Uterine artery embolisation for the treatment of symptomatic uterine fibroids

---

January 2006

MSAC application 1081

Assessment report

ISBN 0 642 82860 1

ISSN (Print) 0 642 82860 1

ISSN (Online) 0 642 82861 X

First printed September 2006

Paper-based publications

Internet sites

Electronic copies of the report can be obtained from the Medical Services Advisory Committee's internet site at http://www.msac.gov.au/

Printed copies of the report can be obtained from:

The Secretary
Medical Services Advisory Committee
Department of Health and Ageing
Mail Drop 106
GPO Box 9848
Canberra ACT 2601

Enquiries about the content of the report should be directed to the above address.

The Medical Services Advisory Committee (MSAC) is an independent committee which has been established to provide advice to the Minister for Health and Ageing on the strength of evidence available on new and existing medical technologies and procedures in terms of their safety, effectiveness and cost-effectiveness. This advice will help to inform government decisions about which medical services should attract funding under Medicare.

MSAC recommendations do not necessarily reflect the views of all individuals who participated in the MSAC evaluation.

This report was prepared by the Medical Services Advisory Committee with the assistance of Dr Anthony Brooks, Ms Tracy Merlin, Ms Linda Mundy, Ms Hedyeh Hedayati, Mr John Moss and Professor Janet Hiller from Adelaide Health Technology Assessment (AHTA), Department of Public Health, University of Adelaide. Karen Hall, Business Manager from the Radiology Department of Alfred Hospital assisted with the costing of uterine artery embolisation. The report was edited by Ms Jo Mason from Mason Edit. The report was endorsed by the Minister for Health and Ageing on 28th March 2006.

Publication approval number: 3810

Contents

Tables

Figures

Executive summary

The procedure

Uterine artery embolisation (UAE) is a uterine-conserving, minimally invasive technique that treats symptomatic uterine fibroids. UAE achieves its aim by blocking blood supply to the dominant fibroid via the injection of embolic material into the uterine arteries. The dominant fibroid undergoes cell death and necrosis due to a lack of blood supply, resulting in a reduction in size of the fibroid and relief in the primary patient-relevant symptoms of menorrhagia, pelvic pain and pelvic bulk. Existing procedures available in Australia for the treatment of symptomatic uterine fibroids include hysteroscopic resection, myomectomy and hysterectomy. These procedures are currently reimbursed under Medicare. Hysterectomy, which removes the uterus, is by far the most commonly performed procedure in Australia.

The Medical Services Advisory Committee – role and approach

The Medical Services Advisory Committee (MSAC) was established by the Australian Government to strengthen the role of evidence in health financing decisions in Australia. The MSAC advises the Minister for Health and Ageing on the evidence relating to the safety, effectiveness and cost-effectiveness of new and existing medical technologies and procedures, and under what circumstances public funding should be supported.

A rigorous assessment of evidence is thus the basis of decision-making when funding is sought under Medicare. A team from Adelaide Health Technology Assessment (AHTA) at the Department of Public Health, University of Adelaide, was engaged to conduct a systematic review of the literature on uterine artery embolisation for the treatment of symptomatic fibroids. Literature from the period 1990 – March, 2005 was canvassed for inclusion in the review. An advisory panel with expertise in this area then evaluated the evidence presented in the review and provided advice to the MSAC.

The MSAC's assessment of uterine artery embolisation

Clinical need

Uterine fibroids are the most common benign tumours in women. The population prevalence of asymptomatic uterine fibroids is commonly quoted at 25 per cent, but the literature contains a median 13 per cent estimate. Using the literature based prevalence estimate and assuming that 10 to 40 per cent of these cases are symptomatic, the approximate number of women with symptomatic uterine fibroids in Australia (based on 2001 census figures) ranges from 81,459 to 325,838. In Australia 14,760 hospital separations for uterine fibroids were recorded for 2002–03. It is therefore apparent that only a minority of uterine fibroids cause symptoms severe enough for women to seek surgical intervention.

Safety

In order to assess the safety of UAE, the procedure was compared to hysterectomy and uterine-conserving fibroid surgery. Comparative treatments for which there was evidence available were abdominal hysterectomy and abdominal myomectomy.

On the basis of one level II and three level III-2 studies, UAE appeared to be as safe as, or safer than, hysterectomy. None of the comparative studies reported cases of death, septic shock, serious non-target embolisation or uterine perforation. Major complications of haemorrhage, deep vein thrombosis and organ damage were more prevalent after hysterectomy compared to UAE. Conversely, UAE was associated with higher rates of minor complications such as vaginal discharge, thigh paraesthesia, renoureteral colic and vulvovaginitis. The two procedures were equivalent for reoperation or rehospitalisation as a consequence of complications, and for the preservation of ovarian function. UAE case reports highlight the potential for rare infective complications associated with tissue necrosis *in situ*.

On the basis of limited evidence, UAE appears to be as safe as, or safer than, myomectomy. Comparative safety data on UAE and myomectomy were primarily based on one medium quality level III-2 study, with one additional poor quality level III-2 study contributing to the evidence base for some outcomes. Comparative studies reported no serious complications such as death, septic shock, serious non-target embolisation, uterine perforation or thrombo-embolism. Overall, abdominal myomectomy was associated with a higher rate of safety complications compared to UAE.

Effectiveness

The effectiveness of treating symptomatic uterine fibroids using UAE was compared to treatment using abdominal hysterectomy and myomectomy. Based on level II and III-2 evidence, UAE appears to be less effective for controlling menorrhagia, pain and pressure symptoms associated with uterine fibroids compared to hysterectomy. UAE patients are also more likely to undergo further intervention to resolve their symptoms than hysterectomy patients. Nevertheless, improvements in quality of life after the two procedures have been shown to be equivalent. Convalescence time for UAE is approximately one-third that of hysterectomy. In terms of the primary outcomes, UAE is therefore less effective than hysterectomy, but this conclusion needs to be considered in the context of patient preference for an intact uterus.

Based primarily on one medium quality level III-2 study, UAE appears to be as, or more, effective than abdominal myomectomy. Menorrhagic and pain symptoms are more likely to be resolved or significantly improved after UAE compared to myomectomy, whereas the converse applies for pressure symptoms. Convalescence is significantly shorter after the minimally invasive UAE procedure when compared to abdominal myomectomy; and rehospitalisation or reoperation rate, due to failure of the procedure to resolve symptoms, is equivalent.

Cost-effectiveness

Although UAE appears to be as safe as, or safer than, abdominal myomectomy and just as effective, the study on which these conclusions are predominately based has a small sample size. Proceeding with a cost-effectiveness analysis based on the results of one

small study could result in large confidence intervals around estimates, introducing a significant element of random error which might not be resolvable by sensitivity analysis. Until more data are published that reinforce the effectiveness equivalence or superiority of UAE compared to myomectomy (abdominal or otherwise), a cost-effectiveness analysis is unlikely to provide much guidance for policy makers. A cost-comparison analysis was therefore conducted for UAE and its comparators, abdominal hysterectomy and abdominal myomectomy. The perspective of this analysis was that of the Australian health system overall rather than a societal approach.

