysed: varied at different time points
Change in symptoms- menorrhagia
<table>
<tr><th>Timing-months; (n)</th><th>Complete resolution %(n)</th><th>Improved but not resolved %(n)</th><th>Same %(n)</th></tr>
<tr><td>6 (n=18)</td><td>44 (8)</td><td>44(8)</td><td>12(2)</td></tr>
<tr><td>12 (n=16)</td><td>29(5)</td><td>50(8)</td><td>7(1)</td></tr>
<tr><td>24 (n=11)</td><td>36.3(4)</td><td>18.2(2)</td><td>0</td></tr>
<tr><td>36(n=11)</td><td>18.2(2)</td><td>36.3(3)</td><td>0</td></tr>
</table>
Change in symptoms- dysmenorrhoea
<table>
<tr><th>Timing-months</th><th>Complete resolution %(n)</th><th>Improved but not resolved %(n)</th><th>Same %(n)</th></tr>
<tr><td>6 (n=18)</td><td>38(7)</td><td>38(7)</td><td>18(3)</td></tr>
<tr><td>12 (n=16)</td><td>57(9)</td><td>36(6)</td><td>7(1)</td></tr>
<tr><td>24 (n=11)</td><td>36.3(4)</td><td>45.5(5)</td><td>9.1(1)</td></tr>
<tr><td>36(n=11)</td><td>63.6(7)</td><td>18.2(2)</td><td>0</td></tr>
</table>
Change in symptoms- bulk symptoms
<table>
<tr><th>Timing-months</th><th>Complete resolution %(n)</th><th>Improved but not resolved %(n)</th><th>Same %(n)</th></tr>
<tr><td>6 (n=18)</td><td>38(7)</td><td>38(7)</td><td>18(3)</td></tr>
<tr><td>12 (n=16)</td><td>31(5)</td><td>44(7)</td><td>25(4)</td></tr>
<tr><td>24 (n=11)</td><td>45.5(5)</td><td>36.3(4)</td><td>9.1(1)</td></tr>
<tr><td>36(n=11)</td><td>54.5(6)</td><td>36.3(3)</td><td>9.1(1)</td></tr>
</table>
Treatment failure</td>
<td>Amenorrhoea
4 patients (age range 50-56 years) were amenorrhoeic following UAE because of onset of menopause (all had reported an improvement in bulk symptoms).

Worsening of symptoms
<table>
<tr><th>Timing-months; (n)</th><th>Menorr-hagia %(n)</th><th>Dysmen-orrhoea %(n)</th><th>Bulk-sympt oms %(n)</th></tr>
<tr><td>6 (n=18)</td><td>0</td><td>6(1)</td><td>6(1)</td></tr>
<tr><td>12 (n=16)</td><td>14(2)</td><td>0</td><td>0</td></tr>
<tr><td>24 (n=11)</td><td>45.5(5)</td><td>9.1(1)</td><td>9.1(1)</td></tr>
<tr><td>36 (n=11)</td><td>54.5(6)</td><td>18.2(2)</td><td>9.1(1)</td></tr>
</table>
None of the women who reported worsened symptoms chose hysterectomy but 3 patients opted for hormonal therapy/levenorgesterol to help with symptom relief.</td>
<td>Follow-up issues:
• Lack of completeness in follow-up data
Study design issues:
• Retrospective review of data collected as part of prospective study on UAE for fibroids.
• Non validated questionnaire used to assess severity of symptoms on a 4-point scale (none, mild, moderate or severe symptoms).
• Data on presenting symptoms was available in 78% (21/27) of patients.

Study population issues:
• Adenomyosis was diagnosed by MRI and confirmed histologically by transvaginal scan in 5 patients.18 patients had diffuse adenomyosis, 8 focal adenomyosis and not classified in 1 patient.</td>
</tr>
</table>

Abbreviations used: HRQoL, health-related quality of life; NS, not significant; PVA, polyvinyl alcohol; QoL, quality of life; UAE, uterine artery embolisation; UFS, uterine fibroid symptom.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr><td></td><td>

1 patient (in whom one of the arteries could not be catheterised because of a ‘sharp kink’) underwent hysterectomy (2 months after UAE). The patient had not shown any improvement in symptoms.
Another patient underwent hysterectomy at 8 months following UAE because of lack of clinical response.

Severity scores-(n= 14 ; patients with pure adenomyosis (n=6) and remaining in patients with associated fibroids) timing: range 24-65 months. (extracted from graph)
<table>
<tr><th></th><th>Menorrhagia (n)</th><th>Dysmen-orrhoea (n)</th><th>Bulk symptoms[a] (n)</th></tr>
<tr><td>None</td><td>0</td><td>1</td><td>2</td></tr>
<tr><td>Mild</td><td>2</td><td>8</td><td>7</td></tr>
<tr><td>Moderate</td><td>7</td><td>8</td><td>9</td></tr>
<tr><td>Severe</td><td>12</td><td>4</td><td>3</td></tr>
</table>
[a]bulk symptoms: abdominal swelling, urinary frequency, constipation and sciatica.
[results are reported separately for patients with pure adenomyosis; but only available for 6 patients as 7 had not reached the 2 years post UAE follow-up]
</td><td></td><td></td></tr>
</table>

Abbreviations used: HRQoL, health-related quality of life; NS, not significant; PVA, polyvinyl alcohol; QoL, quality of life; UAE, uterine artery embolisation; UFS, uterine fibroid symptom.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Lohle PNM (2007)[5]
Case series
Netherlands; Germany
Recruitment period: 2001-4

Study population: patients with symptomatic adenomyosis with or without uterine leiomyomas. Presenting symptoms (self-reported) were heavy menstrual bleeding in 97% (37/38), pelvic pain in 79% (30/38), bulk-related symptoms in 39% (15/38).

n=38 (Group A: 15 patients had adenomyosis only; Group B: 14 patients had adenomyosis dominance and fibroid tumours; Group C: 9 patients had adenomyosis and fibroid tumour dominance).

