NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of uterine artery embolisation for fibroids

Uterine fibroids are non-cancerous growths that occur in the womb. They often have no symptoms but they can cause heavy bleeding, pain, and sometimes make it difficult for a woman to conceive or to carry a pregnancy to term. Uterine artery embolisation involves injecting small particles into the blood vessels that take blood to the uterus, via the groin. The aim is to block the blood supply to the fibroids so that they shrink.

Introduction

The National Institute for Health and Clinical 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 March 2010.

Procedure name

- Uterine artery embolisation for fibroids
- Uterine fibroid embolisation

Specialty societies

- British Society of Interventional Radiology
- Royal College of Obstetricians and Gynaecologists (RCOG).

Description

Indications and current treatment

Uterine fibroids, also known as uterine leiomyomas or uterine myomas, are benign tumours of the smooth muscle cells and fibrous tissue that develop within the wall of the uterus. They are classified by their location relative to the layers of the uterus (as subserous, intramural, or submucous) and can be single or multiple.

Uterine fibroids are one of the most common gynaecological problems among women in the UK. They are often asymptomatic but they can cause symptoms such as abnormal uterine bleeding, urinary incontinence, a feeling of pelvic pressure, or pain; they may also be associated with reproductive problems such as infertility and miscarriage.

Treatment depends on whether the fibroids are causing any symptoms, and on the woman's desire to become pregnant. Asymptomatic fibroids (often discovered incidentally) require no treatment. Depending on size, number and location, symptomatic fibroids have historically been managed by hysterectomy (surgical removal of the uterus) or myomectomy (surgical removal of the fibroids). Fibroids are one of the most common indications for a hysterectomy. Smaller submucous fibroids are usually removed by hysteroscopic resection. There are other treatments available, including endometrial ablation, which may be suitable for particular types of fibroid.

Hormone-based treatments may be used on a short-term basis to relieve symptoms, or to shrink the fibroids before surgery.

The advantage of uterine artery embolisation is that it is less invasive than hysterectomy and myomectomy, with a faster recovery time.

What the procedure involves

Uterine artery embolisation of fibroids is usually performed by an interventional radiologist. With the patient under conscious sedation and local anaesthesia, a catheter is inserted into the femoral artery using a bilateral or unilateral technique. Fluoroscopic guidance is used to manipulate the catheter into each uterine artery in turn. Small embolisation particles are injected through the catheter until the blood vessels supplying the fibroids have been blocked, causing the fibroids to shrink. Most patients experience some pain immediately after the procedure.

A range of different embolisation agents available 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 fibroids. Searches were conducted of the following databases, covering the period from 30 October 2003 to 29 March 2010: 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 uterine fibroids.
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 a systematic review of 36 papers (including 1 randomised controlled trial [RCT], 2 comparative studies, 1 patient questionnaire survey and 32 papers from 25 case series) and approximately 5863 patients from 2 registries, 3 RCTs, 1 non-randomised comparative study, 3 case series and 3 case reports[1–15].

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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 fibroids

Abbreviations used: BMI, body mass index; CI, confidence interval; FSH, follicle simulating hormone; HRQoL, health related quality of life; MRI, magnetic resonance imaging; NS, not significant; OR, odds ratio; QoL, quality of life; RCT, randomised controlled trial; RR, relative risk; UAE, uterine artery embolisation; UFSQoL, uterine fibroid symptoms and quality of life.

Study details	Key efficacy findings	Key safety findings	Comments
Coleman P (2004)[1] **Systematic review** UK Search period: November 2003 Study population: women with symptomatic fibroids One RCT, 2 comparative studies, 1 patient questionnaire survey, and 32 papers (1 reporting baseline data only) from 25 case series of patients were reviewed. The inclusion criteria used to filter the literature were: i) Primary papers reporting on safety and/efficacy ii) Published in 2000 or later iii) English language **n = range 11–555** Mean age: 43 years Patient selection criteria: varied between studies. **Follow-up: range 2 months–'between 3 and 5 years' (the most common period of follow-up was 6 months)** Conflict of interest/source of funding: review was commissioned by NICE	***Reduction in mean uterine volume at 6 months =*** 26%–59% ***Reduction in mean fibroid volume at 6 months*** = 40%–75% Where results from more than one follow-up period were available, a continuing reduction in mean fibroid volume has been reported (mean 43% (range 6%–100%) at 2 months; and mean 59% (range 6%-100%) at 6 months). No association was found between reductions in fibroid or uterine volume and clinical data. ***Symptom improvement*** 17 papers reported changes in symptoms following UAE, occurring in 60% to > 90% of patients. 'Improvements' or 'stabilisation' of symptoms were reported most frequently for menorrhagia. The main outcome measure in the RCT reviewed was cessation of bleeding. Success was reported for 79.5% (31/39) of patients. The largest prospective series of patients reviewed (n = 555) reported changes in symptoms in a subset of 538 patients receiving bilateral UAE at 3-month follow-up, based on an 'untested' 8-point scale from 'much improved' through 'no change' to 'much worse'. The symptoms of 58% of patients with menorrhagia (n = 249/429), 53% with dysmenorrhea (n = 170/322), 34% with bulk symptoms (n = 160/464) and 53% with urinary urgency/frequency (n = 163/306) were reported as 'much improved'. One paper reported 'improved' symptoms at 3-months, 6-months and >12-month follow-up in a series of 200 women. The improvements at 3 months (heavy menstrual bleeding 87%; bulk symptoms 93%; satisfaction 93% (n = 181)) were sustained at more than 12 months (90%, 91% and 92% respectively (n = 167)). ***Patient satisfaction*** A questionnaire survey completed by 51 of 57 patients who underwent UAE between 3 and 5 years previously reported that 61% (n = 31/51) were 'at least somewhat satisfied with their choice of procedure' One study reported that 85% (414/487) of patients were willing to undergo	There was a large variation in the reported rate of complications, ranging from 5% to 73%. The most commonly reported complications were the need for hysterectomy in 0.5% (2/400) to 11.8% (6/51) of women, and the late expulsion of a fibroid in 2.2% (9/400) to 7.7% (2/26) of women. Where hysterectomy was reported and reasons were provided, 3 cases were related to the existence of underlying pelvic disease (other than fibroids). In the short-term, postprocedure pain was commonly reported and infection was the main reason leading to emergency presentation and in some cases, emergency surgical intervention. There was 1 death in a series of 21 patients, due to septic shock and multiple organ failure 25 days after UAE. Ovarian dysfunction (characterised by irregular or absent menses and menopausal levels of follicle-stimulating hormone) was reported in 5 studies and ranged from 2.5% (2/80) to 14% (9/66) of patients. In a further study of 555 patients, amenorrhoea following UAE was reported in 3% of women younger than 40 years and in 41% of women aged 50 years or older. Case reports included the following complications:	**This is the systematic review that was commissioned by NICE for previous guidance on UAE (carried out by the Interventional Procedures Review Body).** • All the patients belong to a selected group. How representative they are of the relevant UK patient population is uncertain. The results reported will be affected by selection bias and patients lost to follow up. • Other limitations are variations in reporting, and the use of unvalidated outcome measures that make it difficult to assess the clinical importance of the improvements reported. Only 1 paper reported using a validated outcomes questionnaire. • Comparison of results is affected by different lengths of follow up. The largest series (n = 555) and one of the smallest series (n = 11) reported clinical results obtained

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Study details	Key efficacy findings	Key safety findings	Comments
	another UAE procedure if necessary. ***Pregnancies*** In 2 studies totalling 584 women, 23 women (3.9%) reported pregnancies following UAE. However, it was unclear how many women in these studies wished to become pregnant.	• Delayed detection of sarcoma/ unrecognised underlying leiomyosarcoma • Death from septic shock • Uterine necrosis • Labial necrosis • Bladder necrosis • Extrusion of degenerating fibroid into bladder • Uterine wall defect 14 months after UAE • Complicated pregnancy and subsequent hysterectomy	in follow-ups of 3 months or less. This is unlikely to be sufficient to capture all the changes in symptoms or adverse effects that may occur.

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Study details	Key efficacy findings	Key safety findings	Comments
O'Grady EA (2009)[2] **Case series (registry data)** UK Recruitment period: 2003–6 Study population: women with symptomatic fibroids **n = 1387** Mean age: 43.5 years (range 24–68) Patient selection criteria: at the time of launching the registry, patients who desired future fertility were generally excluded. This changed as UAE became more established. Technique: Two thirds of patients had the procedure performed via a single femoral artery puncture. A microcatheter was used in 16% of cases. 74% of patients were given at least 1 prophylactic antibiotic. A number of different embolic agents were used, including PVA, spheres and Gelfoam. 4% of patients had UAE performed as an outpatient procedure. **Mean follow-up: 12.7 months (range 1–36)** Conflict of interest/source of	Number of patients analysed: **1387** 932 (67%) patients had follow-up at 6 months or later, 662 (48%) had follow-up at 12 months or later, 163 (12%) had follow-up at 24 months or later **Improvement in symptoms reported at clinical review (5 point score: much worse, worse, unchanged, better, much better):** • 6 months (n = 932) = 84% • 12 months (n = 662) = 83% • 24 months (n = 163) = 83% (actual figures not reported) 3.8% of patients reported worsening of symptoms post procedure. Age was the only predictor of outcome after UAE, with increasing age of the patient significantly associated with improved outcomes (p < 0.01). **Mean reduction in uterine volume** = 40.1% (n = 666) **Mean reduction in fibroid diameter** = 2.2 cm (n = 847) **Mean HRQoL scores (component of UFS-QoL)**: • Baseline = 42.7 (n = 862) • Baseline score of patients included in comparison = 44.1 (n = 378) • Final score of patients included in comparison = 79.5 (n = 378), p < 0.001 **Mean symptom scores (component of UFS-QoL)**: • Baseline = 58.0 (n = 953) • Baseline score of patients included in comparison = 56.3 (n = 449) • Final score of patients included in comparison = 23.6 (n = 449), p < 0.001 7 pregnancies were recorded (3 live births, 2 ongoing pregnancies and 2 miscarriages). 65.4% (848/1296) of patients had 1 night in hospital after the procedure. 5.9% (76/1296) of patients required 2 or more nights in hospital after the procedure.	**Adverse events prior to discharge** *Procedural problems:* • Embolisation not performed = 0.1% (2/1387) • Embolisation incomplete = 0.1% (1/1387) • Femoral artery occlusion (no further information) = 0.1% (1/1387) • Artery dissection/perforation (no further information) = 0.1%(2/1387) • Groin bleeding/ pseudoaneurysm = 0.1% (2/1387) • Contrast reaction = 0.1% (2/1387) • Catheter kinked (snared to release) = 0.1% (1/1387) *Urinary tract problems:* • Retention = 0.1% (2/1387) • Urinary tract infection = 0.1% (1/1387) *Pain:* • Problems with pain control = 0.4% (5/1387) • Persistent pain in leg/ femoral nerve irritation = 0.1% (2/1387) *Other:* • Post procedure hypertension = 0.1% (2/1387) • Post embolisation syndrome (= 0.1% (2/1387) • Post procedure rash = 0.1% (2/1387) • Prolonged vaginal discharge = 0.2% (3/1387) • Respiratory arrest = 0.1% (1/1387) (related to the use of a fentanyl patient-controlled analgesia pump) In 15 patients, the adverse event	**Data from the British Society of Interventional Radiology registry, mentioned in original guidance for UAE.** **Follow-up issues**: • 22% (300/1387) of patients were lost to follow-up. **Study design issues**: • For QoL scores, the comparison was made between pairs of observations for patients who had a baseline score plus a latest score after 6 months. • QoL was measured using the UFS-QOL questionnaire, which is specific for fibroids. It has a symptom score and a HRQoL score both ranging from 0 to 100. A lower score on the symptom scale indicates fewer symptoms and a higher score on the HRQoL scale indicates better QoL. **Study population issues**: • 9% of patients had previous myomectomy. • 55% of patients had 4 or more fibroids. • 13% of patients had at least 1 fibroid greater than 10 cm in diameter

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Study details	Key efficacy findings	Key safety findings	Comments
funding: the initial paper-based registry was financially supported by Boston Scientific. Subsequently this was converted into an electronic format supported by NICE.	During follow-up, 10.8% (150/1387) of patients underwent a further intervention (68 repeat UAE, 10 myomectomy, 38 hysterectomy, 4 endometrial ablation, 93 other).	resulted in a delay in hospital discharge. **Adverse events post hospital discharge** • Fibroid expulsion = 2.8% (39/1387) • Persistent vaginal discharge = 1.9% (27/1387) • Amenorrhoea = 0.5% (7/1387) • Deep vein thrombosis = 0.1% (1/1387) • Death = 0.1% (1/1387) (at 28 months, due to uterine sarcoma) • Bleeding = 1.1% (15/1387) • Urinary retention = 0.4% (5/1387) • Post embolisation syndrome = 0.2% (3/1387) • Pressure = 0.1% (1/1387) • Uterine infections = 2.0% (28/1387) • Non-uterine infections = 0.9% (12/1387) • Other/not recorded = 7.4% (103/1387) One patient required a laparotomy 3.5 months post UAE. Findings were suggestive of a walled off bowel perforation. A small section of bowel was resected and the patient made a good recovery. 191 (14%) of patients had a total of 198 adverse events after being discharged from hospital. Of these, 74% (147) occurred within the first 12 months of the UAE procedure. There were significantly more infective complications post discharge for patients who did not receive antibiotic	**Other issues**: • It is not known how many patients attempted to become pregnant after UAE but failed. • The authors note that the rate of hysterectomy (2.7%) post UAE is much lower than reported in other studies (10–15% at 1 year). They suggest that this is due to the relatively poor follow-up rate and patients undergoing hysterectomy without the radiologist being made aware.