Reliable cost estimates per patient were only able to be calculated for UAE in the private sector. Conversely, costs per patient for the comparators abdominal hysterectomy and myomectomy could only be reliably obtained for the public sector. The costs per patient calculated for UAE (private sector), abdominal hysterectomy for non-malignancy (public sector) and uterine myomectomy (public sector) were $5,731, $6,195 and $6,331, respectively. However, because of the inability to estimate the cost per patient for all three procedures within either one or other of the private or public health sectors specifically, it is not yet possible to determine if there are substantial differences between hysterectomy, myomectomy and UAE in the cost per patient to the Australian health system overall.

Financial implications for the Commonwealth

Information from the Schedule of Medicare Benefits was used to estimate the likely impact on Commonwealth expenditure. The maximum additional Commonwealth expenditure, assuming that all private sector uterine-conserving and removal procedures subsidised in 2002–03 (n = 19,036) are replaced by UAE, was estimated at $24.0 million. An alternative estimate, assuming that only the uterine-conserving treatments in the private sector that were subsidised by the Commonwealth in 2002–03 (n = 2,424) are replaced by UAE, resulted in a substantially lower estimate of additional Commonwealth expenditure of $3.1 million.

Recommendation

The evidence suggests that UAE is safe, clinically effective and potentially cost-effective for the treatment of symptomatic uterine fibroids. It appears to be more effective than myomectomy for the control of menorrhagia and pain but less effective in controlling pressure symptoms. It is safer but less effective in controlling symptoms compared with hysterectomy.

The MSAC recommends that UAE be funded on an interim basis for the treatment of women with symptomatic uterine fibroids with a review within 5 years. The MSAC recommends that patients be referred by a specialist gynaecologist.

The Minister for Health and Ageing accepted this recommendation on 28th of March 2006.

Introduction

The Medical Services Advisory Committee (MSAC) has reviewed the use of uterine artery embolisation, which is an interventional procedure to treat symptomatic uterine fibroids. The MSAC evaluates new and existing health technologies and procedures for which funding is sought under the Medicare Benefits Scheme in terms of their safety, effectiveness and cost-effectiveness, while taking into account other issues such as access and equity. The MSAC adopts an evidence-based approach to its assessments, based on reviews of the scientific literature and other information sources, including clinical expertise.

The MSAC's terms of reference and membership are at Appendix A. The MSAC is a multidisciplinary expert body, comprising members drawn from such disciplines as diagnostic imaging, pathology, surgery, internal medicine and general practice, clinical epidemiology, health economics, consumer health and health administration.

This report summarises the assessment of current evidence for uterine artery embolisation for symptomatic uterine fibroids.

Background

Rationale for assessment

The Royal Australian and New Zealand College of Radiologists (RANZCR) applied to the Medical Services Advisory Committee (MSAC) to have uterine artery embolisation (UAE) for the treatment of symptomatic uterine myoma (fibroids) funded under the Medicare Benefits Schedule (RANZCR 2004).

An evidence-based assessment of the safety, effectiveness and cost-effectiveness of UAE for the treatment of symptomatic uterine fibroids was therefore undertaken for consideration by MSAC.

Uterine fibroids

Uterine 'fibroids' – also known as leiomyomas, leiomyofibromas, fibromyomas and myomas – are non-neoplastic (benign) tumours composed of smooth muscle cells and collagenous fibrous tissue that develop within or near the wall of the uterus (myometrium). Uterine fibroids may grow as a single nodule or in clusters, can be hard, and range in size from 1 mm to over 20 cm in diameter. The proportion of fibrous tissue increases with age, and with multiple fibroids the uterus can become enlarged (Pugh 2000; Technology Evaluation Center 2002).

Uterine fibroids are classified according to their location: intracavitary (within the uterine cavity); submucous (spanning the uterine cavity and wall); intramural (in the uterine wall); subserous (outside the uterine wall); and pedunculated (connected to the uterus by a stalk) (Indman 2000; Technology Evaluation Center 2002).

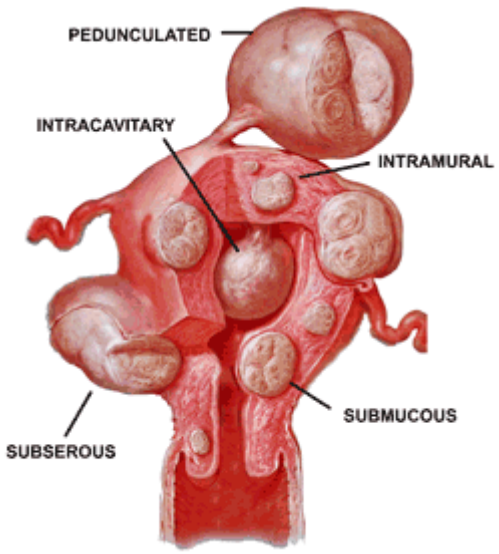

Figure 1 **Various locations of fibroids within the uterus** (Source: Indman 2000)

The factors that initiate the development of uterine fibroids are unknown. It is unclear whether the initial and ongoing stimulus for fibroid growth is genetic, viral, an inflammatory repair response to normal cell loss, or is due to another cause. However, fibroid growth appears to be associated with oestrogen and progesterone (both naturally occurring and from the oral contraceptive pill or hormone replacement therapy), peptide growth factors and the availability of an adequate blood supply (Broder et al 1999). Fibroids grow during the reproductive years, with involution (return of enlarged organ to normal size) and sometimes calcification after menopause (Indman 2000; RANZCR 2004).

Fibroids have a primitive type of blood supply with little resistance to ischaemia (disruption of blood supply). They may be supplied by one uterine artery, although it is more common for fibroids to have a bilateral supply. The uterine arteries have collaterals that communicate with the ovarian and cervical arteries, and in some cases the ovarian artery may supply blood to the fibroid (RANZCR 2004).

Diagnosis of uterine fibroids is made on routine pelvic examination, and confirmed through imaging procedures such as ultrasound, hysteroscopy or magnetic resonance imaging (Braunwald et al 2001; Smith 2000).

In the 10 to 40 per cent of women with problematic uterine fibroids, symptoms can include excessive menstrual blood loss (menorrhagia); cramping; pelvic pain; pressure or bulk symptoms (such as frequent urination or incontinence as a consequence of compression of the bladder or bowel, and lower back pain) in the lower abdomen due to an enlarged fibroid uterus; pain during sexual intercourse; and in some cases infertility or miscarriage (Braunwald et al 2001; Broder et al 1999; Technology Evaluation Center 2002; Topfer & Hailey 2002).

The procedure

The uterine arteries provide the principal blood supply to both the uterus and uterine fibroids. If blood flow from the uterine arteries is disrupted to the myometrium (uterine wall), it usually recovers rapidly because it is supplied by multiple collateral arteries (Smith 2000). However, if blood flow is disrupted to uterine fibroids they are unlikely to recover from the ischaemia (RANZCR 2004).