Age: mean 45 years

Patient selection criteria: Patients with adenomyosis with or without fibroids, self-reported heavy menstrual bleeding, pain and/or bulk-related symptoms for which they had insufficient results when previously treated with medical therapy or conservative surgery were included. Exclusion criteria were postmenopausal status, malignancy, pregnancy and</td>
<td>Number of patients analysed: varied for different outcomes

Complete resolution of symptoms (%[n]) (mean 18 months)
<table>
<tr><th>Symptoms (n ; before UAE)</th><th>Group A (n=12)</th><th>Group B (n=12)</th><th>Group C (n=8)</th></tr>
<tr><td>Bleeding (n=31)</td><td>58.3 (7/12)</td><td>66.7 (8/12)</td><td>42.9 (3/7)</td></tr>
<tr><td>Pain (n=24)</td><td>66.7(6/9)</td><td>70 (7/10)</td><td>40(2/5)</td></tr>
<tr><td>Bulk-related (n=15)</td><td>66.7(2/3)</td><td>66.7(4/6)</td><td>100(6/6)</td></tr>
</table>
Symptoms‘improved in the remaining patients except for pain symptoms in 1 patient in Group C.

The 3 groups did not differ significantly in number of patients reporting complete resolution or improvement of symptoms.

Additional procedures
15.8%(6/38) of patients had additional therapy:
• 1 patient (with pure adenomyosis) underwent adenomyoma resection(13 months after UAE)
• 5 patients (2 with pure adenomyosis) had a hysterectomy because of lack of resolution or improvement of symptoms (between 8 and 34 months after UAE).

Patient satisfaction (at mean 18 months)
• Very satisfied: Group A:83.3%; Group B: 75%; Group C:50%
• Unsatisfied: 6 patients (who had underwent additional surgery)
• The remaining patients reported they were satisfied with</td>
<td>Major complications
(defined as events requiring immediate additional therapy or resulting in permanent adverse sequelae or death)
There were no procedure-related mortality, events requiring immediate additional therapy or hysterectomy.
Permanent amenorrhoea was reported in 15.6% (5/32) of patients (45 years of age or older) in patient who did undergo additional therapy

Minor complications
• Transient amenorrhoea was reported in 32%(8/25) of patients after UAE.
• Spontaneous ‘tumour’ expulsion was reported in 15.6% (5) of patients (timing 3 to 6 months after UAE).
• Pain symptoms in 1 patient in Group C worsened after UAE.</td>
<td>Follow-up issues:
• Patients who underwent a major intervention (n=6) were censored from further follow-up.
Study design issues:
• Prospective study enrolling all eligible consecutive women at 2 centres
• Clinical response assessed using a standardised questionnaire. Patients classified changes in bleeding symptoms, pain and bulk-related symptoms as worsened, unchanged, improved, or resolved.
• Overall satisfaction was scored as very satisfied, satisfied or not satisfied. Authors noted that this scale was asymmetric and skewed in a positive direction.
Study population issues:
• Diagnosis of adenomyosis established with MRI.
• Number of patients with bulk-related symptoms before UAE differed significantly between the 3 groups.</td>
</tr>
</table>

Abbreviations used: HRQoL, health-related quality of life; NS, not significant; PVA, polyvinyl alcohol; QoL, quality of life; UAE, uterine artery embolisation; UFS, uterine fibroid symptom.			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
pedunculated fibroid tumours with a small stalk. Women seeking future fertility were not excluded Technique: Using local anaesthesia, UAE was done with tris-acryl gelatin microspheres (size 500-700 uµm in all cases; additional microspheres 700-900 µm were used in a few cases(Embosphere or EmboGold, Biosphere Medical, Inc.). the angiographic embolisation endpoint was defined as complete stasis of contrast agent in the ascending segment of the uterine artery. Follow-up: **mean 18 months** Conflict of interest/source of funding: 2 authors are consultants to Biosphere Medical, Inc, but did not receive any support from the company. None of the other authors identified a conflict of interest.	treatment.		

Abbreviations used: HRQoL, health-related quality of life; NS, not significant; PVA, polyvinyl alcohol; QoL, quality of life; UAE, uterine artery embolisation; UFS, uterine fibroid symptom.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Pelaje J-P (2005)[b]
Case series
France
Recruitment period: 1997-2002

Study population: premenopausal patients with symptomatic adenomyosis refractory to medical treatment. Presenting symptoms were menorrhagia in 94%(17/18) and pelvic pain or pressure in 61% (11/18) of patients.

n=18
Age: mean 44 years; range 35-57 years
Patient selection criteria: embolisation was offered as an alternative to hysterectomy in all women. Patients with associated uterine fibroids were excluded.