Abbreviations used: BMI, body mass index; CI, confidence interval; FSH, follicle simulating hormone; HRQoL, health related quality of life; MRI, magnetic resonance imaging; NS, not significant; OR, odds ratio; QoL, quality of life; RCT, randomised controlled trial; RR, relative risk; UAE, uterine artery embolisation; UFSQoL, uterine fibroid symptoms and quality of life.			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
		prophylaxis (RR 2.38, $p < 0.01$).	

Abbreviations used: BMI, body mass index; CI, confidence interval; FSH, follicle simulating hormone; HRQoL, health related quality of life; MRI, magnetic resonance imaging; NS, not significant; OR, odds ratio; QoL, quality of life; RCT, randomised controlled trial; RR, relative risk; UAE, uterine artery embolisation; UFSQoL, uterine fibroid symptoms and quality of life.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Goodwin SC (2008)[3]

Case series (registry data)

USA

Recruitment period: 1999 onwards

Study population: women with symptomatic fibroids

n = 2112

Mean age: 43.5 years

Patient selection criteria: not reported

Technique: not reported

Follow-up: 36 months

Conflict of interest/source of funding: two authors declared that they had served as consultants to Biosphere Medical and Boston Scientific.</td>
<td>Number of patients analysed: 2112

Symptom score (score 0 to 100, lower score indicates fewer symptoms)
<table>
<tr><th>Follow-up</th><th>n</th><th>Mean score</th></tr>
<tr><td>Baseline</td><td>2112</td><td>58.61</td></tr>
<tr><td>6 months</td><td>1782</td><td>19.87</td></tr>
<tr><td>1 year</td><td>1664</td><td>19.23</td></tr>
<tr><td>2 years</td><td>1604</td><td>18.26</td></tr>
<tr><td>3 years</td><td>1218</td><td>16.54</td></tr>
</table>
p < 0.001 for changes in symptom score at all follow-up intervals compared with baseline

HRQoL score (score 0 to 100, higher scores indicate better HRQoL)
<table>
<tr><th>Follow-up</th><th>n</th><th>Mean score</th></tr>
<tr><td>Baseline</td><td>2112</td><td>46.95</td></tr>
<tr><td>6 months</td><td>1765</td><td>85.04</td></tr>
<tr><td>1 year</td><td>1645</td><td>86.68</td></tr>
<tr><td>2 years</td><td>1581</td><td>87.43</td></tr>
<tr><td>3 years</td><td>1201</td><td>89.55</td></tr>
</table>
p < 0.001 for changes in HRQoL score at all follow-up intervals compared with baseline

Further surgical intervention (Kaplan-Meier estimates)
• Myomectomy = 2.8%
• Hysterectomy = 9.8%
• UAE = 1.8%

85.7% (1095/1278) of patients agreed or strongly agreed that they would recommend UAE to family members or friends.</td>
<td>At 36 months after UAE, 28.6% (365/1278) of patients had amenorrhoea (excluding those who had undergone hysterectomy).

Of the 365 patients with amenorrhoea, 78.9% were 45 years or older, 15.6% were between 40 and 45, and 5.5% were younger than 40 years.</td>
<td>Follow-up issues:
• At each follow-up interval, patients were sent a questionnaire to complete.
• At 36 months, data were available for 61% (1278/2112) of patients.
• Those patients completing follow-up were 1 year older (median age), more likely to be white, presented with a different mix of predominant symptoms, had a lower BMI, more use of prior medication, less antibiotic use, and a shorter time to return to work (p < 0.05 for all variables).

Study design issues:
• Multicentre study (27 sites).
• Primary outcome measures were symptom scores and HRQoL scores from the UFSQoL questionnaire.
• Scores were analysed using a repeated-measures method.
• Missing values for continuous risk variables were imputed to median values using the non-missing value. Missing values of the categorical variables were imputed to their</td>
</tr>
</table>

Abbreviations used: BMI, body mass index; CI, confidence interval; FSH, follicle simulating hormone; HRQoL, health related quality of life; MRI, magnetic resonance imaging; NS, not significant; OR, odds ratio; QoL, quality of life; RCT, randomised controlled trial; RR, relative risk; UAE, uterine artery embolisation; UFSQoL, uterine fibroid symptoms and quality of life.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr><td></td><td>Change in symptom score: baseline to 36 months (n = 1218), multivariate analysis

<table>
<tr><th>Variable</th><th>Adjusted estimate (95% CI)</th><th>p value</th></tr>
<tr><td>Predominant baseline symptom (compared with other symptoms)

Heavy bleeding

Bulk

Pain</td><td>

-12.3
(-23.3 to -1.38)
0.69
(-10.4 to 11.73)
-0.405
(-12.1 to 11.31)</td><td>

0.027

0.903

0.946</td></tr>
<tr><td>Prior medication (yes vs no)</td><td>-4.20
(-7.03 to -1.37)</td><td>0.004</td></tr>
<tr><td>Fibroid size (per cm increase)</td><td>0.76
(0.24 to 1.27)</td><td>0.004</td></tr>
<tr><td>Fibroid morphology (submucosal vs other)</td><td>-4.72
(-8.61 to -0.82)</td><td>0.018</td></tr>
</table>
A negative estimate indicates that the symptom score decreased at 36 months.

Multivariate analysis showed that higher age, lower BMI and low initial symptom scores were all associated with better outcomes at 3 years.</td><td></td><td>most common value.</td></tr>
</table>

Abbreviations used: BMI, body mass index; CI, confidence interval; FSH, follicle simulating hormone; HRQoL, health related quality of life; MRI, magnetic resonance imaging; NS, not significant; OR, odds ratio; QoL, quality of life; RCT, randomised controlled trial; RR, relative risk; UAE, uterine artery embolisation; UFSQoL, uterine fibroid symptoms and quality of life.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Edwards RD (2007)[4], Moss J (2010)[5]

Randomised controlled trial

UK

Recruitment period: 2000–4

Study population: women with symptomatic fibroids

n = 157 (106 UAE, 51 surgery [43 hysterectomies, 8 myomectomies])

Mean age (years): 43.6 (UAE), 43.3 (surgery)

Patient selection criteria: age ≥ 18 years, 1 or more fibroids > 2 cm in diameter that could be adequately visualised with the use of MRI, symptoms (such as menorrhagia or pelvic pain and pressure). Exclusion criteria included a contraindication to MRI, severe allergy to iodinated contrast media, subserosal pedunculated fibroids, recent or ongoing pelvic inflammatory disease, pregnancy, contraindication to surgery.

Technique: the technique for UAE was not specified, but both uterine arteries had to be embolised and the particle size of the embolic agent was standardised (500 to 710 µm). All the hysterectomies and</td>
<td>Number of patients analysed: 157

Quality of life (SF-36) at 1 month (scores range from 0 to 100, higher scores indicate better function)
<table>
<tr><th>Score</th><th>UAE (n = 95)</th><th>Surgery (n = 47)</th><th>p value</th></tr>
<tr><td>Physical function</td><td>85 ± 16</td><td>57 ± 25</td><td><0.001</td></tr>
<tr><td>Physical role</td><td>37 ± 44</td><td>11 ± 24</td><td><0.001</td></tr>
<tr><td>Bodily pain</td><td>50 ± 22</td><td>44 ± 24</td><td>0.16</td></tr>
<tr><td>General health</td><td>70 ± 19</td><td>74 ± 17</td><td>0.13</td></tr>
<tr><td>Vitality</td><td>47 ± 22</td><td>42 ± 24</td><td>0.11</td></tr>
<tr><td>Social function</td><td>64 ± 27</td><td>44 ± 29</td><td><0.001</td></tr>
<tr><td>Emotional role</td><td>72 ± 41</td><td>64 ± 44</td><td>0.32</td></tr>
<tr><td>Mental health</td><td>72 ± 17</td><td>74 ± 18</td><td>0.39</td></tr>
</table>
Quality of life (SF-36) at 12 months
<table>
<tr><th>Score</th><th>UAE</th><th>Surgery</th><th>p value</th></tr>
<tr><td>Physical function</td><td>92 ± 14</td><td>89 ± 20</td><td>0.85</td></tr>
<tr><td>Physical role</td><td>76 ± 40</td><td>81 ± 34</td><td>0.33</td></tr>
<tr><td>Bodily pain</td><td>76 ± 23</td><td>80 ± 26</td><td>0.28</td></tr>
<tr><td>General health</td><td>74 ± 20</td><td>79 ± 17</td><td>0.07</td></tr>
<tr><td>Vitality</td><td>62 ± 21</td><td>67 ± 22</td><td>0.26</td></tr>
<tr><td>Social function</td><td>84 ± 23</td><td>87 ± 26</td><td>0.22</td></tr>
<tr><td>Emotional role</td><td>81 ± 35</td><td>87 ± 30</td><td>0.22</td></tr>
<tr><td>Mental health</td><td>76 ± 17</td><td>76 ± 21</td><td>0.80</td></tr>
</table>
24- hour pain score (linear analogue score)
• UAE (n = 99) = 3.0 ± 2.1
• Surgery (n =49) = 4.6 ± 2.3, p < 0.001</td>
<td>Minor complications at 1 year:
• UAE = 34% (36/106)
• Surgery = 20% (10/51), p = 0.06

For UAE, there were 50 complications in 36 patients: postembolisation syndrome, including pyrexia, pain and elevated inflammatory markers (n = 26), vaginal discharge (n = 9), sepsis (n = 6), other (n = 9).
Complications in the surgery group included infection (n = 4), haemorrhage (n = 3) and other (n = 9).

Major adverse events (median follow-up = 32 months):
• UAE = 15% (16/106)
• Surgery = 20% (10/51)

During hospital stay
UAE:
• Severe vasovagal event requiring atropine = 0.9% (1/106)
Surgery:
• Operative haemorrhage (1 required left oophorectomy) = 3.9% (2/51)
• Anaesthetic complication = 3.9% (2/51)
• Wound infection = 3.9% (2/51)
• Wound haematoma = 2.0% (1/51)
• Urinary retention = 2.0% (1/51)

During first year of follow-up
UAE:
• Breast cancer = 1.9% (2/106)
• Pain and pelvic infection requiring readmission at 1 and 4 weeks = 1.9% (2/106)
• Severe pain and fibroid expulsion</td>
<td>Follow-up issues:
• 10.8% (17/157) of patients were lost to follow-up at 1 year (11 UAE, 6 surgery).

Study design issues:
• Patients were randomly assigned according to a computer-generated schedule. Randomisation was stratified by centre and performed in 2:1 ratio with twice as many patients in the UAE group.
• The choice between hysterectomy and myomectomy depended on whether the patient wished to retain her uterus for fertility or other reasons.
• The primary outcome measure was quality of life, assessed on the Medical Outcomes Study 36-item short-form General Health Survey (SF-36).
• Intention-to-treat analysis.
• Results were reported for 12-month follow-up except for adverse events and re-intervention rates, which were reported over a longer follow-up period.

Study population issues:</td>
</tr>
</table>

Abbreviations used: BMI, body mass index; CI, confidence interval; FSH, follicle simulating hormone; HRQoL, health related quality of life; MRI, magnetic resonance imaging; NS, not significant; OR, odds ratio; QoL, quality of life; RCT, randomised controlled trial; RR, relative risk; UAE, uterine artery embolisation; UFSQoL, uterine fibroid symptoms and quality of life.

Study details	Key efficacy findings	Key safety findings	Comments
myomectomies were performed through an abdominal incision. **Follow-up: 12 months (5-year follow-up data reported separately below)** Conflict of interest/source of funding: grants were received from 3 companies that manufacture embolic agents used in the trial (William Cook Europe, Cordis and Biocompatibles).	***Symptom score at 1 month (11-point scale, ranging from -5 = markedly worse to +5 markedly better)*** • UAE (n = 98) = 1.5 ± 2.4 • Surgery (n = 48) = 2.8 ± 2.6, p = 0.004 ***Symptom score at 12 months*** • UAE (n = 95) = 3.6 ± 2.0 • Surgery (n = 45) = 4.3 ± 1.7, p = 0.03 ***Patients who would recommend treatment to a friend at 1 months*** • UAE = 76% (74/97) • Surgery = 77% (37/48), p = 0.92 ***Patients who would recommend treatment to a friend at 12 months*** • UAE = 88% (84/95) • Surgery = 93% (42/45), p = 0.32 ***Median hospital stay (days)*** • UAE = 1 • Surgery = 5, p < 0.001 ***Median time to return to work (days)*** • UAE = 20 • Surgery = 62, p < 0.001 ***Median time to sexual intercourse (days)*** • UAE = 21 • Surgery = 53, p < 0.001 ***Further surgical intervention for UAE group:*** • Hysterectomy = 13.2% (14/106) (includes 2 technical failures of primary UAE treatment) • UAE = 6.6% (7/106) 7 pregnancies were reported in the UAE group: 4 resulted in miscarriage, 2 in successful live births and 1 intrauterine death of the fetus at 33 weeks.	at 3,4 and 6 weeks = 2.8% (3/106) • Haematometra at 6 months (not treated) = 0.9% (1/106) • Persistent severe pain requiring hysterectomy at 8 months = 0.9% (1/106) • Pelvic abscess requiring hysterectomy at 10 months = 0.9% (1/106) • Temporary amenorrhoea for 5 and 9 months = 1.9% (2/106) Surgery: • Wound exploration under general anaesthetic = 2.0% (1/51) • Wound infection at 3 weeks = 2.0% (1/51) *After first year of follow-up* UAE: • Death from adrenal cancer at 13 months = 0.9% (1/106) • Severe pain and fibroid expulsion at 13 months = 0.9% (1/106) • Persistent severe pain requiring hysterectomy at 15 months = 0.9% (1/106) Surgery: • none	• There were no statistically significant baseline differences between the groups with regard to age, fibroid size, uterine volume, SF-36 score. The mean EuroQoL score was lower in the surgery group than the UAE group (63 vs 70, p = 0.04). **Other issues**: • For major adverse events after 1 year, only those requiring hospitalisation were reported. • 5% (8/157) of patients did not receive their allocated treatments (5 UAE, 3 surgery).