Interventional radiologists have performed UAE since 1979 to treat women with emergency post-partum haemorrhage, and also in the pre-operative setting. It was, however, an observation by a Parisian gynaecologist that surgery was not required in most cases after embolisation (due to fibroid shrinkage) that led to its first use as a stand-alone treatment in 1994 (Hovsepian et al 2004; Ravina et al 1995b; Smith 2000; Technology Evaluation Center 2002).

Interventional radiologists usually perform UAE upon referral from a gynaecologist. However, if the patient is directly referred from a general practitioner, it is best practice (Society of Interventional Radiology; Spies et al 2003) to refer the patient to a gynaecologist, so that there is an existing patient–gynaecologist relationship in case any complications arise. Prior to and during the embolisation procedure, the uterine arteries are studied via digital subtraction angiography in order to clearly define the anatomy. The patient receives mild intravenous sedation and local anaesthesia. A catheter is introduced into the common femoral artery to provide access to the uterine arteries. Each uterine

artery is then deeply catheterised, in turn, with a microcatheter (Figure 2). Once catheterised, vascular occluding agents – particles of polyvinyl alcohol or tris-acryl gelatin (such as 350–500 micron Ivalon particles or 300 micron embolic microspheres) – are injected into the artery.

The end-point of the embolisation procedure is the cessation of blood flow to the fibroids (causing ischaemic necrosis), with residual flow through the uterine artery. Ischaemia is established between 15 and 30 minutes after the embolisation procedure is completed and the patient develops severe pain, requiring analgesia. However, current sophisticated pain management protocols enable most Australian patients to return home 6 hours after the procedure, although they may experience residual pain over the following week (Broder et al 1999; Hovsepian et al 2004; RANZCR 2004; Technology Evaluation Center 2002; Topfer & Hailey 2002).

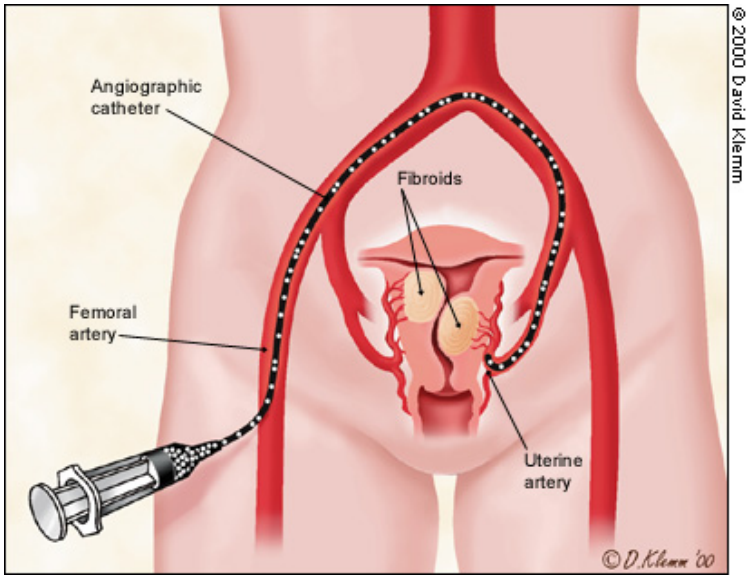

Figure 2 Uterine artery embolisation for the treatment of symptomatic uterine fibroids

A follow-up ultrasound or magnetic resonance imaging (currently not rebatable in Australia) is sometimes performed at 3, 6 and 12 months to objectively assess the effectiveness of the embolisation technique (ie absence of blood supply to the fibroid(s) and fibroid shrinkage). However, these regular post-UAE scans are primarily performed to collect clinical data rather than for patient feedback or monitoring.

Clinical success is measured by reduction in symptom severity, with successful procedures resulting in immediate relief from menorrhagia and a reduction in bulk symptoms within a few weeks (Hovsepian et al 2004; RANZCR 2004). Patients who experience unsatisfactory symptom resolution usually require a magnetic resonance imaging scan to establish the cause of any continuing symptoms. However, in the absence of symptoms an ultrasound visualisation of the uterus is considered satisfactory for post-procedural care.

The primary advantage of UAE over abdominal hysterectomy and myomectomy is that it is a non-invasive procedure and hence is associated with a significantly shorter convalescence. UAE also spares the uterus; however, it is still contraindicated for women

who wish to become pregnant, whereas some myomectomy operations are performed for infertility management.

Intended purpose

The intended purpose of UAE is to treat the symptoms associated with uterine fibroids, while preserving the uterus, via a minimally invasive interventional technique. The currently accepted indications and absolute and relative contraindications – as determined by the joint Standards of Practice Committee of the Cardiovascular and Interventional Radiological Society of Europe and the Society of Interventional Radiology – for UAE for the treatment of symptomatic uterine fibroids are given in Table 1.

Table 1 Indications and contraindications for uterine artery embolisation for fibroid treatment

Indications	Contraindications	
	Absolute	*Relative*
Presence of uterine fibroid(s), confirmed by adequate imaging, causing significant lifestyle-altering symptoms – specifically, mass effect on the bladder or intestines and/or dysfunctional uterine bleeding that is prolonged, associated with severe dysmenorrhea or causing severe anaemia.	A viable pregnancy	Coagulopathy
	Active (untreated) infection	Severe contrast material allergy
	Suspected leiomyosarcoma or adnexal malignancy	Renal impairment
		Immunocompromise
		Previous pelvic irradiation or surgery
		Chronic endometritis
		Partially treated pelvic infection
		Desire to maintain childbearing potential
		Concurrent use of gonadotropin-releasing hormone agonist
		Extensive endometriosis or adenomyosis
		Pedunculated subserosal uterine fibroid (attachment point <50% of diameter) – at risk of uterine detachment

Source: (Hovsepian et al 2004)

By the year 2000 it was estimated that more than 10,000 UAE procedures had been performed worldwide (Hovsepian et al 2004). The American College of Obstetrics and Gynaecology consider UAE as having promising short-term results but have indicated that the procedure is investigational or relatively contraindicated (Table 1) for patients who may wish to become pregnant in the future (ACOG 2004).

Existing procedures

There are two main categories of current treatment for symptomatic uterine fibroids – uterine-removing and uterine-conserving.

If there is no desire for further childbearing, the standard treatment for symptomatic uterine fibroids is hysterectomy. Abdominal or vaginal hysterectomy involves the surgical removal of the uterus and is the most certain cure of fibroids as there is no possibility of fibroid recurrence. Hysterectomy is the most common invasive treatment for

symptomatic uterine fibroids and is 5 to 10 times more common than myomectomy (Broder et al 1999).

A large range of uterine-conserving (although not necessarily fertility-preserving) treatments are also available. The type of treatment may depend on the location, size and number of uterine fibroids (Figure 1) and also whether the treatment is aimed at the fibroid itself or the control of symptoms associated with the fibroid (Smith 2000).