Technique: Under conscious sedation or spinal anaesthesia, unilateral (n=1) or bilateral UAE was performed using PVA particles of 300-500 µm(Contour, Boston Scientific) or 500-900 µm tris-acryl microspheres (EmboSphere, BioSphere Medical) microspheres using fluoroscopic guidance. Embolisation was stopped</td>
<td>Number of patients analysed: varied by time of follow-up
Change in symptoms
<table>
<tr><th>Follow-up (months)</th><th>Menorrhagia (n=17)</th><th>Pelvic pain and pressure (n=11)</th></tr>
<tr><td>5 (n=17)</td><td>Complete resolution: 50% (8/16); Improvement: 94% (15/16)</td><td>Improvement: 80%(8/10)</td></tr>
<tr><td>12 (n=16)</td><td>Complete resolution : 53% (8/15) Improvement:73%(11/15)</td><td>Improvement: 60%(6/10)</td></tr>
<tr><td>24 (n=9)</td><td>Complete resolution : 56% (5/9)</td><td>Improvement: 50% (3/6)</td></tr>
</table>
Duration of menses
<table>
<tr><th>Timing (months)</th><th>Days (mean [range])</th></tr>
<tr><td>baseline</td><td>9.2 (3 to 15)</td></tr>
<tr><td>5[a]</td><td>6.2 (3 to 15)</td></tr>
<tr><td>12[a]</td><td>6.5 (3 to 12)</td></tr>
<tr><td>24[a]</td><td>5.8 (3 to 8)</td></tr>
</table>
[a]mean duration of menses was significantly shorter than before UAE (p=0.002).

Further treatment: 44% (8/18) needed additional treatment for failure or recurrence.
• 28% (5 /18) of patients underwent hysterectomy
-1 patient underwent hysterectomy 3.9 months after UAE (considered an early treatment failure).
-4 patients underwent hysterectomy for recurrent symptoms at 9 (n=1), 13 (n=1), 25(n=1) and 27 months (n=1) after UAE and initial relief of symptoms.</td>
<td>
<table>
<tr><th>Complications</th><th>n</th></tr>
<tr><td>Pain (severe) (timing unclear)</td><td>89% (16/18)</td></tr>
<tr><td>Pain (moderate) (after embolisation)</td><td>2</td></tr>
<tr><td>Recurrent severe cramping pain(4 days after UAE)</td><td>1 (myometrial ischemia was observed; patient was treated by analgesia with full resolution of pain).</td></tr>
<tr><td>Moderate cramping pain[a]</td><td>4</td></tr>
<tr><td>Mild vaginal discharge[a]</td><td>2</td></tr>
<tr><td>Pelvic pain (without haematoma)[a]</td><td>1</td></tr>
</table>
[a]1 week after UAE; spontaneously resolved

No severe vaginal discharge, pelvic infection, or definitive amenorrhoea was observed after UAE.</td>
<td>Study design issues:
• Improvement in menorrhagia was assessed using a 6-point scale ranging from -2 (worsening of symptoms) to 3 (complete resolution). Pelvic pain and pressure were evaluated as ‘still present’ or ‘resolved’ after UAE. Pelvic pain evaluated 6 to 12 hours after UAE using a 3 level scale (no, moderate or intense pain)
• Patients were interviewed by telephone 1 week after UAE to elicit reports of incidents.

Study population issues:
• 14 patients had diffuse adenomyosis and 4 had focal adenomyosis.

Other issues
• Imaging done using transabdominal and endovaginal ultrasonography (n=6) or MRI (n=12) of the pelvis.</td>
</tr>
</table>

Abbreviations used: HRQoL, health-related quality of life; NS, not significant; PVA, polyvinyl alcohol; QoL, quality of life; UAE, uterine artery embolisation; UFS, uterine fibroid symptom.			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
when stasis or near statis was observed in the ascending segment of the uterine artery. Secondary embolisation with gelatin sponge pledgets (Spongel, Yamanuchi; CAPS Recherche) was carried out in 3 patients. Follow-up: 2 years (9 patients followed up for longer than 24 months; range 12-73 months) Conflict of interest/source of funding: One author is a consultant to and has received grants from BioSphere Medical and Boston Scientific. Another author is a patent owner for EmboSphere, manufactured by BioSphere Medical.	• 3 patients who still had improvement at 72 months and 73 monthsafter UAE: -1 patient needed endometrial balloon thermocoagulation. -2 needed medical treatment.		