Abbreviations used: BMI, body mass index; CI, confidence interval; FSH, follicle simulating hormone; HRQoL, health related quality of life; MRI, magnetic resonance imaging; NS, not significant; OR, odds ratio; QoL, quality of life; RCT, randomised controlled trial; RR, relative risk; UAE, uterine artery embolisation; UFSQoL, uterine fibroid symptoms and quality of life.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Moss J (2010)[5] continued.</td>
<td>
Quality of life (SF-36) at 5 years
<table>
<tr><th>Score</th><th>UAE
n = 94</th><th>Surgery
n = 44</th><th>p
value</th></tr>
<tr><td>Physical function</td><td>90 ± 18</td><td>87 ± 24</td><td>0.96</td></tr>
<tr><td>Physical role</td><td>84 ± 32</td><td>81 ± 36</td><td>0.71</td></tr>
<tr><td>Bodily pain</td><td>79 ± 22</td><td>81 ± 27</td><td>0.59</td></tr>
<tr><td>General health</td><td>78 ± 19</td><td>76 ± 24</td><td>0.76</td></tr>
<tr><td>Vitality</td><td>63 ± 22</td><td>63 ± 25</td><td>0.84</td></tr>
<tr><td>Social function</td><td>86 ± 23</td><td>85 ± 29</td><td>0.81</td></tr>
<tr><td>Emotional role</td><td>82 ± 35</td><td>85 ± 34</td><td>0.57</td></tr>
<tr><td>Mental health</td><td>76 ± 17</td><td>74 ± 24</td><td>0.45</td></tr>
</table>
Mean QOL scores at 5-year follow-up (EuroQoL, ranging from 0 being the worst possible and 100 being the best possible):
• UAE = 85
• Surgery = 80, p = 0.29

Symptom score at 5 years
• UAE = 4.5 ± 0.1
• Surgery = 4.8 ± 0.1, p = 0.08

Patients who would recommend treatment to a friend at 5 years
• UAE = 90% (84/93)
• Surgery = 87% (40/46), p = 0.56

There were 12 pregnancies in 5 women (10 UAE, 2 myomectomy).

In the myomectomy group, there were 2 elective caesarean sections resulting in successful live births.

In the UAE group, 4 pregnancies resulted in miscarriage. There was 1 ectopic pregnancy and 1 intrauterine death of the fetus at 33 weeks (there was no evidence of growth retardation).

4 pregnancies resulted in successful live births, including 2 elective caesarean sections (in 1, the placenta was described as ‘morbidly adherent
</td>
<td>
26 women in the UAE group became amenorrhoeic over the 5 year follow-up period.

Ovarian failure at 5 years (defined as FSH > 40 IU/L):
• UAE = 16 patients
• Surgery = 3 patients

14 of these patients were older than 45 years.

Both younger patients and 4 of the older patients had an elevated basal FSH at the time of treatment, indicating their perimenopausal status (all underwent UAE).

There were no cases of premature ovarian failure (age < 40 years).
</td>
<td>
Long-term results from the REST RCT reported above (Edwards et al, 2007).

These data have not yet been published in a peer-reviewed journal but have been submitted to the Scottish Executive Health Department Chief Scientist Office.

Follow-up issues:
• 8.9% (14/157) of patients were lost to follow-up at 5 years (10 UAE, 4 surgery).
</td>
</tr>
</table>

Abbreviations used: BMI, body mass index; CI, confidence interval; FSH, follicle simulating hormone; HRQoL, health related quality of life; MRI, magnetic resonance imaging; NS, not significant; OR, odds ratio; QoL, quality of life; RCT, randomised controlled trial; RR, relative risk; UAE, uterine artery embolisation; UFSQoL, uterine fibroid symptoms and quality of life.

Study details	Key efficacy findings	Key safety findings	Comments
	and difficult to remove' resulting in increased perioperative blood loss) and 1 emergency caesarean section at 34 weeks (delivery was followed by a postpartum haemorrhage due to an atonic uterus). ***Re-interventions for treatment failure at 5 years***: • UAE = 26% (28/106) • Surgery = 2% (1/51) (myomectomy was converted to hysterectomy at the time of the initial operation)		

Abbreviations used: BMI, body mass index; CI, confidence interval; FSH, follicle simulating hormone; HRQoL, health related quality of life; MRI, magnetic resonance imaging; NS, not significant; OR, odds ratio; QoL, quality of life; RCT, randomised controlled trial; RR, relative risk; UAE, uterine artery embolisation; UFSQoL, uterine fibroid symptoms and quality of life.

Study details	Key efficacy findings	Key safety findings	Comments
Mara M (2008)[6] **Randomised controlled trial** Czech Republic Recruitment period: 2001–5 Study population: women with uterine fibroids and unfinished reproductive plans **n = 121 (58 UAE, 63 myomectomy)** Mean age: 32 years Patient selection criteria: ultrasound-verified intramural fibroid at least 4 cm at its largest diameter, age <40 years, serum follicle stimulating hormone (FSH) <30 IU/l (on 3rd day of menstrual cycle), planned pregnancy. Exclusion criteria included non-intramural location of the main fibroid (submucosal or subserous); size of dominant fibroid >12 cm at its largest diameter or uterus enlarged to the size corresponding to >4 months of pregnancy; previous myomectomy, embolisation or hormonal therapy; suspected uterine sarcoma or diffuse adenomyosis; serious disease contraindicating gravidity. Technique: myomectomy included open and laparoscopic	Number of patients analysed: **121** ***Technical success*** • UAE = 89.7% (52/58) • Myomectomy = 92.1% (58/63), p = NS ***Mean length of hospital stay (hours)*** • UAE = 60.2 • Myomectomy = 86.1, p < 0.0001 ***Mean recovery period (days)*** • UAE = 11.9 (range 3–30) • Myomectomy = 22.1 (7–65), p < 0.0001 ***Disability >2 weeks*** • UAE = 22.4% (13/58) • Myomectomy = 57.1% (36/63), p < 0.0001 ***Relief from symptoms*** • UAE = 88.5% (46/52) • Myomectomy = 87.9% (51/58), p = NS ***Mean serum FSH 6 months after procedure*** • UAE = 7.89 (range 4.0–48.9) • Myomectomy = 6.49 (range 3.6–12.3), p = NS ***Re-interventions*** • UAE = 32.8% (19/58) (19 myomectomies, 15 for the persistence of a large fibroid and 4 due to regrowth of a fibroid) • Myomectomy = 3.4% (2/58), p < 0.0001 ***Pregnancy rate in women who have tried to conceive*** • UAE = 50.0% (13/26) (17 pregnancies) • Myomectomy = 77.5% (31/40) (33 pregnancies) p < 0.05 ***Delivery rate in women who have tried to conceive*** • UAE = 19.2% (5/26) • Myomectomy = 47.5% (19/40), p < 0.05 ***Miscarriage rate in women who have tried to conceive (in all cases spontaneous or missed miscarriage in first trimester)*** • UAE = 64%, n = 9	***Periprocedural complications*** • UAE = 6.9% (4/58) (1 artery dissection, 3 uterine artery spasms) • Myomectomy = 7.9% (5/63) (3 unexpected intrauterine penetrations, 2 non-elective laparoconversions) p = NS ***Early postprocedural complications (from day 1 to day 30)*** • UAE = 20.7% (12/58) • Myomectomy = 15.9% (10/63), p = NS ***Hospital stay > 7 days*** • UAE = 1.7% (1/58) (due to severe vaginal bleeding, treated by pharmacotherapy) • Myomectomy = 4.8% (3/63), p = NS ***Readmissions to hospital (within 30 days)*** • UAE = 3.4% (2/58) • Myomectomy = 1.6% (1/63), p = NS Additional complications reported for UAE were 1 case each of subcutaneous haematoma at puncture site in the right groin (managed conservatively), 1 rash as a probable reaction to analgesia, 1 postpuncture headache after epidural anaesthesia. After myomectomy, there were 2 transfusions, 1 urinary tract infection, 1 wound infection and 1 surgical evacuation of subfascial haematoma (1 day after procedure).	**Follow-up issues**: • 2.5% (3/121) of patients were lost to follow-up. **Study design issues**: • Randomisation was done using computer-generated random numbers. • Intent-to-treat analysis. **Study population issues**: • 91% (110/121) of patients were symptomatic at baseline. • There were more women described as 'sterile' in the myomectomy group compared with the UAE group (24 vs 11, p < 0.05). There were no other significant differences between the groups. **Other issues:** • The paper does not specify 'normal' levels for FSH, although the cut-off of 10 IU/L is used. In general, the higher the FSH level the lower the ovarian reserve.

Abbreviations used: BMI, body mass index; CI, confidence interval; FSH, follicle simulating hormone; HRQoL, health related quality of life; MRI, magnetic resonance imaging; NS, not significant; OR, odds ratio; QoL, quality of life; RCT, randomised controlled trial; RR, relative risk; UAE, uterine artery embolisation; UFSQoL, uterine fibroid symptoms and quality of life.

Study details	Key efficacy findings	Key safety findings	Comments
procedures. For UAE, a microcatheter was used with trisacryl gelatin microspheres (Embospheres, BioSphere Medical). After the first 5 patients, only particles larger than 500 µm were used. A single dose of antibiotics was given to every patient 30 min before embolisation. **Mean follow-up: 24.9 months** Conflict of interest/source of funding: none reported.	• Myomectomy = 23%, n = 6, p < 0.05 NB. It is not clear what denominator was used to calculate the reported percentages for miscarriage rates. Of the remaining 3 pregnancies in the UAE group, 1 was ectopic, 1 was terminated and 1 was ongoing. Of the remaining 8 pregnancies in the myomectomy group, 1 was ectopic, 1 was terminated, 5 were ongoing and the outcome of 1 was not described. RR of women treated with UAE not to get pregnant (in women who tried to conceive) = 2.22 (95% CI 1.11 to 4.44) RR of women treated with UAE not to deliver = 1.54 (95% CI 1.08 to 2.18) RR of women treated with UAE to miscarry = 2.79 (95% CI 1.25 to 6.22) ***Perinatal results*** Preterm delivery (<37 weeks) • UAE = 0% (0/5) • Myomectomy = 26.3% (5/19), p = NS Caesarean section • UAE = 60.0% (3/5) • Myomectomy = 68.4% (13/19), p = NS Postpartum haemorrhage • UAE = 20.0% (1/5) • Myomectomy = 0% (0/19), p = NS Fetal intrauterine growth restriction • UAE = 0% (0/5) • Myomectomy = 10.5% (2/19), p = NS	***Late postprocedural complications*** • UAE = 13.8% (8/58) • Myomectomy = 8.1% (5/62), p = NS For UAE, these included 4 complications related to ovarian function, including 2 cases of temporary amenorrhoea. Another 2 patients had raised FSH and unsuccessful therapy for sterility. Late complications after myomectomy included dyspareunia, pelvic pain, endometritis, and 1 episode of metrorrhagia. ***FSH >10 IU/l*** • UAE = 13.8% (8/58) • Myomectomy = 3.2% (2/62), p < 0.05 ***Significant elevation of FSH (≥ 5 IU/l) 6 months after procedure*** • UAE = 5.2% (3/58) • Myomectomy = 0% (0/58), p = NS	

Abbreviations used: BMI, body mass index; CI, confidence interval; FSH, follicle simulating hormone; HRQoL, health related quality of life; MRI, magnetic resonance imaging; NS, not significant; OR, odds ratio; QoL, quality of life; RCT, randomised controlled trial; RR, relative risk; UAE, uterine artery embolisation; UFSQoL, uterine fibroid symptoms and quality of life.

Study details	Key efficacy findings	Key safety findings	Comments
Volkers NA (2007)[7], Hehenkamp WJK (2008)[8] **Randomised controlled trial** The Netherlands Recruitment period: 2002–4 Study population: women with uterine fibroids and heavy menstrual bleeding **n = 177 (88 UAE, 89 hysterectomy)** Mean age: 45 years Patient selection criteria: diagnosis of uterine fibroids confirmed by ultrasound; premenopausal; menorrhagia; treatment options other than hysterectomy were unsuitable or had failed to provide relief; absence of the following disorders: renal failure, active pelvic infection, clotting disorders, allergy to contrast fluid, suspected uterine malignancy, submucosal fibroids protruding by > 50% within the uterine cavity, or pedunculated abdominal fibroids; no desire for a future pregnancy. Technique: UAE was performed using polyvinyl alcohol particles (Contour, Boston Scientific) with a size of	Number of patients analysed: **156 (81 vs 75)** ***Bilateral failure of UAE = 4.9% (4/81)*** ***Unilateral UAE = 12.3% (10/81)*** ***Technical success of hysterectomy = 100% (75/75)*** ***Re-interventions during 2-year follow-up in UAE group:*** 23.5% (19/81) hysterectomies Excluding bilateral technically failed procedures, there were 19.5% (15/77) hysterectomies in women undergoing successful UAE. All but 1 were performed for persistence or relapse of menorrhagia. Multiple regression analysis revealed that only parity was associated with a higher risk for failure. ***Symptom relief*** Proportion of patients reporting at least moderate improvement in pain at 24-month follow-up: • UAE = 84.9% • Hysterectomy = 78.0%, p = 0.30 Analysis of trend for the 5 categories of change compared to baseline for pain favoured hysterectomy at all time points except for 24 months where no significant difference between the 2 groups was observed. Proportion of patients reporting at least moderate improvement in bulk-related symptoms at 24-month follow-up: • UAE = 66.2% • Hysterectomy = 69.2%, p = 0.71 ***Mean percent volume reduction of largest fibroid at 24 months (for UAE) = 60.5%*** ***Mean percent volume reduction of uterus at 24 months (for UAE) = 48.2%***	A total of 30 patients (37%) in the UAE group had amenorrhoea at 24 months, 19 of which were due to hysterectomy and 2 were due to medication.	**Follow-up issues**: • After randomisation, 7 patients in the UAE group and 14 in the hysterectomy group refused the allocated treatment and withdrew from the study. • At 24 months, 2 patients in the hysterectomy group and none in the UAE group were lost to follow-up. **Study design issues**: • Multicentre (28 hospitals). • Randomisation was computer based, stratified by study centre. • Intent-to-treat analysis. **Study population issues**: • Most patients (85%) had already undergone 1 or more treatments before study enrollment. • There were no statistically significant differences in baseline characteristics between the groups. • The authors note that patients participating in the study had severe bleeding problems. They were all candidates for hysterectomy and so represented the severe end of the clinical spectrum. This may

Abbreviations used: BMI, body mass index; CI, confidence interval; FSH, follicle simulating hormone; HRQoL, health related quality of life; MRI, magnetic resonance imaging; NS, not significant; OR, odds ratio; QoL, quality of life; RCT, randomised controlled trial; RR, relative risk; UAE, uterine artery embolisation; UFSQoL, uterine fibroid symptoms and quality of life.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>355–500 µm. Particles of size 500–700 µm were used only if an anastomosis within the ovarian artery was observed. The type of hysterectomy and route of access varied, but the majority were abdominal.