In younger women, myomectomy – also known as fibroidectomy, leiomyomectomy, fibromectomy or hysteromyomectomy – is a common alternative to hysterectomy. It is the surgical removal of uterine fibroids, and may be indicated for women with symptomatic uterine fibroids who have also experienced infertility or repeated miscarriage, or have a desire for future childbearing (Braunwald et al 2001; Pugh 2000). In some cases where the woman has no desire for future pregnancy, myomectomy is supplemented with endometrial ablation (the endometrium is scraped and burned to create amenorrhea). Myomectomy may be performed by gynaecologists, using either an open or laparoscopic technique.

Other, less established, treatments for uterine fibroids include myolysis or cryomyolysis. Myolysis involves the application of a laser probe or electric current to heat-coagulate symptomatic uterine fibroids. Cryomyolysis is a similar treatment, but instead of using a laser or electrical current, a probe is used to deliver a freezing agent such as liquid nitrogen directly to the fibroid to cause it to shrink and necrose. Another treatment for uterine fibroids being investigated in the United States involves the laparoscopic clipping of the uterine arteries. None of these techniques, however, are routinely practised in Australia.

Fibroids can also be treated medically through the administration of progesterone or progesterone-like drugs or gonadotropin releasing hormone (GnRH) antagonists. These medications are currently not listed on the Pharmaceutical Benefits Schedule for the treatment of uterine fibroids. They are believed to have a limited cycle of use (<6 months), produce menopausal symptoms and may increase the risk of osteoporosis. They are often used to treat women with symptomatic uterine fibroids who are close to menopause, or as a debulking agent prior to hysterectomy or myomectomy. Hormone suppression therapy is not a relevant comparator for assessing the safety, effectiveness and cost-effectiveness of UAE because it is considered an adjunct to other fibroid treatments rather than a treatment in itself.

Comparators

Abdominal, vaginal or laparoscopic hysterectomy and myomectomy were the comparators for this report. Vaginal hysteroscopic resection of submucous fibroids was also a comparator. The goal of hysterectomy is to alleviate the symptoms associated with fibroids by removing the offending organ (ie the uterus), whereas myomectomy and hysteroscopic resection remove the fibroids surgically while maintaining the integrity of the uterus. These latter procedures are therefore classified as uterine-conserving treatment for uterine fibroids.

Marketing status of the technology

The occlusion agents currently listed/registered on the Australian Register of Therapeutic Goods, and available on the Australian market, include: Polyvinyl Alcohol foam particles (William A Cook Pty Ltd; ARTG number 21940), PVA particles (Contour; Boston Scientific Corporation; ARTG number 31918), Ivalon particles (Bard Corporation; ARTG number 57792) and Embospheres (Endotherapeutics Pty Ltd; ARTG number 71918).

Current reimbursement arrangement

There is currently no reimbursement arrangement for uterine artery embolisation (UAE) per se. However, Medicare Benefits Schedule (MBS) numbers used for digital subtraction angiography of the abdomen (4–6 data acquisition runs; MBS number 60027) and the initiation of management of anaesthesia for digital subtraction angiography (MBS number 21922) during UAE would be used. The RANZCR have suggested that UAE could be included under item number 35321 on the Medicare Benefits Schedule (Box 1), as the service comprises the introduction of agents to occlude an artery – in this instance referring to the occlusion of the uterine arteries supplying blood to the fibroids (RANZCR 2004).

Box 1 MBS item number 35321 and explanatory notes

MBS item no: 35321

PERIPHERAL ARTERIAL OR VENOUS CATHETERISATION to administer agents to occlude arteries, veins or arterio-venous fistulae or to arrest haemorrhage, percutaneous or by open exposure, excluding associated radiological services or preparation, and excluding aftercare, not being a service associated with photodynamic therapy with verteporfin (Anaes.) (Assist.)

(See Explanatory Note T8.35.1)

Fee: $675.85 Benefit: 75% = $506.90 85% = $617.25

Explanatory Notes

T8.35 Peripheral Arterial or Venous Embolisation (Item 35321)

T8.35.1 Uterine artery embolisation for the treatment of uterine fibroids cannot be claimed under this or any other item.

This is a new medical procedure which requires assessment by the Medical Services Advisory Committee (MSAC) to determine whether it should be supported for listing on the MBS. Further information is available from the MSAC Secretariat (see para 8.4 of the General Explanatory Notes).

Peripheral Arterial or Venous Embolisation - Item 35321 - has been amended and new note T8.35 has been added to clarify that benefits for uterine artery embolisation for the treatment of uterine fibroids cannot be claimed under this or any other item.

Source: MBS Online. July 2004. Available at: http://www7.health.gov.au/pubs/mbs/mbsjul04/MBS_Updated_July_2004_PDF/MBS%20Updated%20July%202004.pdf. [accessed 26/10/04]

UAE remains approved for the following indications: uterine artery haemorrhage after myomectomy, lacerated uterus, uncontrolled bleeding after dilatation and curettage, uncontrolled post-partum uterine bleeding, uterine arteriovenous malformation and bleeding from advanced uterine malignancy after surgery.

The current reimbursement arrangements via MBS numbers for hysterectomy, myomectomy and hysteroscopic resection are listed in Table 2.

Table 2 Current MBS item numbers for the treatment of symptomatic uterine fibroids

Treatment category	MBS item no.	Description
(1) Discriminatory item numbers [a]		
Myomectomy	35649	HYSTEROTOMY or UTERINE MYOMECTOMY, abdominal
Hysteroscopic resection	35636	HYSTEROSCOPY, involving resection of myoma, or resection of myoma and uterine septum (where both are performed)
	35623	HYSTEROSCOPIC RESECTION of myoma, or myoma and uterine septum resection (where both are performed), followed by endometrial ablation by laser or diathermy
(2) Non-discriminatory item numbers [b]		
Hysterectomy	35653	HYSTERECTOMY, ABDOMINAL, SUBTOTAL or TOTAL, with or without removal of uterine adnexae
	35657	HYSTERECTOMY, VAGINAL, with or without uterine curettage, not being a service to which item 35673 applies
	35750	LAPAROSCOPICALLY ASSISTED HYSTERECTOMY, including any associated laparoscopy
	35753	LAPAROSCOPICALLY ASSISTED HYSTERECTOMY with one or more of the following procedures: salpingectomy, oophorectomy, excision of ovarian cyst or treatment of moderate endometriosis, one or both sides, including any associated laparoscopy
	35673	HYSTERECTOMY, VAGINAL (with or without uterine curettage) with salpingectomy, oophorectomy or excision of ovarian cyst, 1 or more, 1 or both sides
	35661	HYSTERECTOMY, ABDOMINAL, requiring extensive retroperitoneal dissection, with or without exposure of 1 or both ureters, for the management of severe endometriosis, pelvic inflammatory disease or benign pelvic tumours, with or without conservation of the ovaries

[a] items approximate procedures performed for fibroid indication; [b] items include procedures for fibroid indication, as well as several other patient indications

Approach to assessment

Objective

To determine whether there is sufficient evidence, in relation to clinical need, safety, effectiveness and cost-effectiveness, to have uterine artery embolisation (UAE) for the treatment of symptomatic uterine fibroids listed on the Medicare Benefits Schedule. Benefits are currently not payable under Medicare for this procedure.