Abbreviations used: HRQoL, health-related quality of life; NS, not significant; PVA, polyvinyl alcohol; QoL, quality of life; UAE, uterine artery embolisation; UFS, uterine fibroid symptom.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Siskin GP (2001)[7]
Case series
USA
Recruitment period: not reported
Study population: patients treated with UAE for menorrhagia in the presence of adenomyosis. All patients presented with abnormal uterine bleeding, 73.3% (11/15) patients presented with dysmenorrhoea, and 46.7% (7/15) presented with bulk-related symptoms, including abdominal distension and bladder compression with frequent urination.
n=15
Age: mean 47 years; range 37 to 56 years
Patient selection criteria:
Patients who had diagnosis of adenomyosis.
Technique: Arterial access was via right femoral artery, bilateral UAE was undertaken with PVA particles measuring 355-500 µm (Contour, Interventional Therapeutics) until stasis of flow was achieved.
Follow-up: mean 8 months (clinical follow-up)
Conflict of interest/source of funding: not reported.</td>
<td>Number of patients analysed: 13
Changes in QoL (median response); (n=13) (mean 8 months)
<table>
<tr><th>Variables</th><th>Before UAE</th><th>After UAE</th></tr>
<tr><td>Ability to perform activities of daily life[a]</td><td>7</td><td>2</td></tr>
<tr><td>Ability to socialise outside the home[a]</td><td>7</td><td>1</td></tr>
<tr><td>Overall energy level[a]</td><td>8</td><td>1</td></tr>
<tr><td>Pain or cramping during menstruation[a]</td><td>8</td><td>2</td></tr>
<tr><td>Interest in sexual intercourse[b]</td><td>7.5</td><td>3</td></tr>
<tr><td>Pain during sexual intercourse[c]</td><td>5.5</td><td>1</td></tr>
</table>
[a]p<0.001; [b]NS; [c]p=0.02
Symptomatic improvement:
92.3% (12/13) reported symptomatic improved at 3 month follow-up.
A statistically significant (p<0.05) improvement in the number of days of bleeding during menstrual cycle (actual numbers not reported) and time between changes of sanitary pads or tampons was reported.
Treatment failure
1 patient (with diffuse adenomyosis and multiple uterine fibroids) continued to experience heavy bleeding during menstrual period 4 months after UAE (the patient did not undergo any additional procedures).</td>
<td>Amenorrhoea
1 patient (with diffuse adenomyosis and no fibroids), who had initially presented with abnormal bleeding, had not resumed menstrual periods for 5 months after UAE.

Post-procedure symptoms, including pelvic pain, nausea and fever, occurred in all patients and were treated with medication.</td>
<td>Follow-up issues:
• 1 patient was lost to follow-up; reasons not reported.

Study design issues:
• Retrospective analysis.
• Patients selected embolisation as treatment option.
• QoL (self-assessment)- degree of severity or impairment assessed on a scale of 1 to 10, with 1 representing ‘no severity or impairment’ and 10 representing ‘severe severity or impairment’.

Study population issues:
• Patients included were initially diagnosed with uterine fibroids (based on sonography and clinical symptoms). Diagnosis of adenomyosis based on established MRI criteria. 9 patients had adenomyosis with one or more fibroids, 5 patients had diffuse adenomyosis without evidence of uterine fibroids, and 1 had focal adenomyosis without evidence of uterine fibroids.

• 3 patients underwent a trial of hormonal therapy before UAE. None of the patients underwent myomectomy or endometrial ablation for UAE.</td>
</tr>
</table>

Abbreviations used: HRQoL, health-related quality of life; NS, not significant; PVA, polyvinyl alcohol; QoL, quality of life; UAE, uterine artery embolisation; UFS, uterine fibroid symptom.			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Huang L-Y (2003)[8] **Case report** Taiwan Recruitment period: not reported Study population: patient with symptomatic adenomyosis with a 3 year history of severe dysmenorrhoea and heavy menorrhagia with anaemia. n=1 Age: 41 years old Technique: Bilateral UAE performed via right femoral artery using 10 ml 38% lipiodol followed by gelfoam pledgets. Conflict of interest/source of funding: not reported.	**Vaginal expulsion of a large focal pyoadenomyosis associated with sepsis and focal bladder necrosis** Patient presented with severe abdominal cramping, dysuria and fever 5 days after UAE. Blood culture showed *Escheria Coli* (treated by antibiotics and recovered by 16 days after UAE). Heavy vaginal discharge with a tender uterus and yellowish, foul odour leucorrhoea was reported at 19 days following UAE. Focal pyoadnomyosis had protruded to the cervix and was 'twisted out' with negligible bleeding on day 42. Symptoms of dysuria, leucorrhoea and cramping resolved completely by 49 days after UAE.		• Patient opted for UAE instead of hysterectomy. • Authors proposed that focal bladder necrosis secondary to UAE of uterine leiomyoma or adenomyosis may occur if: there is vascular communications between uterine and vesicle arteries and this may result in untargeted embolisation of bladder during UAE ; retention of lipiodol in the distal vessels of the non-target tissue may result in more ischaemia ; or if lipiodol escapes from uterine arteries. However, no flow of contrast into vesicle branches were observed in this study.

Abbreviations used: HRQoL, health-related quality of life; NS, not significant; PVA, polyvinyl alcohol; QoL, quality of life; UAE, uterine artery embolisation; UFS, uterine fibroid symptom.			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
MAUDE adverse event report[9] US FDA Date report accessed: 28 May 2013 Case report Adverse event occurred in 2004; reported in 2008. Technique: UAE with PVA microspheres	Patient experienced bruising and numbness on one side and has been unable to walk since the procedure (needing walking aids). Patient has continued to have severe hip pain with necrosis of the hip. Report noted adverse event 'required intervention'- no further details.		It is unclear if the patient underwent UAE for treatment of adenomyosis.