Follow-up: 24 months

Conflict of interest/source of funding: Boston Scientific partly sponsored the embolic agent used in the trial. They were not involved in the trial.</td>
<td>Patient satisfaction at 6 months
<table>
<tr><th></th><th>UAE (n = 81)</th><th>Hysterectomy (n = 75)</th></tr>
<tr><td>Very satisfied</td><td>29 (35.8%)</td><td>42 (56.0%)</td></tr>
<tr><td>Satisfied</td><td>18 (22.2%)</td><td>15 (20.0%)</td></tr>
<tr><td>Moderately satisfied</td><td>18 (22.2%)</td><td>6 (8%)</td></tr>
<tr><td>Neither satisfied nor unsatisfied</td><td>7 (8.6%)</td><td>2 (2.7%)</td></tr>
<tr><td>Moderately unsatisfied</td><td>3 (3.7%)</td><td>2 (2.7%)</td></tr>
<tr><td>Unsatisfied</td><td>2 (2.5%)</td><td>1 (1.3%)</td></tr>
<tr><td>Very unsatisfied</td><td>1 (1.2%)</td><td>1 (1.3%)</td></tr>
</table>
p = 0.044

Patient satisfaction at 24 months
<table>
<tr><th></th><th>UAE (n = 81)</th><th>Hysterectomy (n = 75)</th></tr>
<tr><td>Very satisfied</td><td>34 (42.0%)</td><td>45 (60.0%)</td></tr>
<tr><td>Satisfied</td><td>29 (35.8%)</td><td>16 (21.3%)</td></tr>
<tr><td>Moderately satisfied</td><td>11 (13.6%)</td><td>5 (6.7%)</td></tr>
<tr><td>Neither satisfied nor unsatisfied</td><td>2 (2.5%)</td><td>3 (4.0%)</td></tr>
<tr><td>Moderately unsatisfied</td><td>3 (3.7%)</td><td>0 (0%)</td></tr>
<tr><td>Unsatisfied</td><td>1 (1.2%)</td><td>1 (1.3%)</td></tr>
<tr><td>Very unsatisfied</td><td>0 (0%)</td><td>3 (4.0%)</td></tr>
</table>
p = 0.02</td>
<td></td>
<td>partly explain the relatively high rate of subsequent hysterectomy in the UAE group.
• Re-embolisations were not allowed in the study and recurrence was seen as a definite failure.</td>
</tr>
</table>

Abbreviations used: BMI, body mass index; CI, confidence interval; FSH, follicle simulating hormone; HRQoL, health related quality of life; MRI, magnetic resonance imaging; NS, not significant; OR, odds ratio; QoL, quality of life; RCT, randomised controlled trial; RR, relative risk; UAE, uterine artery embolisation; UFSQoL, uterine fibroid symptoms and quality of life.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Dutton S (2007)[9], Hirst A (2008)[10]

Non-randomised comparative study

UK

Recruitment period: 2004–5

Study population: women with symptomatic uterine fibroids

n = 1108 (649 UAE, 459 hysterectomy)

Mean age (years): UAE = 43.8, hysterectomy = 46.5

Patient selection criteria: not reported

Technique: All UAE centres used poly(vinyl alcohol) (PVA) embolic particles and in addition some used gelfoam or coils. Most hysterectomies were total abdominal (86.7%) with the remainder being subtotal (5.0%), vaginal (5.2%) or laparoscopically assisted vaginal (2.6%). Prophylactic antibiotics were given to 65% (422/649) of women undergoing UAE.

Mean follow-up (years): UAE = 4.6, hysterectomy = 8.6

Conflict of interest/source of</td>
<td>Number of patients analysed: 1108

Efficacy outcomes from patient questionnaire
<table>
<tr><th></th><th>UAE (n = 589)</th><th>Hysterectomy (n = 397)</th><th>p value</th></tr>
<tr><td>Relief from symptoms</td><td>85.2% (472/554)</td><td>99.2% (352/355)</td><td>< 0.0001</td></tr>
<tr><td>Felt better since treatment</td><td>83.8% (434/518)</td><td>95.8% (320/334)</td><td>< 0.0001</td></tr>
<tr><td>Would recommend to a friend</td><td>91.4% (510/558)</td><td>85.5% (278/325)</td><td>0.007</td></tr>
<tr><td>Expectations fulfilled</td><td>73.5% (417/567)</td><td>93.5% (343/367)</td><td>< 0.0001</td></tr>
<tr><td>Reported problems caused by treatment</td><td>79.5% (388/488)</td><td>75.4% (221/293)</td><td>0.18</td></tr>
</table>
Further surgical intervention for UAE patients:
• Hysterectomy = 11.2% (73/649)
• UAE = 4.5% (29/649)
• Myomectomy = 4.9% (32/649)
(some patients underwent more than one re-intervention)

After adjusting for differential time of follow-up using survival analysis to first further treatment, women in the UAE group had a 23% (95% CI 19 to 27%) chance of requiring further treatment for fibroids within the first 7 years.

28.8% (187/649) of women in the UAE cohort indicated a hope to have any/more children in the future and 22% were uncertain or did not answer the question.

27 women achieved 37 pregnancies after UAE (8.5% of those women who indicated that they wished or were uncertain of their wish for children. There were 15 miscarriages, 2 ectopic pregnancies, 1 termination and 19 successful live births (from 16 women). Of the live births, 79% were delivered by caesarean section, 6 due to complications of pregnancy or delivery.</td>
<td>Complications:
• UAE = 17.6% (114/649)
• Hysterectomy = 26.1% (120/459)
OR (adjusted for confounders, clustering by centre and missing values) = 0.48,
95% CI: 0.26 to 0.89.
There were 341 complications in 234 women.
'Severe complications'
Pulmonary embolus
• UAE = 0% (0/649)
• Hysterectomy = 0.7% (3/459)
Organ failure
• UAE = 0% (0/649)
• Hysterectomy = 0.2% (1/459)
'Other severe'
• UAE = 0.2% (1/649)
• Hysterectomy = 0.2% (1/459)
'Major complications'
Permanent amenorrhoea (age <40 years)
• UAE = 0.2% (1/649)
• Hysterectomy = 0% (0/459)
Blood transfusion required
• UAE = 0.6% (4/649)
• Hysterectomy = 7.4% (34/459)
Structural damage caused by treatment
• UAE = 0.8% (5/649)
• Hysterectomy = 3.5% (16/459)
Septicaemia, emergency myomectomy/hysterectomy
• UAE = 2.6% (17/649)
• Hysterectomy = 0.4% (2/459)
Thrombosis
• UAE = 0% (0/649)
• Hysterectomy = 0.4% (2/459)
'Other major'
• UAE = 0.2% (1/649)
• Hysterectomy = 2.0% (9/459)</td>
<td>Follow-up issues:
• A total of 1734 women were eligible for the study and data were available for 64% (n = 1108).

Study design issues:
• The hysterectomy cohort underwent their index treatment in 1994–5. Patients in the UAE cohort had all received their index UAE from 1996 to 2002.
• Multicentre, retrospective study.
• General side effects of the treatment, including post-embolisation syndrome, were not included as complications.

Study population issues:
• The two cohorts presented a different baseline profile for many confounders including age (UAE younger), educational level (UAE higher), ethnicity (UAE more ethnically diverse), and parity (more UAE women nulliparous).
• There was a significantly higher proportion of patients receiving prophylactic antiobiotics in the hysterectomy group (89% vs 65%,</td>
</tr>
</table>

Abbreviations used: BMI, body mass index; CI, confidence interval; FSH, follicle simulating hormone; HRQoL, health related quality of life; MRI, magnetic resonance imaging; NS, not significant; OR, odds ratio; QoL, quality of life; RCT, randomised controlled trial; RR, relative risk; UAE, uterine artery embolisation; UFSQoL, uterine fibroid symptoms and quality of life.			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
funding: not reported		***'Minor complications'*** *Minor infections (< 30 days)* • UAE = 5.9% (38/649) • Hysterectomy = 13.5% (62/459) *Haematoma requiring treatment* • UAE = 0.6% (4/649) • Hysterectomy = 1.3% (6/459) *Adverse drug reaction* • UAE = 1.2% (8/649) • Hysterectomy = 0.7% (3/459) *Permanent amenorrhoea (age ≥ 40 years)* • UAE = 1.4% (9/649) • Hysterectomy = 0.2% (1/459) *Urinary retention requiring catheterisation* • UAE = 1.4% (9/649) • Hysterectomy = 2.2% (10/459) *Fibroid extraction requiring assistance* • UAE = 6.3% (41/649) • Hysterectomy = 0% (0/459) *'Other minor (< 30 days)'* • UAE = 4.2% (27/649) • Hysterectomy = 5.7% (26/459) Being obese, having a later onset of menarche, an existing medical comorbidity, or having undergone prior pelvic surgery raised the odds of experiencing a complication. Using prophylactic antibiotics at the time of the procedure reduced the odds of experiencing a complication. Anticipated general side effects of UAE included chronic, although self-limiting vaginal discharge (12.6%), spontaneous fibroid expulsions (7.6%) and postembolisation syndrome (17.7%).	p < 0.0001). • The general heath of both cohorts was similar at baseline.

Abbreviations used: BMI, body mass index; CI, confidence interval; FSH, follicle simulating hormone; HRQoL, health related quality of life; MRI, magnetic resonance imaging; NS, not significant; OR, odds ratio; QoL, quality of life; RCT, randomised controlled trial; RR, relative risk; UAE, uterine artery embolisation; UFSQoL, uterine fibroid symptoms and quality of life.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Spies JB (2005)[11]

Case series

USA

Recruitment period: 1997–9

Study population: women with symptomatic uterine fibroids

n = 200

Mean age: 43.1 years

Patient selection criteria: at least 1 of the following symptoms: heavy menstrual bleeding; pelvic pain or pressure, or back, flank or leg pain caused by fibroids; urinary frequency or other bladder symptoms caused by compression of the bladder by fibroids or compression of the ureters with hydronephrosis. Medical therapy must have failed or been unsuitable. Exclusion criteria included current pregnancy or a suspicion of uterine, ovarian, or cervical cancer. Anatomical exclusion criteria included pedunculated submucosal fibroids that were hysteroscopically resectable and uterus size >24 weeks.

Technique: bilateral embolisation was performed in each case, using polyvinyl</td>
<td>Number of patients analysed: 200

Improvement of symptoms
<table>
<tr><th>Follow-up</th><th>Improved</th><th>Not improved</th><th>Major intervention*</th></tr>
<tr><td>3 months</td><td>93.3% (180/193)</td><td>4.7% (9/193)</td><td>2.1% (4/193)</td></tr>
<tr><td>1 year</td><td>87.4% (166/190)</td><td>5.3% (10/190)</td><td>7.4% (14/190)</td></tr>
<tr><td>2 years</td><td>84.5% (136/161)</td><td>5.0% (8/161)</td><td>10.6% (17/161)</td></tr>
<tr><td>3 years</td><td>83.1% (152/183)</td><td>3.8% (7/183)</td><td>13.7% (25/183)</td></tr>
<tr><td>4 years</td><td>79.4% (143/180)</td><td>3.3% (6/180)</td><td>16.7% (30/180)</td></tr>
<tr><td>5 years</td><td>73.1% (133/182)</td><td>5.5% (10/182)</td><td>19.8% (36/182)</td></tr>
</table>
* hysterectomy, definitive myomectomy or repeat embolisation, resulted in patient being censored for follow-up
Mean change score (range from -5 = markedly worse to +5 = markedly improved, only includes those who are not failed)
<table>
<tr><th>Follow-up</th><th>Bleeding</th><th>Pain</th></tr>
<tr><td>3 months</td><td>3.33</td><td>3.47</td></tr>
<tr><td>1 year</td><td>3.73</td><td>3.68</td></tr>
<tr><td>2 years</td><td>3.83</td><td>3.56</td></tr>
<tr><td>3 years</td><td>3.84</td><td>3.81</td></tr>
<tr><td>4 years</td><td>4.07</td><td>3.84</td></tr>
<tr><td>5 years</td><td>3.98</td><td>3.72</td></tr>
</table>
Mean percent volume reduction of largest fibroid:
• 3 months (n = 175) = 43.6% (95% CI 39.6 to 47.6)
• 1 year (n = 124) = 57.8% (95% CI 52.7 to 62.8)
Mean percent volume reduction of uterus:
• 3 months (n = 175) = 28.5% (95% CI 24.7 to 32.3)
1 year (n = 124) = 39.4% (95% CI 34.6 to 44.2)

Hysterectomy rate at 5 years = 13.7% (25/182)

Logistic regression showed long-term failure was more likely in those not improved at 1 year (RR 5.73; 95% CI 2.32 to 14.12) and in those with</td>
<td>Amenorrhoea:
• 1 year = 4.2% (8/190)
• 5 years = 23.2% (42/181)

Mean age at embolisation of women reporting amenorrhoea = 46.0 years

Mean age of first report of amenorrhoea = 50.0 years (95% CI 48.9 to 51.2)

Mean interval until onset of amenorrhoea = 4.1 years after embolisation.</td>
<td>Follow-up issues:
• Follow-up data were available for 91% (182/200) of patients at 5 years. Three patients died during follow-up (1 of breast cancer, 1 of colon cancer, 1 of pre-existing cardiomyopathy).
• Some follow-up questionnaires were self-administered whereas other were completed by telephone interview.