Research questions

Burden of disease

1. What is the prevalence of symptomatic uterine fibroids in Australia?

2. What is the risk of developing lifestyle-altering symptoms for Australian women with uterine fibroids?

Safety

3. Is UAE as safe as, or safer than, hysterectomy for the treatment of symptomatic uterine fibroids in women?

4. Is UAE as safe as, or safer than, other uterine-conserving treatments for the treatment of symptomatic uterine fibroids in women?

Effectiveness

5. Is UAE as, or more, effective at treating symptomatic uterine fibroids in women compared to hysterectomy?

6. Is UAE as, or more, effective at treating symptomatic uterine fibroids in women compared to other uterine-conserving treatments?

Cost-effectiveness

7. Is UAE a cost-effective treatment option for symptomatic uterine fibroids in women compared to hysterectomy?

8. Is UAE a cost-effective treatment option for symptomatic uterine fibroids in women compared to other uterine-conserving treatments?

Expert advice

An advisory panel with expertise in gynaecology, interventional radiology and consumer interests was established to evaluate the evidence and provide advice to the MSAC from a clinical or consumer perspective. In selecting members for advisory panels the MSAC's practice is to approach the appropriate medical colleges, specialist societies and

associations and consumer bodies for nominees. Membership of the advisory panel is provided at Appendix B.

Review of literature

Literature sources and search strategies

The medical literature was searched to identify relevant studies concerning uterine artery embolisation (UAE) for the period between 1990 and November 2004, as UAE for the treatment of symptomatic uterine fibroids was believed to be first performed in 1994. A search of 'Embase' was extended to March 2005. Appendix C describes the electronic databases that were used for this search, as well as the other sources of evidence – particularly grey literature – that were investigated. Appendix D lists the health technology assessment and specialty websites that were searched in November 2004.

The search terms used to identify literature in electronic databases on the incidence of uterine fibroids and the safety, effectiveness and cost-effectiveness of UAE are also presented in Appendix C.

Inclusion/exclusion criteria

The criteria for including articles varied depending on the type of research question being addressed. Often a study was assessed more than once because it addressed more than one research question. Three researchers separately applied the inclusion criteria to the collated literature. In general, articles were excluded if they did not:

- address the research question;
- provide information on the pre-specified target population;
- include uterine artery embolisation;
- compare results to the relevant comparator(s);
- address one of the pre-specified outcomes and/or provide inadequate numerator and/or denominator data; or
- have the appropriate study design.

Grey literature[1] was included in the search strategy. Unpublished literature, however, was not canvassed as it is difficult to search for this literature exhaustively and systematically, and trials that are difficult to locate are often smaller and of lower methodological quality (Egger et al 2003). It is, however, possible that these unpublished data could affect the results of this review. A post-hoc change to the protocol was made because of an abundance of level IV evidence. Effectiveness data were not extracted from case series with ≤20 patients because they were unlikely to affect the outcome of the report. Safety data were extracted from all included papers regardless of sample size.

[1] Literature not usually obtainable through conventional channels like publishers eg conference abstracts, health technology assessment reports

The inclusion criteria relevant to each of the research questions posed in this assessment are provided in Boxes 2–4 in the results section of this report.

The process of study selection went through six phases (Figure 3).

Figure 3 Study selection process

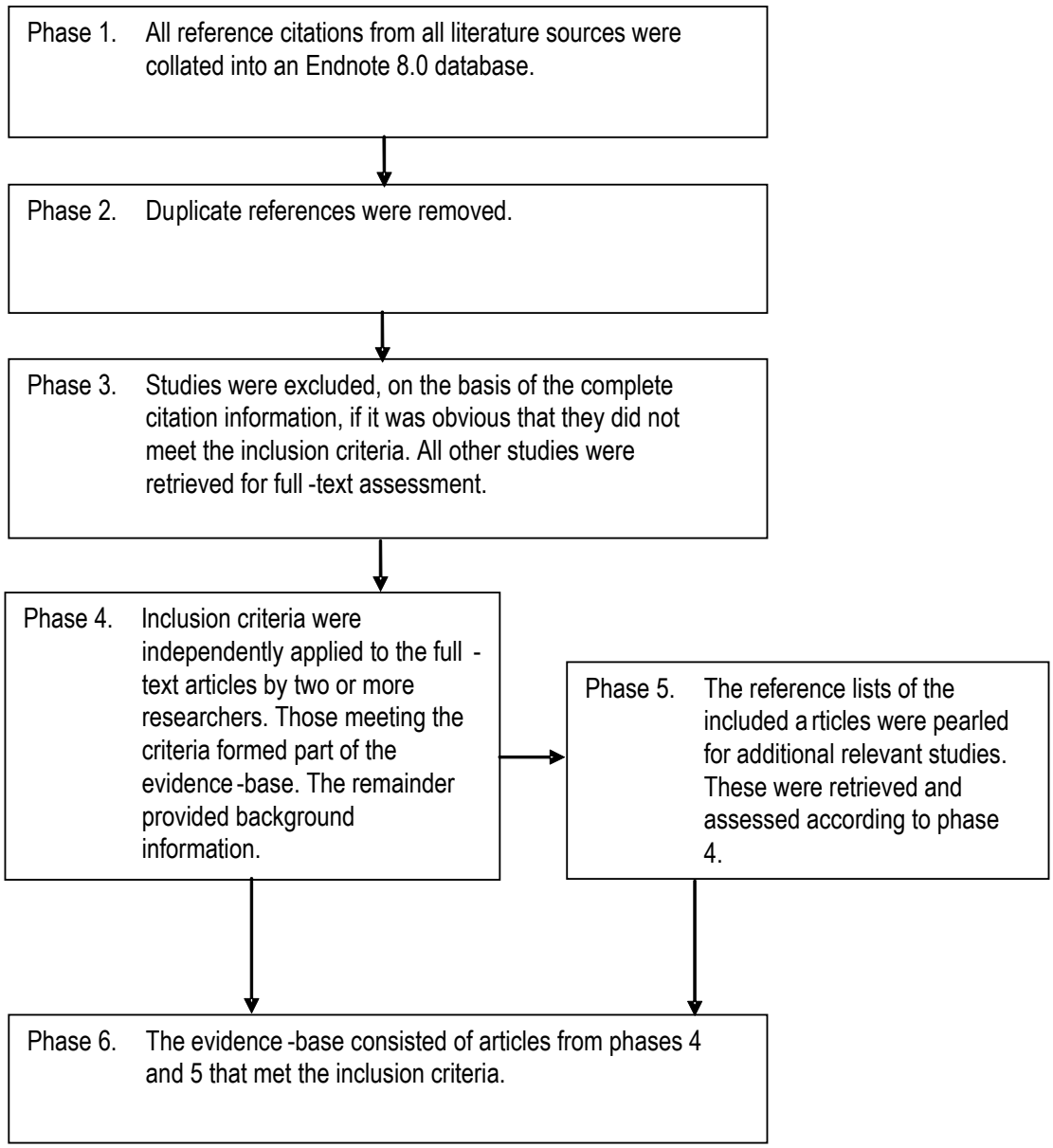

Table 3 provides a breakdown of the study selection process in terms of the number of literature citations or articles retrieved and retained from the search. Any doubt concerning inclusions at phase 4 was resolved by group consensus.