Efficacy

Resolution of menorrhagia

In a case series of 54 patients, with 78% (42/54) of patients presenting with symptoms of menorrhagia, resolution of symptoms was reported in 93% (39/42) of patients at 3 month follow-up and additional resolution of menorrhagia was reported in 26% (10/39) at mean follow-up of 5 years[1].

In a case series of 40 patients (90% [36/40] presenting with menorrhagia), symptoms had resolved in 78% (28/36) of patients at median follow-up of 40 months [3].

Resolution of dysmenorrhoea

In a case series of 27 patients, complete resolution of dysmenorrhoea was reported in 38% (7/18), 57% (9/16), 36% (4/11) and 64%(7/11) of patients at 6,12, 24 and 36 months respectively[4].

In the case series of 40 patients (85% [34/40] presenting with dysmenorrhea), symptoms had resolved in 68% (23/34) of patients at median 40 months follow-up[3].

Resolution of 'bulk-related' symptoms

In the case series of 54 patients with adenomyosis, with 43% (23/54) of patients presenting with bulk-related symptoms, complete resolution of bulk-related symptoms was reported in 35% (8/23) of patients at meanfollow-up of 5 years[1].

In the case series of 27 patients, complete resolution of bulk-related symptoms was reported in 38% (7/18), 31% (5/16), 46% (5/11) and 55% (6/11) of patients at 6, 12, 24 and 36 months respectively[4].

In a case series of 38 patients, complete resolution of bulk-related symptoms was reported in 67% (2/3) of patients with adenomyosis only, in 67% (4/6) of patients with dominant adenomyosis and fibroid tumours and in 100% (6/6) of patients with adenomyosis and dominant fibroid tumours; mean follow-up was 18 months[5].

Quality of life

In the case series of 54 patients, 70% (35/50) of patients were satisfied at long-term follow-up. In 19 patients with symptom recurrence, 37% (7/19) of patients were satisfied for the following reasons: less severe symptoms, pregnancy, a long symptom-free period, and delay of hysterectomy[1].

In a case series of 15 patients, a significant improvement in quality of life was reported on the following domains: ability to perform activities of daily life, ability

to socialise outside the home, overall energy level, pain or cramping during menstruation ($p<0.001$) and pain during sexual intercourse ($p=0.02$). There was an improvement in interest in sexual intercourse, but this was not significant [7].

Fertility

In the case series of 54 patients with adenomyosis, 5 patients had uneventful intrauterine pregnancies (3 delivered successfully and 2 opted for abortion)[1].

Treatment failure

In a case series of 54 patients with adenomyosis, treatment failure (defined as unsuccessful embolisation or no resolution of symptoms after the procedure) was reported in 7%(4/54) of patients (immediately after the procedure) and 38% (19/50) of patients had symptom recurrence (timing ranged from 4 to 48 months). Five patients with symptom recurrence underwent hysterectomy. There were no details on the remaining patients[1].

In a case series of 40 patients, additional therapy (because of insufficient symptom relief) was reported in 20% (8/40) of patients. Seven patients underwent hysterectomy (5 within 18 months and 2 after more than 5 years after uterine artery embolisation). One patient underwent second uterine artery embolisation (timing unclear)[2].

In a case series of 18 patients with adenomyosis, 44% (8/18) of patients had additional treatment because of treatment failure or recurrent symptoms. Twenty-eight per cent (5/18) of patients underwent hysterectomy (4 months after the procedure in 1 patient because of treatment failure, and between 9 and 27 months after the procedure in 4 patients because of recurrent symptoms). Eleven per cent (2/18) of patients needed additional medication and 6% (1/18) of patients needed endometrial balloon thermocoagulation because of recurrent symptoms (timing unclear)[6].

Safety

Amenorrhoea

Amenorrhoea was reported in 4% (2/54) of patients (aged 41 and 44 years) immediately after the procedure in the case series of 54 patients[1].

Amenorrhoea following the procedure because of onset of menopause was reported in 4 patients (age range 50 to 56 years) in a case series of 27 patients[4].

Vaginal discharge

Transient increased vaginal discharge was reported in 8% (3/40) of patients in the case series of 40 patients (timing unclear)[2].

Mild vaginal discharge (which spontaneously resolved) was reported in 2 patients in a case series of 18 patients 1 week after the procedure[6].

Tumour expulsion
Spontaneous 'tumour' expulsion was reported in 15.6% (5) of patients in a case series of 38 patients, 3–6 months after the procedure[5].

Pain
Recurrent severe cramping pain (4 days after the procedure; treated successfully by analgesia) was reported in 1 patient in the case series of 18 patients[6].

Worsening of symptoms
Worsening of symptoms (menorrhagia:55%;[6/11]; dysmenorrhoea: 18%[2/11]; bulk-symptoms: 9%[1/11]) was reported in 82% (9/11) of patients in the case series of 27 patients at 3 years follow-up. Three patients opted for hormonal therapy to help with symptom relief and none chose hysterectomy[4].

Worsening of menorrhagia was reported in 31% (12/39) of patients in the case series of 54 patients[1].