Study design issues:
• Consecutive patients (first 200 treated at study centre).

Study population issues:
• The 18 women who were missing at year 5 did not differ significantly from the remaining cohort on age, race, bleeding and pain scores at 3 months, baseline uterine and fibroid volumes, number and location of fibroids and volume reductions.
• The enrolment criteria were expanded after the 50th patient to include those who wanted to maintain their fertility if their only treatment alternatives were hysterectomy or</td>
</tr>
</table>

Abbreviations used: BMI, body mass index; CI, confidence interval; FSH, follicle simulating hormone; HRQoL, health related quality of life; MRI, magnetic resonance imaging; NS, not significant; OR, odds ratio; QoL, quality of life; RCT, randomised controlled trial; RR, relative risk; UAE, uterine artery embolisation; UFSQoL, uterine fibroid symptoms and quality of life.

Study details	Key efficacy findings	Key safety findings	Comments
alcohol particles (Contour, Boston Scientific; Ivalon, Cook Inc.; Trufill, Cordis), 500 to 710 µm size. **Follow-up: 5 years** Conflict of interest/source of funding: not reported.	baseline fibroid volumes greater than the median (RR 2.18; 95% CI 1.05 to 4.51). ***Patient satisfaction*** 76.4% (146/191) of patients consistently reported satisfaction scores of 3 or higher during their follow-up (scale -5 = very dissatisfied to +5 = very satisfied). 23.6% (45/191) of patients reported at least 1 satisfaction score below 3. Poorer bleeding and pain or pressure scores at year 1 and less fibroid volume reduction were significantly associated with an increased risk of dissatisfaction.		extensive myomectomy.

Abbreviations used: BMI, body mass index; CI, confidence interval; FSH, follicle simulating hormone; HRQoL, health related quality of life; MRI, magnetic resonance imaging; NS, not significant; OR, odds ratio; QoL, quality of life; RCT, randomised controlled trial; RR, relative risk; UAE, uterine artery embolisation; UFSQoL, uterine fibroid symptoms and quality of life.

Study details	Key efficacy findings	Key safety findings	Comments
Gabriel-Cox K (2007)[12] **Case series** USA Recruitment period: 1997–2001 Study population: women with symptomatic uterine fibroids **n = 562** Mean age: 45.0 years Patient selection criteria: indication to include 1 or more of bleeding, pain and pressure. UAEs performed emergently or in preparation for same-day hysterectomy were excluded. Exclusion criteria included postmenopausal status, desired fertility, symptom profile not likely attributable to fibroids. Technique: prophylactic antibiotics were usually administered.Choice of particles was by operator preference; polyvinyl alcohol particle was the primary particle of choice until tris-acryl gelatin microspheres were introduced in 2000. **Median follow-up: 4.8 years** Conflict of interest/source of funding: none	Number of patients analysed: **562** ***Bilateral UAE successfully performed = 94.1% (529/562)*** (although 7 required 2 procedures) ***Unilateral UAE = 5.9% (33/562)*** (17 were unilateral for technical reasons and 16 anatomic, with the majority being successful only on the left). ***Length of hospital stay after UAE*** • < 2 nights = 90.7% • 2 nights = 8.4% • 3 nights = 0.9% ***Subsequent hysterectomy after UAE*** = 17.8% (100/562) (none within 30 days, 39 within the first year) The only factor significantly associated with an increased risk of hysterectomy was the number of vessels embolised (16.6% for bilateral and 36.4% for unilateral, p = 0.0006) ***Rate of hysterectomy at 5 years*** (life-table method) = 19.7% Beyond 5 years, no additional hysterectomies were performed among 192 women with follow-up ranging from 5–7.7 years. 5.7% (32/562) of women underwent additional uterine conserving procedures for fibroid-related symptoms (12 myomectomies, 11 attempted repeat UAEs, 9 endometrial ablations). 7 pregnancies occurred from 7–30 months after UAE.	Technical difficulties cited: spasm, inability to cannulate or catheterise, vessel dissection. 9.6% (54/562) of patients had 63 emergency department visits for fibroid or post-UAE related symptoms within 2 years of UAE (30 were within 7 days). Pain was the most common indication for visit (54%). Readmission = 3.0% (17/562) (12 for infection, 3 for pain, 2 for bleeding) 3 readmissions led to hysterectomy (2 for bleeding, 1 for infection, occurring 33–130 days after UAE)	**Follow-up issues**: • 4 cases in which the procedure was attempted were excluded because no vessels were embolised. **Study design issues**: • Retrospective cohort study of all 'Kaiser Permanente Northern California' members. • 8 study centres (16 radiologists). • All statistical tests were 2-sided. **Study population issues**: • Most of the study cohort were aged between 40 and 50 years so many will have transitioned into menopause during the study period.

Abbreviations used: BMI, body mass index; CI, confidence interval; FSH, follicle simulating hormone; HRQoL, health related quality of life; MRI, magnetic resonance imaging; NS, not significant; OR, odds ratio; QoL, quality of life; RCT, randomised controlled trial; RR, relative risk; UAE, uterine artery embolisation; UFSQoL, uterine fibroid symptoms and quality of life.

Study details	Key efficacy findings	Key safety findings	Comments
Walker WJ (2006)[13] **Case series** UK Recruitment period: not reported Study population: women becoming pregnant after UAE **n = 56 pregnancies** Mean age: not reported Patient selection criteria: not reported Technique: not described **Follow-up: not reported** Conflict of interest/source of funding: not reported.	**56 completed pregnancies were identified in approximately 1200 women after UAE.** 108 patients were attempting to become pregnant and 33 of these became pregnant (30.6%). 18 women had unintentional pregnancies. 58.9% (33/56) of pregnancies had a successful outcome (in 27 women), including 18.2% (6/33) preterm (< 37 weeks) deliveries. 30.4% (17/56) of pregnancies miscarried (13 during the first trimester) (the rate in the general obstetric population is quoted as 10–15%). There were 3 terminations, 2 stillbirths and 1 ectopic pregnancy. One of the stillbirths was at 33 weeks' gestation and there was a true knot in the cord. The second was at 37 weeks' gestation and the uterus ruptured through a previous caesarean scar. There was 1 case of placenta previa. Premature rupture of membranes = 9.1% (3/33) Of the 33 deliveries, 24 (72.7%) were delivered by caesarean section (13 elective); 9 were because of fibroids. Postpartum haemorrhage = 18.2% (6/33). There was 1 case of intrauterine growth retardation requiring a caesarean section at 33 weeks' gestation for impaired uterine artery blood flow.		**Study design issues**: • Retrospective analysis of all pregnancies after UAE by a single interventional radiologist. **Study population issues:** • The mean age at cessation of all pregnancies 37 years (described as 'extremely high'). • 58% of all pregnancies were first conceptions and these patients generally have higher rates of pregnancy-related complications. **Other issues:** • The authors note that compared with the general obstetric population, there was a significant increase in delivery by caesarean section and an increase in preterm delivery, postpartum haemorrhage, miscarriage and lower pregnancy rates. These results can be partly explained by the demographics of the study population.

Abbreviations used: BMI, body mass index; CI, confidence interval; FSH, follicle simulating hormone; HRQoL, health related quality of life; MRI, magnetic resonance imaging; NS, not significant; OR, odds ratio; QoL, quality of life; RCT, randomised controlled trial; RR, relative risk; UAE, uterine artery embolisation; UFSQoL, uterine fibroid symptoms and quality of life.

Study details	Key efficacy findings	Key safety findings	Comments
Hamoda H (2009)[14] **Case report** UK Recruitment period: 2008 Study population: woman with symptomatic uterine fibroids **n = 1** Age: 44 years Patient selection criteria: not reported Technique: Polyvinyl alcohol particles of 350–500 µm and 510 – 700 µm in diameter were used. **Follow-up: not reported** Conflict of interest/source of funding: not reported	**Fatal pulmonary embolus after UAE** The largest fibroid was 6 cm in diameter. The UAE procedure was apparently uneventful and no immediate complications were noted. The patient developed sudden-onset shortness of breath and went into cardiac arrest 19 hours after UAE. Postmortem autopsy confirmed that the cause of death was a pulmonary embolism. It was not clear if the embolus was from the pelvic or the lower-limb veins. There was a history of previous pelvic surgery but no clinical history of thrombotic tendency.		The authors note that to their knowledge this is the first such case in the UK.

Abbreviations used: BMI, body mass index; CI, confidence interval; FSH, follicle simulating hormone; HRQoL, health related quality of life; MRI, magnetic resonance imaging; NS, not significant; OR, odds ratio; QoL, quality of life; RCT, randomised controlled trial; RR, relative risk; UAE, uterine artery embolisation; UFSQoL, uterine fibroid symptoms and quality of life.

Study details	Key efficacy findings	Key safety findings	Comments
Reinblatt SL (2008)[15] **Case report** Canada Recruitment period: 2006 Study population: women with symptomatic uterine fibroids **n = 2** Age: 50 and 54 years Patient selection criteria: not reported Technique: not described **Follow-up: not reported** Conflict of interest/source of funding: not reported	**Septic uterus after UAE for uterine fibroids triggered by endometrial biopsy** Uterine sepsis developed at 4 and 9 months after UAE, and at 10 and 16 days after endometrial sampling. Case 1 After UAE, symptoms initially improved but after several months vaginal bleeding became irregular and heavy. Repeat MRI 6 months after UAE showed complete necrosis of the fibroid. Intimate contact between the fibroid and the endometrium was seen. An endometrial biopsy was done 9 months after UAE, which showed benign necrotic endometrium. Ten days later, the patient developed sepsis and a large pelvic abscess was found. The patient underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy. Case 2 Four months after UAE, patient presented with vaginal discharge, painful cramping and increased uterine bleeding. An endometrial biopsy showed secretory endometrium. Sixteen days later, the patient presented with urinary retention and foul-smelling vaginal discharge. Imaging showed that an intramural fibroid had become submucous and had prolapsed into the uterine cavity. She underwent laparoscopic total hysterectomy and bilateral salpingo-oophorectomy, during which a large, foul-smelling necrotic uterus with a large prolapsing fibroid was found.		The authors state that women who have had UAE and present with necrotic fibroid adjacent to the endometrium should not undergo endometrial biopsy.

Abbreviations used: BMI, body mass index; CI, confidence interval; FSH, follicle simulating hormone; HRQoL, health related quality of life; MRI, magnetic resonance imaging; NS, not significant; OR, odds ratio; QoL, quality of life; RCT, randomised controlled trial; RR, relative risk; UAE, uterine artery embolisation; UFSQoL, uterine fibroid symptoms and quality of life.

Study details	Key efficacy findings	Key safety findings	Comments
Wagreich A (2009)[16] **Case report** USA Recruitment period: not reported **n = 1** Age: 46 years Technique: not described **Follow-up: 9 months** Conflict of interest/source of funding: not reported	**Advanced ovarian carcinoma following bilateral UAE** Patient was treated with bilateral UAE for symptomatic uterine fibroids following pelvic sonography and MRI, which depicted bilateral normal adnexa. The patient was noncompliant with planned post-procedure follow-up. Nine months after UAE, a routine MRI showed a mass in the cul-de-sac that was not present previously. A total abdominal hysterectomy, bilateral salpingo-oophorectomy, appendectomy, pelvic and paraaortic lymph node sampling and tumour debulking were performed. Histopathology confirmed stage III ovarian carcinoma.		The authors note that this is the first report of ovarian cancer following UAE.
Lazarou S (2005)[17] **Case report** Canada Recruitment period: 2000 **n = 1** Age: 40 years Technique: not described Conflict of interest/source of funding: not reported	**Ureteric obstruction requiring nephrectomy after uterine fibroid embolisation** UAE performed in May 2000. There were no identified complications during or immediately after the procedure. In January 2003, the patient developed right flank and lower quadrant pain. Ultrasonography and nuclear imaging revealed a non-functioning hydronephrotic right kidney. Cystoscopy and right retrograde pylogram showed complete obstruction of the right ureter 6 cm above the ureteroovesical junction. The patient elected to undergo laparoscopic nephrectomy. The authors postulate that embolisation of the uterine artery may have resulted in segmental infarction of the ureter or fibroid infarction may have created periureteral or ureteral inflammation and fibrosis.		

Efficacy

Symptom relief

The UK registry of 1387 patients reported that 84% had improved symptoms at 6 months and 83% at 24 months after uterine artery embolisation (UAE)[2]. Data from the US registry showed that patients had significantly fewer symptoms at follow-up compared with before UAE (at 3-year follow-up, the mean symptom score for 1218 patients was 16.5 compared with 58.6 at baseline, $p < 0.001$)[3].

An RCT comparing UAE with myomectomy, with a mean follow-up of 25 months, reported that 88% (46/52) of patients had relief from symptoms in the UAE group, compared with 88% (51/58) of patients in the myomectomy group (p = not significant)[6].

An RCT of 177 patients comparing UAE with hysterectomy reported similar proportions of patients in each group with at least moderate improvement in pain at 24-month follow-up (85% vs 78%, $p = 0.3$)[7,8]. The proportion of patients reporting at least moderate improvement in bulk related symptoms was also similar in the 2 groups (66% vs 69%, $p = 0.71$).

An RCT of 157 patients comparing UAE with surgery (hysterectomy or myomectomy) reported improvement in symptoms for patients in both groups[4]. Patients in the surgery group, however, showed a statistically significantly bigger improvement than those in the UAE group ($p = 0.004$ at 1 month, $p = 0.03$ at 12 months).