Table 3 Number of citations initially retrieved and then retained at each phase [a]

Search	Phase 2	Phase 3	Phase 4	Phase 5	Phase 6 (total Included)
Incidence and prevalence of uterine fibroids	2,137	33	6	0	6
Safety of UAE	1,511	136	111	0	111
Effectiveness of UAE	2,267	265	75	0[A]	75

[a] Additional pearled studies were only assessed/reviewed if they were comparative

Validity assessment

The evidence presented in the selected studies was assessed and classified using the dimensions of evidence defined by the National Health and Medical Research Council (NHMRC 2000).

These dimensions (Table 4) consider important aspects of the evidence supporting a particular intervention and include three main domains: strength of evidence, size of effect and relevance of evidence. The first domain is derived directly from the literature identified as informing a particular intervention. The last two require expert clinical input as part of their determination.

Table 4 Evidence dimensions

Type of evidence	Definition
Strength of evidence	
Level	The study design used, as an indicator of the degree to which bias has been eliminated by design [a]
Quality	The methods used by investigators to minimise bias within a study design
Statistical precision	The p-value or, alternatively, the precision of the estimate of the effect. It reflects the degree of certainty about the existence of a true effect
Size of effect	The distance of the study estimate from the 'null' value and the inclusion of only clinically important effects in the confidence interval
Relevance of evidence	The usefulness of the evidence in clinical practice, particularly the appropriateness of the outcome measures used

[a] See Table 5

Strength of evidence

Level

The three subdomains (level, quality and statistical precision) are collectively a measure of the strength of the evidence. The NHMRC is currently piloting a revised hierarchy of 'levels of evidence' where various study designs are ranked by type of research question

(NHMRC 2005). This revised hierarchy of evidence was used to assess the strength of evidence included in this review. Designations of these levels of evidence are shown in Table 5.

Table 5 Designations of levels of evidence [a] according to type of research question

Level	Intervention [b]	Diagnosis [e]	Prognosis	Aetiology [k]	Screening
I [a]	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies
II	A randomised controlled trial	A study of test accuracy with: an independent, blinded comparison with a valid reference standard [f] among consecutive patients with a defined clinical presentation [g]	A prospective cohort study [i]	A prospective cohort study	A randomised controlled trial
III-1	A pseudorandomised controlled trial (ie alternate allocation or some other method)	A study of test accuracy with: an independent, blinded comparison with a valid reference standard [f] among non-consecutive patients with a defined clinical presentation [g]	All or none [j]	All or none [j]	A pseudorandomised controlled trial (ie alternate allocation or some other method)
III-2	A comparative study with concurrent controls: Non-randomised, experimental trial [c] Cohort study Case-control study Interrupted time series with a control group	A comparison with reference standard that does not meet the criteria required for level II and III-1 evidence	Analysis of prognostic factors among untreated control patients in a randomised controlled trial	A retrospective cohort study	A comparative study with concurrent controls: Non-randomised, experimental trial Cohort study Case-control study
III-3	A comparative study without concurrent controls: Historical control study Two or more single arm studies [d] Interrupted time series without a parallel control group	Diagnostic case-control study [g]	A retrospective cohort study	A case-control study	A comparative study without concurrent controls: Historical control study Two or more single arm studies
IV	Case series with either post-test or pre-test/post-test outcomes	Study of diagnostic yield (no reference standard) [h]	Case series, or cohort study of patients at different stages of disease	A cross-sectional study	Case series

Tablenotes

[a] A systematic review will only be assigned a level of evidence as high as the studies it contains, excepting where those studies are of level II evidence.

[b] Definitions of these study designs are provided in NHMRC 2000, pp 7–8.

[c] This also includes controlled before-and-after (pre-test/post-test) studies, as well as indirect comparisons (ie using A vs B and B vs C to determine A vs C).

[d] Comparing single arm studies, ie case series from two studies.

[e] The dimensions of evidence apply only to studies of diagnostic accuracy. To assess the effectiveness of a diagnostic test there also needs to be a consideration of the impact of the test on patient management and health outcomes. See MSAC (2004) *Guidelines for the assessment of diagnostic technologies*. Available at: www.msac.gov.au.

[f] The validity of the reference standard should be determined in the context of the disease under review. Criteria for determining the validity of the reference standard should be pre-specified. This can include the choice of reference standard and its timing in relation to the index test. The validity of the reference standard can be determined through quality appraisal of the study. See Whiting et al (2003).

[g] Well-designed population based case-control studies (eg population based screening studies where test accuracy is assessed on all cases, with a random sample of controls) do capture a population with a representative spectrum of disease and thus fulfil the requirements for a valid assembly of patients. However, in some cases the population assembled is not representative of the use of the test in practice. In diagnostic case-control studies a selected sample of patients already known to have the disease are compared with a separate group of normal/healthy people known to be free of the disease. In this situation patients with borderline or mild expressions of the disease, and conditions mimicking the disease, are excluded, which can lead to exaggeration of both sensitivity and specificity. This is called spectrum bias because the spectrum of study participants will not be representative of patients seen in practice.

[h] Studies of diagnostic yield provide the yield of diagnosed patients, as determined by an index test, without confirmation of the accuracy of this diagnosis by a reference standard. Using such studies may be the only alternative when there is no reliable reference standard.

[i] At study inception members of the cohort are either non-diseased or all at the same stage of the disease.

[j] All or none of the people with the risk factor(s) experience the outcome. For example, no smallpox develops in the absence of the specific virus; and clear proof of the causal link has come from the disappearance of smallpox after large-scale vaccination.

[k] If it is possible and/or ethical to determine a causal relationship using experimental evidence, then the 'intervention' hierarchy of evidence should be used. If it is only possible and/or ethical to determine a causal relationship using observational evidence (eg cannot allocate groups to a potential harmful exposure, such as nuclear radiation), then the 'aetiology' hierarchy of evidence should be used.

Note 1: Assessment of comparative harms/safety should occur according to the hierarchy presented for each of the research questions, with the proviso that this assessment occurs within the context of the topic being assessed. Some harms are rare and cannot feasibly be captured within randomised controlled trials; physical harms and psychological harms may need to be addressed by different study designs; harms from diagnostic testing include the likelihood of false positive and false negative results; harms from screening include the likelihood of false alarm and false reassurance results.

Note 2: When a level of evidence is attributed in the text of a document, it should also be framed according to its corresponding research question, eg level II intervention evidence; level IV diagnostic evidence; level III-2 prognostic evidence.