Validity and generalisability of the studies

- Studies in table 2 are mainly case series – prospective and retrospective studies.
- The majority of the studies reported that diagnosis of adenomyosis was established according to MRI diagnostic criteria.
- Studies included patients with adenomyosis with or without fibroids.
- Different types and sizes of embolic agents were used.
- 3 studies which included patients with adenomyosis with or without associated fibroids evaluated quality of life. In 2 studies[2-3], quality of life was assessed using a disease specific questionnaire for fibroids and in the remaining study[7] a self-reported questionnaire was used.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Uterine artery embolisation for fibroids. NICE interventional procedure guidance 367 (2010). Available from www.nice.org.uk/guidance/IPG367
- Endometrial cryotherapy for menorrhagia. NICE Interventional Procedure Guidance 157 (2006). Available from http://www.nice.org.uk/guidance/IPG157

Technology appraisals

- Fluid-filled thermal balloon and microwave endometrial ablation techniques for heavy menstrual bleeding. NICE Technology Appraisal 78 (2004). Available from http://www.nice.org.uk/guidance/TA78

Clinical guidelines

- Heavy menstrual bleeding. NICE clinical guideline 44 (2007). Available from www.nice.org.uk/guidance/CG44

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

Prof. Anna Belli, Dr Kashif Burney, Dr Susan Ingram and Prof. Anthony Watkinson (British Society of Interventional Radiology).

- Two specialist advisers indicated that they perform this procedure regularly and 1 specialist adviser noted they have performed this procedure at least once
- All 4 specialist advisers considered this to be a minor variation on an existing procedure, which is unlikely to alter that procedure's safety and efficacy. One specialist adviser comment that the technique is identical to that used in the treatment of fibroids with one possible difference being that some operators may start embolisation using smaller particles.
- Two specialist advisers noted that 10% to 50% of specialist engaged in this area of work are performing the procedure, 1 specialist adviser noted

more than 50% and another specialist adviser stated an estimate cannot be given.

- The specialist advisers reported quality of life ,symptom resolution and need for further treatment to be a key efficacy outcomes and listed that the following adverse events to be reported in literature: infection, uterine ischaemia, hysterectomy, premature menopause, complications common to all arterial interventions, post embolisation syndrome and non target embolisation
- Three specialist advisers stated that if safe and efficacious, this procedure is likely to be carried out in most or all district general hospitals and the potential impact of this procedure on the NHS would be moderate. One specialist adviser stated the effect would be major.

Patient Commentators' opinions

NICE's Public Involvement Programme sent 40 questionnaires to 2 NHS trusts for distribution to patients who had the procedure (or their carers). NICE received 9 completed questionnaires.

Patient commentaries were received after the Committee had met to consider the evidence on the procedure. These commentaries will be considered alongside the consultation comments and updated literature search.

Issues for consideration by IPAC

- There were no ongoing trials identified.

References

1. Kim MD, Kim S, Kim NK et al. (2007) Long-term results of uterine artery embolization for symptomatic adenomyosis. American Journal of Roentgenology 188:176-81

2. Smeets AJ, Nijenhuis RJ, Boekkooi PF et al. (2012) Long-term follow-up of uterine artery embolization for symptomatic adenomyosis. Cardiovascular & Interventional Radiology 35:815-9

3. Froeling V, Scheurig-Muenkler C, Hamm B et al. (2012) Uterine artery embolization to treat uterine adenomyosis with or without uterine leiomyomata: results of symptom control and health-related quality of life 40 months after treatment. Cardiovascular & Interventional Radiology 35:523-9

4. Bratby MJ and Walker WJ. (2009) Uterine artery embolisation for symptomatic adenomyosis--mid-term results. European Journal of Radiology 70:128-32

5. Lohle PN, De VJ, Klazen CA et al. (2007) Uterine artery embolization for symptomatic adenomyosis with or without uterine leiomyomas with the use of calibrated tris-acryl gelatin microspheres: midterm clinical and MR imaging follow-up. Journal of Vascular & Interventional Radiology 18:835-41

6. Pelage JP, Jacob D, Fazel A et al. (2005) Midterm results of uterine artery embolization for symptomatic adenomyosis: initial experience. Radiology 234:948-53

7. Siskin GP, Tublin ME, Stainken BF et al. (2001) Uterine artery embolization for the treatment of adenomyosis: clinical response and evaluation with MR imaging. American Journal of Roentgenology 177:297-302

8. Huang LY, Cheng YF, Huang CC et al. (2003) Incomplete vaginal expulsion of pyoadenomyoma with sepsis and focal bladder necrosis after uterine artery embolization for symptomatic adenomyosis: case report. Human Reproduction 18:167-71

9. Food and Drug Administration (FDA). Manufacturer and user facility device experience (MAUDE) database. Available from: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfmaude/detail.cfm?mdrfoi__id=1084861 [accessed 28 May 2013]

Appendix A: Additional papers on uterine artery embolisation for treating adenomyosis