A non-randomised comparative study reported that a significantly lower proportion of patients treated by UAE had symptom relief compared with those treated by hysterectomy (85% [472/554] vs 99% [352/355], $p < 0.0001$)[9,10].

A case series of 200 patients reported that the proportion of patients with improvement of symptoms fell from 93% (180/193) at 3 months to 73% (133/182) at 5 years[11].

Quality of life

The UK registry reported a statistically significant improvement in health-related quality of life scores after UAE (79.5 after 6 months vs 44.1 at baseline, $p < 0.001$)[2]. The US registry also reported a significant improvement in quality of life (at 3 year follow-up, the mean quality of life score for 1201 patients was 89.6 compared with 46.9 at baseline, $p<0.001$)[3].

The RCT of 157 patients comparing UAE with surgery reported that some aspects of quality of life were better for women in the UAE group compared with the surgery group at 1-month follow-up. At 12 months, the quality of life was similar for women in the 2 groups[4].

Reduction in uterine and fibroid volume

The UK registry data showed a mean reduction in uterine volume of 40% (n = 666). The mean reduction in fibroid diameter was 2.2 cm (n = 847)[2]. An RCT including 88 patients treated by UAE reported a mean reduction in uterine volume of 48% and a mean volume reduction of the largest fibroid of 60%, at 24 month follow-up[7,8]. A case series of 200 patients reported that the mean volume reduction of the largest fibroid was 58% at 12 months and the mean volume reduction of the uterus was 39%[11].

Re-interventions

The UK registry reported that 11% (150/1387) of patients underwent a further intervention during a mean follow-up of 13 months, including 38 (3%) hysterectomies, 68 (5%) repeat UAE and 10 (1%) myomectomies[2]. The US registry reported a re-intervention rate of 15% during a 3-year follow-up (10% hysterectomy, 3% myomectomy and 2% repeat UAE)[3].

An RCT reported that 33% (19/52) of patients had a further intervention after UAE compared with 3% (2/58) of patients after myomectomy ($p < 0.0001$)[5]. Another RCT reported that 24% (19/81) of patients required hysterectomy during the 2 years after UAE[7,8].

A non-randomised comparative study reported that 11% (73/649) of patients underwent hysterectomy after UAE, 5% (32/649) underwent myomectomy and 5% (29/649) had repeat UAE during a mean follow-up of 5 years[9,10]. Two case series including 762 patients reported hysterectomy rates of 14% (25/182) and 20% at 5 years after UAE[11,12].

Pregnancies

An RCT of 121 women with a mean follow-up of 25 months reported that 50% (13/26) of women who tried to conceive after UAE became pregnant compared with 78% (31/40) of women after myomectomy ($p < 0.05$)[6]. The live birth rate was 19% (5/26) for women in the UAE group and 48% (19/40) for women in the myomectomy group ($p < 0.05$). The rate of spontaneous abortion or missed miscarriage was 64% in the UAE group and 23% in the myomectomy group ($p < 0.05$).

In a non-randomised comparative study including 649 women treated with UAE, 27 women achieved 37 pregnancies after UAE (representing 9% of those women who indicated that they wished or were uncertain of their wish for children). There were 15 miscarriages, 2 ectopic pregnancies, 1 termination and 19 successful live births (from 16 women). Of the live births, 79% were delivered by caesarean section; 6 due to complications of pregnancy or delivery[9,10].

Safety

The systematic review reported a large variation in the reported rate of complications, ranging from 5% to 73%[1]. In the UK registry report, 14% (191/1387) of patients had a total of 198 adverse events after being discharged from hospital[2]. Of these, 74% (147) occurred within the first 12 months of the UAE procedure.

Procedural problems

The UK registry of 1387 patients reported 2 cases each of artery dissection or perforation and groin bleeding or pseudoaneurysm. There was 1 case of femoral artery occlusion[2]. Another study reported artery dissection in 1 out of 58 patients[6]. One study reported a severe vasovagal event requiring atropine in 1 out of 106 patients[4].

Structural damage

One study reported that 1% (5/649) of patients had structural damage caused by UAE, which was not further specified[9,10]. The UK registry reported 1 bowel perforation that was treated by laparotomy[2].

Infection

In the systematic review, there was 1 death in a series of 21 patients, due to septic shock and multiple organ failure 25 days after UAE[1]. A non-randomised comparative study reported that 3% (17/649) of patients had septicaemia and emergency myomectomy or hysterectomy[9,10]. The UK registry reported uterine infection in 2% (28/1387) of patients[2]. It noted that there were significantly more infective complications post discharge for those patients who did not receive prophylactic antibiotics.

Amenorrhoea

In 4 studies, the reported rates of amenorrhoea after UAE ranged from 0.5% (7/1387) at 13 months after UAE to 29% (365/1278) at 36 months[2,3,9,10,11].

Validity and generalisability of the studies

- There are several studies from the UK, including a large registry, an RCT and a large non-randomised comparative study[2,4,10].
- The study reporting data from the UK registry had a relatively high loss to follow-up. It is likely that the re-intervention rate reported by this study is an

underestimate. The authors note that some women may have undergone hysterectomy without the interventional radiologist being made aware[2,3].

- The UK registry originally excluded women who desired future fertility, but this changed as UAE became more established. Although some pregnancies are reported, it is not known how many women tried to become pregnant after UAE but failed[2].
- One RCT of UAE versus hysterectomy and a case series specifically excluded women who desired future pregnancy[7,12].
- In general, data about the number of women actively seeking pregnancy and the number of live births achieved after UAE are very limited.
- One RCT of UAE versus myomectomy only included women who were planning a future pregnancy[6]. This is the only study that did not exclusively include symptomatic patients.
- Some studies excluded women with particular types of fibroid. In particular, subserosal, submucosal and/or pedunculated fibroids were listed as exclusion criteria in 4 studies[4,6,7,11].
- One study excluded women if the size of the dominant fibroid was greater than 12 cm or the uterus was enlarged to a size corresponding to more than 4 months of pregnancy[6]. Another study excluded women if the uterus size corresponded to more than 24 weeks of pregnancy[11].
- Studies differed in the way complications are defined.
- A number of different embolic agents were used.

Existing assessments of this procedure

In 2009, the Royal College of Radiologists (RCR) and the RCOG jointly produced guidelines on 'Clinical recommendations on the use of uterine artery embolisation in the management of fibroids'[18]. The summary of recommendations includes the following statements:

- Early and mid-term results of UAE are promising, indicating that it is at least as safe as the surgical alternatives. It provides good symptom relief and is particularly effective for heavy menstrual bleeding.
- For women with symptomatic fibroids, UAE should be considered as one of the treatment options.
- UAE as treatment for fibroids in women of child-bearing age who wish, or might wish, to become pregnant in the future should only be offered after fully informed discussion and should be considered on a case-by-case basis. The increased risks of caesarean section and the possibility of increased pregnancy complications should be fully understood.
- UAE is contraindicated in women who have evidence of current or recent infection, women who are unwilling to have a hysterectomy under any circumstances and where there is significant doubt about the diagnosis of benign pathology.
- Accurate pre-treatment diagnosis is essential.

- The procedure should only be undertaken by radiologists with specialised experience in embolisation who have undergone appropriate training.

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

- Laparoscopic techniques for hysterectomy. NICE interventional procedures guidance 239 (2007). Available from www.nice.org.uk/guidance/IPG239
- Magnetic resonance image-guided focused ultrasound for uterine fibroids NICE interventional procedures guidance 231 (2007). Available from www.nice.org.uk/guidance/IPG231
- Uterine artery embolisation for the treatment of fibroids. NICE interventional procedures guidance 94 (2004). Available from www.nice.org.uk/guidance/IPG94
  Current guidance under review.
- Magnetic resonance (MR) image-guided percutaneous laser ablation of uterine fibroids. NICE interventional procedures guidance 30 (2003). Available from www.nice.org.uk/guidance/IPG30
- Laparoscopic laser myomectomy. NICE interventional procedures guidance 23 (2003). Available from www.nice.org.uk/guidance/IPG23

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 A Watkinson, Dr J Moss (British Society of Interventional Radiology),.Dr M Lumsden (Royal College of Obstetricians and Gynaecologists).

- Two Specialist Advisers considered this procedure to be established practice and no longer new. One Specialist Adviser commented that although the procedure is not new, there are still major areas of uncertainty, particularly related to impact on pregnancy.

- Appropriate comparators to the procedure are hysterectomy and myomectomy.
- Adverse events reported in the literature include death, infection, ovarian damage, uterine infarction, bladder and vulval damage.
- One Adviser listed anecdoctal adverse events as post-embolisation syndrome, pain, non-offensive discharge, hysterectomy and premature menopause.
- If patients are considering pregnancy there is a theoretical risk of placental insufficiency leading to small for gestational age, increased caesarean section and prematurity.
- One Adviser commented that the safety of the procedure in women who wish to reproduce is not known.
- Key efficacy outcomes include symptom improvement, quality of life and the need for further treatment.
- One Adviser commented that the long-term outcomes are still unclear and that there are no data on pregnancy outcomes. Another commented that the evidence supports the efficacy of UAE in the short and medium term up to 5 years.
- Appropriate training is necessary.
- One Adviser commented that not all NHS trusts provide or recommend this procedure.
- One Adviser thought that the procedure is likely to have a moderate impact on the NHS and one thought the impact was likely to be major.

Patient Commentators' opinions

NICE's Patient and Public Involvement Programme sent 60 questionnaires to 1 trust for distribution to patients who had the procedure (or their carers). NICE received 22 completed questionnaires. In addition, 17 responses were received from a survey carried out by the British Fibroid Trust, on behalf of the Patient and Public Involvement Programme.

The Patient Commentators' views on the procedure were consistent with the published evidence and the opinions of the Specialist Advisers.

Issues for consideration by IPAC

- There is a lot of published literature on this procedure; appendix A lists a large number of relevant articles including several RCTs comparing different embolic agents. There are also several case reports of complications not mentioned in table 2.

References

1. Coleman P, Ayiku L, Nicholl J, et al. (2004) Systematic review of the efficacy and safety of uterine artery embolisation in the treatment of fibroids. Sheffield: Review Body for Interventional Procedures.

2. O'Grady EA, Moss JG, Belli AM, et al. (2009) UK uterine artery embolisation for fibroids registry 2003–2008. The British Society of Interventional Radiology.

3. Goodwin SC, Spies JB, Worthington-Kirsch R, et al. (2008) Uterine artery embolization for treatment of leiomyomata. Obstetrics & Gynecology 111; 22–33.

4. Edwards RD, Moss JG, Lumsden MA, et al. (2007) Uterine-artery embolization versus surgery for symptomatic uterine fibroids. New England Journal of Medicine 356: 360–70.

5. Moss JG, Lumsden MA, Murray GD, et al. (2010) Long term (3-5 year) follow up and MRI imaging of the REST trial cohort. Unpublished personal communication.

6. Mara M, Maskova J, Fucikova Z, et al. (2008) Midterm clinical and first reproductive results of a randomized controlled trial comparing uterine fibroid embolization and myomectomy. Cardiovascular & Interventional Radiology 31: 73–85.

7. Volkers NA, Hehenkamp WJK, Birnie E, et al. (2007) Uterine artery embolization versus hysterectomy in the treatment of symptomatic uterine fibroids: 2 years' outcome from the randomized EMMY trial. American Journal of Obstetrics & Gynecology 196: 519.e1–519.e11.

8. Hehenkamp WJK, Volkers NA, Birnie E, et al. (2008) Symptomatic uterine fibroids: treatment with uterine artery embolization or hysterectomy – results from the randomized clinical embolisation versus hysterectomy (EMMY) trial. Radiology 246: 823–32.

9. Dutton S, Hirst A, McPherson K, et al. (2007) A UK multicentre retrospective cohort study comparing hysterectomy and uterine artery embolisation for the treatment of symptomatic uterine fibroids (HOPEFUL study): main results on medium-term safety and efficacy. BJOG 114: 1340–51.

10. Hirst A, Dutton S, Wu O, et al. (2008) A multi-centre retrospective cohort study comparing the efficacy, safety and cost-effectiveness of hysterectomy and uterine artery embolisation for the treatment of symptomatic uterine fibroids. The HOPEFUL study. Health Technology Assessment 12 (5).

11. Spies JB, Bruno J, Czeyda-Pommersheim F, et al. (2005) Long-term outcome of uterine artery embolization of leiomyomata. Obstetrics & Gynecology 106: 933–9.

12. Gabriel-Cox K, Jacobson GF, Armstrong MA, et al. (2007) Predictors of hysterectomy after uterine artery embolization for leiomyoma. American Journal of Obstetrics & Gynecology 196: 588.e1–588.e6.

13. Walker WJ, McDowell SJ. (2006) Pregnancy after uterine artery embolization for leiomyomata: a series of 56 completed pregnancies. American Journal of Obstetrics & Gynecology 195: 1266–71.

14. Hamoda H, Tait P, Edmonds DK. (2009) Fatal pulmonary embolus after uterine fibroid embolisation. Cardiovascular & Interventional Radiology 32: 1080–2.

15. Reinblatt SL, Krishnamurthy S, Valenti D, et al. (2008) Septic uterus after uterine artery embolization for uterine myomas triggered by endometrial biopsy. Journal of Obstetrics & Gynaecology Canada 30: 344–6.

16. Wagreich A, Salame G, Lee YC, et al. (2009) Advanced ovarian carcinoma following bilateral uterine artery embolization: a case report. Journal of Reproductive Medicine 54: 325–6.

17. Lazarou S, Herschorn S. (2005) Ureteric obstruction requiring nephrectomy after uterine fibroid embolization. The Canadian Journal of Urology 12: 2553–4.