Hierarchies adapted and modified from: (Bandolier 1999; Lijmer et al 1999; NHMRC 1999; Phillips et al 2001)

Quality

Studies providing information on the prevalence and incidence of symptomatic and asymptomatic uterine fibroids were not appraised for quality as no intervention or association was being tested.

Controlled studies of uterine artery embolisation (UAE) effectiveness were assessed using a modified version of the checklist developed by Downs and Black (Appendix E) (Downs & Black 1998). This checklist is suitable for trials, cohort and case-control studies, and has been psychometrically assessed to have overall high internal consistency, good test-retest and inter-rater reliability, and high criterion validity (Downs & Black 1998). The checklist contains subscale scores for reporting, external validity, bias and confounding, summing to an overall quality index score of 27. Information on specific methodological components shown empirically to impact on treatment effect sizes are also included in this checklist and were identified during the critical appraisal process and in the report – specifically, concealment of allocation, blinding and completeness of data (Juni et al 2001; Moher et al 1998; Schulz et al 1995).

The majority of studies were uncontrolled pre-test/post-test case series, which represent a poorer level of evidence for effectiveness assessment. Their quality was assessed using a checklist developed by the West Midlands Development and Evaluation Committee (Young et al 1999) that appraises selection, misclassification and reviewer bias, which sum to an overall quality score of 3 (Appendix E).

Statistical precision

Statistical precision was determined using standard statistical principles. Small confidence intervals and p-values give an indication as to the probability that the reported effect is real (NHMRC 2000). However, in studies without a control group, it is difficult to determine whether statistically significant differences can be attributed to the intervention or to other factors.

Size of effect

For the controlled studies evaluating UAE, it was important to assess whether statistically significant differences were also clinically important. The size of the effect needs to be determined, as well as whether the 95% CI includes only clinically important effects. Rank scoring methods were used to determine the clinically important benefit of the effect size in the few controlled studies available (NHMRC 2000) (Appendix E).

Relevance of evidence

Similarly, the outcome being measured in the studies should be appropriate and clinically relevant. Inadequately validated (predictive) surrogate measures of a clinically relevant outcome should be avoided (NHMRC 2000). Rank scoring methods were used to determine the clinical relevance of the safety or effectiveness outcome being assessed in UAE studies (Appendix E) (NHMRC 2000).

Data extraction and analysis

A profile was developed for each study outlining the level of evidence, quality score, inclusion/exclusion criteria for study participants, authors, publication year, location, study design, study population characteristics, type of intervention, outcomes assessed and follow-up period (Appendix F). Studies that were unable to be retrieved or that met the inclusion criteria but contained insufficient or inadequate data are provided in Appendix G. Definitions of all technical terms and abbreviations are provided in the appended Glossary.

Descriptive statistics were extracted or calculated for all safety and effectiveness outcomes (defined in the assessment protocol) in the individual studies – including numerator and denominator information, and means and standard deviations (mean±SD). Medians and inter-quartile ranges were reported for data that were not normally distributed.

Relative risk/rate ratios (RR), absolute risk differences, number needed to treat to benefit or harm and associated 95% confidence intervals (95% CIs) were calculated from individual comparative studies containing count data. Number needed to treat statistics are prefixed by NNTB (number needed to treat to benefit) or NNTH (number needed to treat to harm). They represent the number of patients who would need to be treated with the target intervention to prevent one additional harmful outcome (or facilitate one additional beneficial outcome) compared to treatment with the comparator intervention. Independent t-tests were used to examine mean differences and 95% CIs were calculated for normally distributed continuous outcomes in individual studies. In instances where both baseline and follow-up data were provided on an outcome for both UAE and its comparator, a within-groups change score and a relative change score were calculated.

Meta-analysis was not undertaken as the evidence base was heterogenous and there were only a few controlled trials comparing dissimilar treatments with outcomes that were measured differently. A qualitative synthesis of the data was therefore undertaken.

All statistical calculations and testing were performed using the statistical computer package *Stata version 8.2* (Stata Corporation 2004).

Results of assessment

Clinical need / burden of disease

Uterine fibroids are one of the most common disorders of the uterus and the most prevalent tumour in women (one in four women are affected). However, uterine fibroids are predominantly asymptomatic and do not require treatment in approximately 60 to 90 per cent of the women affected. Ethnicity may have an impact on the incidence of fibroids, with a higher incidence documented in African American women (Broder et al 1999; Technology Evaluation Center 2002; Topfer & Hailey 2002).

The clinical need in the private sector is reflected in estimates obtained from usage of items on the Australian Medicare Benefits Schedule (MBS) by Australian private patients for current (rebated) treatments for uterine fibroids. MBS items used for uterine fibroid treatment are presented in Table 6 and have been separated into discriminatory and non-discriminatory items, which respectively categorise treatments primarily used to treat fibroids and treatments that may be used for indications other than uterine fibroids. Using the discriminatory item numbers for the period July 2003 – June 2004, the total number of rebated procedures was 2,424; whilst over the same period for the non-discriminatory item numbers there were 16,612 procedures rebated. In a later section of this report these data have been used to calculate the financial implications for the Commonwealth of potentially listing uterine artery embolisation.

Hospitalisations due to uterine leiomyoma (fibroids) in both the public and private hospital sectors in 2002–03 (n=14,760; (AIHW 2005)) probably underestimate symptomatic uterine fibroid disease in Australia. Only severe symptomatic uterine fibroids are treated with hospital procedures (usually hysterectomy or myomectomy), whereas less severe symptoms would be treated in an outpatient setting.

In an attempt to capture the full burden of disease from symptomatic uterine fibroids – ie to produce an estimate that includes those women who would not necessarily undergo an invasive, surgical treatment (represented in the estimates above) but who may have symptoms sufficiently severe to opt for the less invasive uterine artery embolisation procedure - a systematic review of the literature was conducted.

Table 6 MBS item usage for current treatments for symptomatic uterine fibroids

Treatment Category	MBS item number	Total procedures (Jul 03 – Jun 04)	Description
(1) Discriminatory item numbers [a]			
Myomectomy	35649	830	HYSTEROTOMY or UTERINE MYOMECTOMY, abdominal
Hysteroscopic resection	35636	975	HYSTEROSCOPY, involving resection of myoma, or resection of myoma and uterine septum (where both are performed)
	35623	619	HYSTEROSCOPIC RESECTION of myoma, or myoma and uterine septum resection (where both are performed), followed by endometrial ablation by laser or diathermy
Total		2,424	
(2) Non-discriminatory item numbers [b]			
Hysterectomy	35653	5,362	HYSTERECTOMY, ABDOMINAL, SUBTOTAL or TOTAL, with or without removal of uterine adnexae
	35657	5,934	HYSTERECTOMY, VAGINAL, with or without uterine curettage, not being a service to which item 35673 applies
	35750	1,225	LAPAROSCOPICALLY ASSISTED HYSTERECTOMY, including any associated laparoscopy
	35753	1,394	LAPAROSCOPICALLY ASSISTED HYSTERECTOMY with one or more of the following procedures: salpingectomy, oophorectomy, excision of ovarian cyst or treatment of moderate endometriosis, one or both sides, including any associated laparoscopy
	35673	530	HYSTERECTOMY, VAGINAL (with or without uterine curettage) with salpingectomy, oophorectomy or excision of ovarian cyst, 1 or more, 1 or both sides
	35661	2,167	HYSTERECTOMY, ABDOMINAL, requiring extensive retroperitoneal dissection, with or without exposure of 1 or both ureters, for the management of severe endometriosis, pelvic inflammatory disease or benign pelvic tumours, with or without conservation of the ovaries
Total		16,612	

Source: Health Insurance Commission. Medicare Benefits Schedule Statistics. Available at: http://www.hic.gov.au (accessed 27/10/04).
[a] items approximate procedures performed for fibroid indication; [b] items include procedures for fibroid indication, as well as several other patient indications.