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Bai SW, Jang JB, Lee DY et al. (2002) Uterine arterial embolization for the treatment of uterine leiomyomas. Yonsei Medical Journal 43:346-350.	N= 37 (in patients with uterine leiomyoma accompanied by adenomyosis) Follow-up=mean 13 months	Post embolisation symptoms of pain (79%), nausea and vomiting (25%) and fever (14%) were reported. All symptoms treated conservatively.	Larger studies included in table 2.
Goodwin SC (1999) Uterine artery embolization for the treatement of uterine leiomyomata midterm results Journal of Vascular and Interventional Radiology 10(9):1159-66	N=60 (3 patients with pre-existing diagnosis of adenomyosis) Follow-up= mean 16 months	3 patients with pre-existing diagnosis of adenomyosis had a clinically successful outcome. Six patients underwent hysterectomy at 5 weeks (because of infectious complication); adenomyosis was subsequently diagnosed by postsurgical histopathology in 3 of these patients.	Larger studies included in table 2.
Jha RC, Takahama J, Imaoka I et al. (2003) Adenomyosis: MRI of the uterus treated with uterine artery embolization. American Journal of Rotegenology181:851-856.	N=31 Follow-up= 1 year	All 3 patients with pure adenomyosis and all 6 patients with dominant adenomyosis reported an improvement in symptoms.	Larger studies included in table 2.
Kim JY, Kim MD, Cho JH et al. (2011) Uterine artery embolization for symptomatic adenomyosis in a patient with uterus didelphys. Journal of Vascular and Interventional Radiology 22(10):1489-1491.	N=1 Follow-up= 7 months	Abdominal cramping pain was reported immediately after the procedure. Symptom severity scores decreased from 10 to 4 for menorrhagia and from 10 to 0 for dysmenorrhoea at 3 months and remained same at 7 months.	Larger studies included in table 2.
Kim MD, Won JW, Lee DY et al. (2004) Uterine artery embolization for adenomyosis without fibroids. Clinical Radiology 59:520-526.	N=43 Follow-up= range 1-8 months	Significant improvement of dysmenorrhoea (95.2%) and menorrhagia (95.0%) were reported.	There may be some overlap with patients included in Kim (2007)[1] in table 2.
Kim MD, Kim NK, Kim HJ et al. (2005) Pregnancy following uterine artery embolization with polyvinyl alcohol particles for patients with uterine fibroid or adenomyosis. Cardiovascular &	N=94 (reports on 6 patients who desired future pregnancy;4 patients with adenomyosis) Follow-up= mean 35 months	83%(5/6) succeeded in becoming pregnant (twice in 1 patient). Of 8 pregnancies, 7 were successfully delivered (1 preterm) and 1 patient underwent abortion.	Outcome reported in table 2. There may be some overlap with patients included in Kim (2007)[1] in table 2.

Interventional Radiology 28:611-615.			
Kitamura Y, Allison SJ, Jha RC et al. (2006) MRI of adenomyosis: changes with uterine artery embolization. AJR American:855-864.	N=19 Follow-up=1 year	88.9%(16/18) patients reported an improvement in symptoms and no change in the remaining 2 patients. 10/11 patients reported continued improvement and 1 patient reported a worsening of symptoms at 12 months.	Larger studies included in table 2.
Liang E, Brown B, Kirsop R et al. (2012) Efficacy of uterine artery embolisation for treatment of symptomatic fibroids and adenomyosis - An interim report on an Australian experience. Australian & New Zealand Journal of Obstetrics & Gynaecology 52:106-113.	N=76 (17 patients with adenomyosis) Follow-up= range 3 to 24 months	Primary success rate was 96% and secondary success rate (after repeat procedure) was 100%. No significant procedural-related acute complications. Three possible cases of endometritis (2 managed conservatively and 1 needed hysterectomy) and 1 patient with calf deep vein thrombosis at 2 weeks post procedure was reported.	Larger studies included in table 2.
Popovic M, Puchner S, Brezaczy D et al. (2011) Uterine artery embolisation for the treatment of adenomyosis: A review Journal of Vascular Interventional Radiology 22:901-9	N= 511 (15 studies) Follow-up= median 27months	Symptomatic relief was reported by 75.7% (311).Outcomes need to be verified over the long term with respect to sustained symptomatic relief to validate UAE as an effective option for women with adenomyosis who wish to retain their fertility and/or for a minimally invasive treatment approach.	Review article. Relevant studies included in table 2 or Appendix A.
Toh CH, Wu CH, Tsay PK et al. (2003) Uterine artery embolization for symptomatic uterine leiomyoma and adenomyosis. Journal of the Formosan Medical Association 102:701-706.	N=46 (13 patients with adenomyosis) Follow-up= mean 11 months	Four complications occurred in the adenomyosis group: permanent amenorrhoea in 1 patient, pelvic inflammatory disease in 1 patient and severe low back pain in 2 patients.	Larger studies included in table 2.
Wood C. (2001) Adenomyosis: difficult to diagnose, and difficult to treat. Diagnostic & Therapeutic Endoscopy 7:89-95.	N=2 Follow-up= 'short term'	In both patients the posterior myometrial thickness was reduced, small myometrial cystic spaces were present in1 patient and myometrial scarring increased in the other patient.	Larger studies included in table 2.