18. Royal College of Obstetricians and Gynecologists and the Royal College of Radiologists (2009) Clinical recommendations on the use of uterine artery embolisation in the management of fibroids. Second edition. Available from http://www.rcog.org.uk/files/rcog-corp/uploaded-files/WPRUterineArteryEmbolisation2009.pdf

Appendix A: Additional papers on uterine artery embolisation for fibroids

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. Case series with fewer than 100 patients have not been included unless they are describing a series of pregnancies.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Cochrane Review			
Gupta JK, Sinha A, Lumsden MA et al. (2006) Uterine artery embolisation for symptomatic uterine fibroids. Cochrane Database of Systematic Reviews. Issue 1. Art No: CD005073. DOI: 10.1002/14651858.CD005073.pub2.	3 RCTs n = 297	UAE has a shorter hospital stay and quicker return to normal activities than hysterectomy. There was a higher rate of minor post procedural complications in the UAE group.	Search date: 2005 1 RCT was included in the ReBIP systematic review and the other 2 have been described in detail in table 2.
RCTs			
Cunningham E, Barreda L, Ngo M, et al. (2008) Uterine artery embolization versus occlusion for uterine leiomyomas: a pilot randomized clinical trial. Journal of Minimally Invasive Gynecology 15: 301–7.	RCT n = 14 Follow-up = 3 months	**UAE vs transcatheter uterine artery occlusion** Uterine artery occlusion had less postprocedural pain, reduced requirements for analgesia and shorter hospital stays than UAE.	Larger studies are included.
Hald K, Noreng HJ, Istre O et al. (2009) Uterine artery embolization versus laparoscopic occlusion of uterine vessels: long-term results of a randomized controlled trial. Journal of Vascular and Interventional Radiology 20: 1303–10.	RCT n = 66 Median follow-up = 48 months	**UAE vs laparoscopic occlusion** Clinical failure: • UAE = 17% • Laparoscopic occlusion = 48%, p = 0.02	Larger RCTs are included.
Hehenkamp WJK, Volkers NA, Bartholomeus W, et al. (2007) Sexuality and body image after uterine artery embolization and hysterectomy in the treatment of uterine fibroids: a randomized comparison. Cardiovascular & Interventional Radiology 30: 866–75.	RCT n = 177 Follow-up = 2 years (EMMY trial)	**UAE vs hysterectomy** There were no differences between the groups with regard to sexual function at 24 months. Body image improved significantly more in UAE patients than in hysterectomy patients.	Other outcomes from the same RCT are included.

Hehenkamp WJK, Volkers NA, Broekmans FJM, et al. (2007) Loss of ovarian reserve after uterine artery embolization: a randomized comparison with hysterectomy. Human Reproduction 22: 1996–2005.	RCT n = 177 Follow-up = 2 years (EMMY trial)	**UAE vs hysterectomy** Both UAE and hysterectomy affect ovarian reserve. This results in older women becoming menopausal after the intervention.	Other outcomes from the same RCT are included.
Siskin GP, Beck A, Schuster M, et al. (2008) Leiomyoma infarction after uterine artery embolization: a prospective randomized study comparing tris-acryl gelatin microspheres versus polyvinyl alcohol microspheres. Journal of Vascular & Interventional Radiology 19: 58–65.	RCT n = 53	**tris-acryl gelatin microspheres versus polyvinyl alcohol microspheres** There was a significantly greater degree of fibroid infarction in patients treated with tris-acryl gelatin microspheres than in those treated with polyvinyl alcohol microspheres.	Comparison of different embolic agents.
Spies JB, Allison S, Flick P, et al. (2004) Polyvinyl alcohol particles and tris-acryl gelatin microspheres for uterine artery embolization for leiomyomas: results of a randomized comparative study. Journal of vascular and interventional radiology: JVIR 15: 793-800.	RCT n = 100 Follow-up = 3 months	**Polyvinyl alcohol particles vs tris-acryl gelatin microspheres** No substantive differences were detected between the two groups.	Comparison of different embolic agents.
Spies JB, Allison S, Flick P et al. (2005) Spherical polyvinyl alcohol versus tris-acryl gelatin microspheres for uterine artery embolization for leiomyomas: results of a limited randomized comparative study. Journal of vascular and interventional radiology: JVIR 16: 1431-1437.	RCT n = 36 Follow-up = 3 months	**Spherical polyvinyl alcohol versus tris-acryl gelatin microspheres** The use of spherical PVA particles resulted in an unacceptably high rate of failed fibroid infarction and the study was terminated.	Comparison of different embolic agents.
Non-randomised comparative studies			
Galvez JA, McCarthy S, Weinreb J, et al. (2008) Comparison of MRI outcomes of uterine artery embolization for uterine leiomyoma using tri-acryl gelatin microspheres, polyvinyl alcohol spheres and polyvinyl alcohol particles. Journal of Computer Assisted Tomography 32: 356–61.	Non-randomised comparative study n = 101	Patients embolised with spherical polyvinyl alcohol have a higher risk of having residual enhancement on follow-up MRI than those embolised with tri-acryl gelatin microspheres or polyvinyl alcohol particles.	Comparison of dfferent embolic agents.
Goldberg J, Pereira L, Berghella V, et al. (2004) Pregnancy outcomes after treatment for fibromyomata: uterine artery embolization versus laparoscopic myomectomy. American Journal of Obstetrics and Gynecology 191: 18–21.	Non-randomised comparative study n = 192 pregnancies (53 after UAE)	**UAE vs laparoscopic myomectomy** Pregnancies after UAE had higher rates of preterm delivery (OR 6.2, 95% CI 1.4 to 27.7) and malpresentation (OR 4.3, 95% CI 1.0 to 20.5) than after myomectomy. The rates of postpartum haemorrhage and miscarriage were also higher but the differences were not statistically significant.	Review of pregnancies from multiple series. A large series of pregnancies from the UK is included.
Healey S, Buzaglo K, Seti L et al. (2004) Ovarian function after uterine artery embolization and	Non-randomised comparative	**UAE vs hysterectomy** Ovarian function, as indicated by	Larger studies are included

hysterectomy. Journal of the American Association of Gynecologic Laparoscopists: 348–52.	study n = 84	day 3 FSH levels, was not affected by UAE or hysterectomy.	
Hovsepian DM, Ratts VS, Rodriguez M, et al. (2006) A prospective comparison of the impact of uterine artery embolization, myomectomy, and hysterectomy on ovarian function. Journal of Vascular & Interventional Radiology 17: 1111–15.	Non-randomised comparative study n = 55 Follow-up = 6 months	**UAE vs myomectomy and hysterectomy** There was no significant difference between the groups with regard to ovarian function.	Larger studies are included
Holub Z, Mara M, Kuzel D, et al. (2008) Pregnancy outcomes after uterine artery occlusion: prospective multicentric study. Fertility and Sterility 90: 1886–91.	Non-randomised comparative study n = 58 pregnancies	**Reproductive outcomes after laparoscopic uterine artery occlusion and UAE** Spontaneous abortion: • UAE = 56% • Occlusion = 10.5% Rate of caesarean section after UAE = 80%	Larger studies are included.
McLucas B, Chespak L, Kaminsky D. (2008) Myoma necrosis following Gelfoam™ embolization of uterine myomata. Minimally Invasive Therapy 17: 200–4.	Non-randomised comparative study n = 54	**Gelfoam™ vs traditional particles** Purulent necrosis of leiomyomata: • Gelfoam™ = 36% (4/11) • Traditional particles = 2% (1/43) p = 0.005	Comparison of different embolic agents. Small sample size.
Ohgi S, Nakagawa K, Inoue H, et al. (2007) Uterine artery embolization should not be recommended without careful consideration in the treatment of symptomatic uterine fibroids. Journal of Obstetrics & Gynaecology Research 33: 506–11.	Non-randomised comparative study n = 136 Follow-up = 12 months	**UAE vs laparoscopic surgery (myomectomy)** Convalescence was similar for the 2 groups. UAE had a higher incidence of adverse symptoms than laparoscopic surgery.	Larger studies are included.
Rasuli P, Hammond I, Al-Mutairi B, et al. (2008) Spherical versus conventional polyvinyl alcohol particles for uterine artery embolization. Journal of Vascular & Interventional Radiology 19: 42–6.	Non-randomised comparative study n = 149 Follow-up = 12 months	**Conventional vs spherical polyvinyl alcohol particles** The use of spherical particles resulted in less fibroid shrinkage and less improvement in clinical symptoms compared with conventional particles.	Comparison of different embolic agents.
Siskin GP, Shlansky-Goldberg RD, Goodwin SC, et al. (2006) A prospective multicenter comparative study between myomectomy and uterine artery embolization with polyvinyl alcohol microspheres: Long-term clinical outcomes in patients with symptomatic uterine fibroids. Journal of Vascular & Interventional Radiology 17: 1287-1295.	Non-randomised comparative study n = 149 Follow-up = 24 months	UAE with PVA microspheres was associated with greater sustained improvements in symptom severity and HRQoL and with fewer complications compared with myomectomy.	Larger studies are included.
Spies JB, Cooper JM, Worthington-Kirsch R et al. (2004) Outcome of uterine embolization and hysterectomy for leiomyomas: results of a multicenter study. American Journal of Obstetrics &	Non-randomised comparative study n = 152	**UAE vs hysterectomy** Both procedures substantially improved symptoms for most patients, with an advantage for hysterectomy at 12 months for	Larger studies are included.

Gynecology 191: 22-31.	Follow-up = 12 months	pelvic pain.	
Case series			
Abbara S, Nikolic B, Pelage JP et al. (2007) Frequency and extent of uterine perfusion via ovarian arteries observed during uterine artery embolization for leiomyomas. AJR American Journal of Roentgenology. 188: 1558-1563.	Case series n = 145	The presence of residual fibroid perfusion is more likely if the ovarian arteries are large, have rapid flow or have flow that extends into the pelvis.	Larger studies are included.
Chrisman HB, Liu DM, Bui JT et al. (2005) The safety and efficacy of a percutaneous closure device in patients undergoing uterine artery embolization. Journal of Vascular & Interventional Radiology 16: 347-51.	Case series n = 342	The suture-mediated closure device provided safe and effective haemostasis in patients undergoing UAE.	Study focused on the safety and efficacy of closure device.
Huang J Y, Kafy S, Dugas A et al. (2006) Failure of uterine fibroid embolization. Fertility & Sterility 85: 30–35.	Case series n = 233 Mean follow-up = 13 months	Overall failure rate of UAE = 9.4%	Studies with longer follow-up are included.
Firouznia K, Ghanaati H, Sanaati M, et al. (2008) Uterine artery embolization in 101 cases of uterine fibroids: do size, location, and number of fibroids affect therapeutic success and complications? Cardiovascular & Interventional Radiology 31: 521–6.	Case series n = 101 Follow-up = 1 year	Neither the success rate nor the complication rate was affected by the primary fibroid size, location or total number of fibroids.	Larger studies are included.
Firouznia K, Ghanaati H, Sanaati M, et al. (2009) Pregnancy after uterine artery embolization for symptomatic fibroids: a series of 15 pregnancies. AJR American 192: 1588–92.	Case series n = 15 pregnancies	61% (14/23) of women wishing to become pregnant succeeded. There were 2 miscarriages. The other 13 pregnancies went to term, were uncomplicated and ended in elective caesarean section.	Larger studies are included.
Katsumori T, Kasahara T, Tsuchida Y, et al. (2008) Amenorrhea and resumption of menstruation after uterine artery embolization for fibroids. International Journal of Gynecology & Obstetrics 103: 217–21.	Case series n = 221 Mean follow-up = 44.5 months	The rates of onset of permanent amenorrhoea changed over time and differed according to age at the time of UAE. There was no onset of permanent amenorrhoea after up to 6-year follow-up in women who were younger than 40 years at the time of UAE.	Larger studies are included.
Katsumori T, Kasahara T, Kin Y et al. (2008) Infarction of uterine fibroids after embolization: relationship between postprocedural enhanced MRI findings and long-term clinical outcomes. Cardiovascular & Interventional Radiology 31: 66–72.	Case series n = 221 Mean follow-up = 29.6 months	The degree of infarction of uterine fibroids after embolisation on enhanced MRI was related to long-term clinical outcomes.	Larger studies are included.

Katsumori T, Nakajima K, Mihara T (2003) Is a Large Fibroid a High-Risk Factor for Uterine Artery Embolization? American Journal of Roentgenology 181: 1309–14.	Case series n = 152	There was no increased risk of complications with fibroids larger than 10 cm.	Larger studies are included.
Katsumori T, Akazawa K, Mihara T. (2005) Uterine artery embolization for pedunculated subserosal fibroids. AJR American Journal of Roentgenology. 184: 399-402.	Case series n = 196 Follow-up = 1 year	There were no serious complications after UAE for pedunculated subserosal fibroids with stalk diameters 2 cm or larger.	Larger studies are included.
Kim HS, Tsai J, Lee JM et al. (2006) Effects of utero-ovarian anastomoses on basal follicle-stimulating hormone level change after uterine artery embolization with tris-acryl gelatin microspheres. Journal of Vascular & Interventional Radiology 17: 965–71.	Case series n = 124 Follow-up = 6 months	44% (55/124) of patients had patent anastomoses between the uterine and ovarian arteries. UAE in patients with anastomoses was associated with a greater risk of significant increase in basal FSH level.	Larger studies are included.
Lohle PNM, Voogt MJ, De Vries J, et al. (2008) Long-term outcome of uterine artery embolization for symptomatic uterine leiomyomas. Journal of Vascular & Interventional Radiology 19: 319–26.	Case series n = 93 Follow-up = 1 year	Symptom relief = 72% (67/93) Patient satisfied or very satisfied = 90%.	Larger studies are included.
Lohle PNM, Boekkooi FP, Smeets AJ, et al. (2006) Limited uterine artery embolization for leiomyomas with tris-acryl gelatin microspheres: 1-Year follow-up. Journal of Vascular & Interventional Radiology 17: 283-287.	Case series n = 158 Follow-up = 1 year	93% of patients were satisfied or very satisfied. Mean uterine volume and fibroid volume were significantly decreased.	Larger studies are included.
Park AJ, Bohrer JC, Bradley LD, et al. (2008) Incidence and risk factors for surgical intervention after uterine artery embolization. American Journal of Obstetrics and Gynaecology 199: 671.e1–671.e6.	Case series n = 454 Median follow-up = 14 months	22% risk for requiring additional surgical intervention.	Case series with longer follow-up is included.
Park HR, Kim MD, Kim NK. et al. (2005) Uterine restoration after repeated sloughing of fibroids or vaginal expulsion following uterine artery embolization. European Radiology 15: 1850-1854.	Case series n = 124	Vaginal expulsion or fibroid sloughing is a possible course following UAE that is manageable.	Larger studies are included.
Pinto Pabon I, Porras Magret J, Ayerbe Unzurrunzaga E, et al. (2008) Pregnancy after uterine fibroid embolization: follow-up of 100 patients embolized using tri-acryl gelatin microspheres. Fertility and Sterility 90: 2356–60.	Case series n = 57 Follow-up: up to 3 years	Pregnancy rate = 19% (11/57) 8 live births (4 caesarean deliveries), 3 early miscarriages. There were no cases of abnormal placental implantation.	Small case series.

Pisco JM, Bilhim T, Duarte M, et al. (2009) Management of uterine artery embolization for fibroids as an outpatient procedure. Journal of Vascular & Interventional Radiology 20: 730–5.	Case series n = 234 Follow-up = 6 months	Improvement in menorrhagia = 92% (146/158) Improvement in bulk symptoms = 89% (39/44) Improvement in pain = 80% (20/25) Decrease in uterine volume = 34% Decrease in fibroid volume = 39%	Studies with longer follow-up are included.
Rajan DK, Beecroft JR, Clark TW et al. (2004) Risk of intrauterine infectious complications after uterine artery embolization. Journal of Vascular & Interventional Radiology 15: 1415-1421.	Case series n = 410	Technical success rate = 99% No specific risk factor for intrauterine infection following UAE was identified.	Studies with longer follow-up are included.
Smeets AJ, Lohle PN, Vervest HA et al. (2006) Mid-term clinical results and patient satisfaction after uterine artery embolization in women with symptomatic uterine fibroids. Cardiovascular & Interventional Radiology 29: 188-191.	Case series n = 135 Median follow-up = 14 months	Improvement of symptoms and patient satisfaction were both good in the vast majority of patients.	Larger studies are included.
Spies JB, Cornell C, Worthington-Kirsch R, et al. (2007) Long-term outcome from uterine fibroid embolization with tris-acryl gelatin microspheres: results of a multicenter study. Journal of Vascular & Interventional Radiology 18: 203-207.	Case series n = 96 Follow-up = 3 years	Much or moderate improvement in pelvic pain = 83% 84% of patients were moderately or very satisfied with their outcome.	Larger studies are included.
Walker WJ, Barton-Smith P. (2006) Long-term follow up of uterine artery embolisation – an effective alternative in the treatment of fibroids. BJOG: An International Journal of Obstetrics & Gynaecology 113: 464–8.	Case series n = 172 Follow-up = 5 – 7 years	75% of women had either a return to normal or an improvement in menstrual flow compared to baseline. 16% of women required further treatment. Premature menopause was diagnosed in 1 woman. 88% of women were satisfied with the outcome.	Larger studies are included.
Case reports (adverse events)			
Aungst M, Wilson M, Vournas K et al. (2004) Necrotic leiomyoma and gram-negative sepsis eight weeks after uterine artery embolization. Obstetrics & Gynecology 104: 1161–4.	Case report n = 1	**Necrotic fibroid and sepsis 8 weeks after UAE** Required hysterectomy and bilateral salpingo-oophorectomy.	Complication already described.
Bedaiwy MA, Paraiso MFR. (2004) Pelvic organ prolapse after uterine artery embolization for uterine myoma. International Urogynecology Journal 15: 214– 5.	Case report n = 1	**Pelvic organ prolapse developed 16 months after UAE**	Case report

Czeyda-Pommersheim F, Magee ST, Cooper C et al. (2006) Venous thromboembolism after uterine fibroid embolization. Cardiovascular & Interventional Radiology 29: 1136–40.	Case series n = 8	**Nonfatal thromboembolism complications** Estimate frequency of non-fatal thromboembolism complications = 0.4%	Complication already described.
De Blok S, De Vries C, Prinssen H et al. (2003) Fatal sepsis after uterine artery embolization with microspheres. Journal of Vascular & Interventional Radiology 14: 779–83.	Case report n = 1	**Fatal sepsis** UAE with microspheres.	Complication already described.
Dietz DM, Stahlfeld KR, Bansal S et al. (2004) Buttock necrosis after uterine artery embolization. Obstetrics & Gynecology 104: 1159–61.	Case report n = 1	**Buttock necrosis** After surgical debridement, healing occurred over 14 weeks.	Nontarget embolisation is already described in table 2.
Gavrilescu T, Sherer DM, Temkin S, et al. (2006) Small bowel volvulus after uterine artery embolization requiring bowel resection: A case report. Journal of Reproductive Medicine for the Obstetrician & Gynecologist 51: 739-741.	Case report n = 1	**Small bowel volvulus requiring bowel resection** Bowel obstruction diagnosed 7 days after UAE, treated by laparotomy.	Complication already described.
Gonsalves C, Franciosa SV, Shah S, et al. (2007) Patient presentation and management of labial ulceration following uterine artery embolization. Cardiovascular & Interventional Radiology 30: 1263–6.	Case reports n = 2	**Labial ulceration (non-target embolisation)** Both cases completely resolved within 1 week.	Complication already described.
Naeem S, Aitkens L, Evans AS, et al. (2009) Leiomyosarcoma following uterine artery embolisation. Journal of Obstetrics & Gynaecology 29: 74–7.	Case report n = 1	**Leiomyosarcoma following UAE** Sarcomatous change within a pre-existing fibroid, diagnosed 3 months after UAE.	Complication already mentioned.
Nikolic B, Nguyen K, Martin LG et al. (2004) Pyosalpinx Developing from a Preexisting Hydrosalpinx after Uterine Artery Embolization. Journal of Vascular & Interventional Radiology 15: 297-301.	Case report n = 1	**Pyosalpinx developing from a pre-existing hydrosalpinx** Treated by hysterectomy and oophorectomy.	Case report (super-infection)
Ogliari KS, Mohallem SV, Barrozo P et al. (2005) A uterine cavity-myoma communication after uterine artery embolization: Two case reports. Fertility & Sterility 83: 220-222.	Case report n = 2	**Communication between uterine cavity and a degenerated fibroid** Required laparoscopic correction of the uterine wall defect.	Case report (fistula)
Papadia A, Salom EM, Fulcheri E et al. (2007) Uterine sarcoma occurring in a premenopausal patient after uterine artery embolization: A case report and review of the literature. Gynecologic Oncology 104: 260-263.	Case report n = 1	**Uterine leiomyosarcoma diagnosed 13 months after UAE**	Complication already described.

Rastogi S, Wu Y-H, Shlansky-Goldberg et al. (2004) Acute renal failure after uterine artery embolization. Cardiovascular & Interventional Radiology 29: 188-191.	Case report n = 1	**Acute renal failure** Patient was admitted to hospital for renal failure 7 days after UAE. The patient responded to persistent hydration and was discharged after 4 days.	Case report.
Vilos GA, Urian R, Chang P, et al. (2008) Femoral artery puncture site pseudoaneurysm formation following uterine artery embolization for symptomatic fibroids: a case report. Journal of Obstetrics and Gynaecology Canada 31: 263–6.	Case report n = 1	**Pseudoaneurysm after UAE** Ruptured pseudoaneurysm required surgical repair. The wound was healing well at 3 months after UAE.	Complication already mentioned.

Appendix B: Related NICE guidance for uterine artery embolisation for fibroids

Guidance	Recommendations
Interventional procedures	**Laparoscopic techniques for hysterectomy. NICE interventional procedures guidance 239 (2007).** 1.1 Current evidence on the safety and efficacy of laparoscopic techniques for hysterectomy (including laparoscopically-assisted vaginal hysterectomy [LAVH], laparoscopic hysterectomy [LH], laparoscopic supracervical hysterectomy [LSH] and total laparoscopic hysterectomy [TLH]) appears adequate to support their use, provided that normal arrangements are in place for consent, audit and clinical governance. 1.2 Clinicians should advise women that there is a higher risk of urinary tract injury and of severe bleeding associated with these procedures, in comparison with open surgery. 1.3 Advanced laparoscopic skills are required for these procedures, and clinicians should undergo special training and mentorship. The Royal College of Obstetricians and Gynaecologists has developed an Advanced Training Skills Module, 'Benign Gynaecological Surgery: Laparoscopy' (www.rcog.org.uk/index.asp?PageID=1951). This would need to be supplemented by further training in order to achieve the skills required for total laparoscopic hysterectomy. **Magnetic resonance image-guided focused ultrasound for uterine fibroids NICE interventional procedures guidance 231 (2007).** 1.1 Current evidence on the safety and efficacy of magnetic resonance image (MRI)-guided transcutaneous focused ultrasound for uterine fibroids is such that this procedure should only be used with special arrangements for consent and for audit or research. 1.2 Clinicians wishing to use MRI-guided transcutaneous focused ultrasound ablation for uterine fibroids should take the following actions. • Inform the clinical governance leads in their Trusts. • Ensure that patients understand the uncertainty about the procedure's safety and efficacy and provide them with clear written information. In addition, use of the Institute's information for patients ('Understanding NICE guidance') is recommended (available from www.nice.org.uk/IPG231publicinfo). • Audit and review clinical outcomes of all patients having

	MRI-guided transcutaneous focused ultrasound ablation for uterine fibroids (see section 3.1). 1.3 Further research on the procedure and publication of long-term outcomes would be useful. The Institute will review the procedure upon publication of further evidence **Uterine artery embolisation for the treatment of fibroids. NICE interventional procedures guidance 94 (2004).** *This guidance is currently under review.* 1.1 Current evidence on uterine artery embolisation (UAE) suggests that it is safe enough for routine use and that there is symptomatic benefit in the majority of patients in the short term. However, more evidence is required on the degree and duration of the procedure's benefits, and of its effects on fertility. 1.2 Clinicians wishing to undertake UAE should take the following actions. • Ensure that patients understand the uncertainty about the degree and duration of the procedure's benefits and provide them with clear written information. Use of the Institute's Information for the Public is recommended. • Audit and review clinical outcomes of all patients having UAE. Data should be submitted to the British Society of Interventional Radiology registry (www.bsir.org). 1.3 Patient selection should be made with the involvement of a multidisciplinary team, which should include a gynaecologist and an interventional radiologist. 1.4 The Institute may review the procedure upon publication of further evidence. **Magnetic resonance (MR) image-guided percutaneous laser ablation of uterine fibroids. NICE interventional procedures guidance 30 (2003).** 1.1 Evidence on safety and efficacy outcomes of MR image-guided percutaneous laser ablation of uterine fibroids is insufficient to support its use without special arrangements for consent and for audit or research. Clinicians wishing to undertake MR image-guided percutaneous laser ablation should inform the clinical governance leads in their Trusts. They should ensure that women offered the procedure understand the uncertainty about its safety and efficacy and should provide them with clear written information. Use of the Institute's Information for the Public is recommended. Clinicians should ensure that appropriate arrangements are in place for audit or research. Publication of safety and efficacy outcomes will be useful in reducing the current uncertainty. NICE is not undertaking further investigation at present.

	Laparoscopic laser myomectomy. NICE interventional procedures guidance 23 (2003). 1.1 Current evidence on the safety and efficacy of laparoscopic laser myomectomy does not appear adequate to support the use of this procedure without special arrangements for consent and for audit or research. Clinicians wishing to undertake laparoscopic laser myomectomy should inform the clinical governance leads in their Trusts. They should ensure that patients offered it understand the uncertainty about the procedure's safety and efficacy and should provide them with clear written information. Use of the Institute's Information for the Public is recommended. Clinicians should ensure that appropriate arrangements are in place for audit or research. Publication of safety and efficacy outcomes will be useful in reducing the current uncertainty. NICE is not undertaking further investigation at present. 1.2 Clinicians undertaking this procedure should undergo training as recommended by the Royal College of Obstetricians and Gynaecologists Working Party on Training in Endoscopic Surgery (www.rcog.org.uk).
Clinical guidelines	**Heavy Menstrual Bleeding. NICE clinical guideline 44 (2007).** • 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. • 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. • When surgery for fibroid-related HMB is felt necessary then UAE, myomectomy and hysterectomy must all be considered, discussed and documented. • Women should be informed that UAE or myomectomy will potentially allow them to retain their fertility. • UAE is recommended for women with HMB associated with uterine fibroids and who want to retain their uterus and/or avoid surgery. • 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. • 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 fibroids

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	29/03/2010	March 2010
Database of Abstracts of Reviews of Effects – DARE (CRD website)	29/03/2010	-
HTA database (CRD website)	29/03/2010	-
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	29/03/2010	March 2010
MEDLINE (Ovid)	29/03/2010	1950 to March Week 3 2010
MEDLINE In-Process (Ovid)	29/03/2010	March 26, 2010
EMBASE (Ovid)	29/03/2010	1980 to 2010 Week 12
CINAHL (NLH Search 2.0)	29/03/2010	-
BLIC (Dialog DataStar)	29/03/2010	-

MEDLINE search strategy

The MEDLINE search strategy was adapted for use in the other sources.

1	Uterine Neoplasms/
2	Leiomyoma/
3	Myoma/
4	(uter$ adj3 (neoplasm$ or cancer$ or tumo$ or growth$)).tw.
5	leiomyom$.tw.
6	myom$.tw.
7	myofibro$.tw.
8	or/1-7
9	Embolization, Therapeutic/
10	UAE.tw.
11	embolotherap$.tw.

12	(uter$ adj3 arter$ emboli$).tw.
13	or/9-12
14	8 and 13
15	Animals/
16	Humans/
17	15 not (15 and 16)
18	14 not 17