Appendix B: Related NICE guidance for uterine artery embolisation for treating adenomyosis

Guidance	Recommendations
Interventional procedures	**Uterine artery embolisation for fibroids. NICE Interventional Procedure Guidance 367 (2010).** 1.1 Current evidence on uterine artery embolisation (UAE) for fibroids shows that the procedure is efficacious for symptom relief in the short and medium term for a substantial proportion of patients. There are no major safety concerns. Therefore this procedure may be used provided that normal arrangements are in place for clinical governance and audit. 1.2 During the consent process patients should be informed, in particular, that symptom relief may not be achieved in some women, that symptoms may return and that further procedures may therefore be required. Patients contemplating pregnancy should be informed that the effects of the procedure on fertility and on pregnancy are uncertain. 1.3 Patient selection should be carried out by a multidisciplinary team, including a gynaecologist and an interventional radiologist. 1.4 NICE encourages further research into the effects of UAE compared with other procedures to treat fibroids, particularly for women wishing to maintain or improve their fertility. **Endometrial cryotherapy for menorrhagia. NICE Interventional Procedure Guidance 157 (2006).** 1.1 Limited short-term evidence on the safety and efficacy of endometrial cryotherapy for menorrhagia appears adequate to support the use of this

	procedure in carefully selected patients provided that normal arrangements are in place for consent, audit and clinical governance. 1.2 Clinicians should ensure that patients understand that there are alternative treatment options with different likelihoods of achieving complete amenorrhea or normal periods. Appropriate patient selection and patient choice are both important. In addition, use of the Institute's information for the public is recommended.
Technology appraisals	**Fluid-filled thermal balloon and microwave endometrial ablation techniques for heavy menstrual bleeding. NICE Technology Appraisal 78 (2004).** 1.1 Fluid-filled thermal balloon endometrial ablation and microwave endometrial ablation are recommended as treatment options for women with heavy menstrual bleeding in cases where it has been decided (by the woman and the clinician responsible for her treatment) that surgical intervention is appropriate for the management of the condition. 1.2 For heavy menstrual bleeding, the choice of surgical treatment should be made jointly by the woman and the clinician responsible for treatment. The decision should be made after an informed discussion taking into account the desired outcome of the treatment (such as reduced menstrual bleeding or complete cessation of menstrual bleeding [amenorrhoea]), the relative benefits of all other treatment options and the adverse events associated with them, as well as the clinical condition, anatomical suitability and preferences of the woman.

Clinical guidelines	**Heavy menstrual bleeding. NICE Clinical Guideline 44 (2007).** 1.7 Further interventions for uterine fibroids associated with HMB 1.7.1 For women with large fibroids and HMB, and other significant symptoms such as dysmenorrhoea or pressure symptoms, referral for consideration of surgery or uterine artery embolisation (UAE) as first-line treatment can be recommended. 1.7.2 UAE, myomectomy or hysterectomy should be considered in cases of HMB where large fibroids (greater than 3 cm in diameter) are present and bleeding is having a severe impact on a woman's quality of life. 1.7.3 When surgery for fibroid-related HMB is felt necessary then UAE, myomectomy and hysterectomy must all be considered, discussed and documented. 1.7.4 Women should be informed that UAE or myomectomy may potentially allow them to retain their fertility. 1.7.5 Myomectomy is recommended for women with HMB associated with uterine fibroids and who want to retain their uterus. 1.7.6 UAE is recommended for women with HMB associated with uterine fibroids and who want to retain their uterus and/or avoid surgery. 1.7.7 Prior to scheduling of UAE or myomectomy, the uterus and fibroid(s) should be assessed by ultrasound. If further information about fibroid position, size, number and vascularity is required, MRI should be considered. 1.7.8 Pretreatment before hysterectomy and myomectomy with a gonadotrophin-releasing hormone analogue for 3 to 4

	months should be considered where uterine fibroids are causing an enlarged or distorted uterus. 1.7.9 If a woman is being treated with gonadotrophin-releasing hormone analogue and UAE is then planned, the gonadotrophin-releasing hormone analogue should be stopped as soon as UAE has been scheduled.

Appendix C: Literature search for uterine artery embolisation for treating adenomyosis

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	25/04/2013	Issue 3 of 12, March 2013
Database of Abstracts of Reviews of Effects – DARE (Cochrane Library)	25/04/2013	Issue 1 of 4, January 2013
HTA database (Cochrane Library)	25/04/2013	Issue 1 of 4, January 2013
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	25/04/2013	Issue 3 of 12, March 2013
MEDLINE (Ovid)	25/04/2013	1946 to April Week 3 2013
MEDLINE In-Process (Ovid)	25/04/2013	April 24, 2013
EMBASE (Ovid)	25/04/2013	1974 to 2013 Week 16
CINAHL (NLH Search 2.0 or EBSCOhost)	25/04/2013	n/a
BLIC (Dialog DataStar)	25/04/2013	n/a

Trial sources searched on 25/04/2013

- Current Controlled Trials metaRegister of Controlled Trials – mRCT
- Clinicaltrials.gov
- National Institute for Health Research Clinical Research Network Coordinating Centre (NIHR CRN CC) Portfolio Database

Websites searched

- National Institute for Health and Care Excellence (NICE)
- Food and Drug Administration (FDA) - MAUDE database
- French Health Authority (FHA)
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- Conference search
- Evidence Updates (NHS Evidence)
- General internet search

MEDLINE search strategy

1	embolization, therapeutic/ or uterine artery embolization/
2	(uter* adj3 arter* adj3 emboli*).tw.
3	(emboli* adj3 therap*).tw.
4	embolotherap*.tw.
5	UAE.tw.
6	or/1-5
7	Adenomyosis/
8	adenomyos*.tw.
9	endometrium/
10	endometri*.tw.
11	Uterine Diseases/
12	(uter* adj3 diseas*).tw.
13	or/7-12
14	6 and 13
15	animals/ not humans/
16	14 not 15