A total of six studies met the inclusion criteria outlined in Box 2. To assess the burden of disease from uterine fibroids systematically, the collated studies were evaluated against the criteria delineated in the review protocol. Five of these studies provided prevalence data and one assessed both point prevalence and cumulative incidence. While no Australian study met the criteria for inclusion in this review, one study assessing disease incidence was from the United States and the studies measuring prevalence of symptomatic uterine fibroids were either based in European countries (five studies) or the United States (one study). Results from these studies are therefore likely to be transferable to the Australian setting.

Box 2 Study selection criteria for burden of disease

Research questions

(1) What is the prevalence of symptomatic uterine fibroids in Australia?

(2) What is the risk of developing lifestyle-altering symptoms for Australian women with uterine fibroids?

Selection criteria	Inclusion criteria
Population	Women (post-menarche) in (1) Australia or, if this information is unavailable, in (2) Western countries of similar demographic composition.
Outcome	Prevalence – proportion of women with uterine fibroids, diagnosed clinically [a], causing patient-relevant symptoms at a specific point in time.
	Incidence – proportion of women with uterine fibroids, diagnosed clinically [a], who developed lifestyle-altering symptoms during a specific time period.
Study design	Cross-sectional surveys (with random sampling), case series of consecutive people, or cohort studies.
Search period	In order to obtain relatively recent burden of disease estimates, studies published before 1990 were not included.
Language	Studies relevant to Australia's demographic composition are most likely to be published in English. Therefore, studies in languages other than English were not included.

[a] not presenting to the clinician with symptoms, but fibroids discovered during clinical evaluation for other procedures

What is the prevalence of symptomatic uterine fibroids in Australia?

The prevalence of uterine fibroids was found to vary amongst the included studies from 3 to 27 per cent. From the six studies measuring prevalence, there were two with prevalence data at the low end of the range (Borgfeldt & Andolf 2000; Van der Leij & Lammes 1997), two in the middle (Lippman et al 2003; Maggino et al 1990) and two with high prevalence figures (DeWaay et al 2002; Marino et al 2004).

Borgfeldt and Andolf (2000) conducted a cross-sectional study in a random sample of women between 25 and 40 years of age. The prevalence of asymptomatic uterine fibroids in these women was 5.4 per cent (95% CI 3.0–7.8%) overall, with 3.3 per cent (95% CI 0.7–6.0%) in the 25–32 year-olds and 7.8 per cent (95% CI 3.6–12.0%) in the 33–50 year-olds. Although the prevalence rate may to some extent be explained by the predominately young age of the women, the rate is still quite low for this to be the sole reason. The study conducted by Van der Leij and Lammes (1997) also showed a low prevalence rate (3.4%) of uterine fibroids amongst 503 patients who were about to undertake sterilisation and did not have gynaecological complaints. The age range was recorded as being 22–47 years with a mean of 34.7 years. Therefore, both these studies have similar age compositions and were both conducted in European countries, with an expected similar demographic composition. This could contribute to the similar prevalence rates.

Two Italian studies by Maggino et al (1990) and Lippman et al (2003) found similar prevalence rates of 11.5 per cent and 15 per cent, respectively. As in the studies by Borgfeldt and Andolf (2000) and Van der Leij and Lammes, age appeared to affect the prevalence rates, with younger age being associated with a lower prevalence of fibroids. In the study by Maggino et al (1990) over 50 per cent of the women were 24–31 years of age, and in the study by Lippman et al (2003) 47 per cent of the women were less than 35 years of age.

Lippman et al (2003), together with a third Italian study conducted by Marino et al (2004), made use of the same data source – an original prospective cohort study of 981 women known as the Seveso Women's Health Study (SWHS). This initial study aimed to assess the reproductive health of women living near Seveso, where a chemical plant explosion occurred in 1976. Lippman et al (2003) included 635 women in their analysis because of their decision to include all women with intact uteri, whereas Marino et al (2004) assessed 451 women from the cohort. Marino et al (2004) excluded women with previous hysterectomy, those that had not menstruated in the past year, those using oral contraceptives or intra-uterine devices, and those who were pregnant or lactating. This difference in population selection meant that prevalence rates varied substantially, with a 15 per cent rate reported by Lippman et al (2003) in a comparatively younger patient population, while Marino et al (2004) found a 21.4 per cent prevalence rate. Marino et al (2004) suggested that this was an underestimation of the true prevalence because 90 per cent of the excluded hysterectomy patients received the surgery to treat uterine fibroids; hence, a higher prevalence rate would have been expected.

Finally, the study conducted by DeWaay et al (2002) was a prospective cohort study which calculated both the cumulative incidence and the point prevalence of uterine fibroids in an asymptomatic population of premenopausal women. The prevalence rate was identified to be 27 per cent, which was the highest recorded from the included studies. It appears that increasing age towards menopause correlates with increasing risk of developing uterine fibroids, and the DeWaay study (DeWaay et al 2002) included the older age range leading up to menopause. The high prevalence rate cannot be explained by the racial distribution in this particular study as the population consisted of over 90 per cent white women.

Differences between the reported prevalence data in these studies could be due to: 1) the sensitivity of the methods used to diagnose uterine fibroids and 2) the populations of women being studied, in that Caucasian populations are at a lower risk of developing uterine fibroids than Black populations.

Table 7 Prevalence of asymptomatic uterine fibroids

Country	Study	Population	Prevalence [95% CI]
USA	DeWaay et al (2002)	Prospective cohort study of 64 initially asymptomatic, premenopausal women	17/64 = 27% [16,39%]
Italy	Maggino et al (1990)	Cross-sectional study of 885 asymptomatic women attending for screening	102/885 = 11.5% [9,14%]
	Lippman et al (2003)	Cross-sectional study of 635 non–care-seeking (asymptomatic) women with an intact uterus	96/635 = 15% [12,18%]
	Marino et al (2004)	Cross-sectional study of 341 premenopausal women, 30–60 years old, who had an intact uterus and were menstruating	73/341 = 21.4% [17,26%]
Sweden	Borgfeldt & Andolf (2000)	Cross-sectional study of asymptomatic women 25–40 years old selected from the Swedish register in March 1996	18/335 = 5.4% [3,8%]
The Netherlands	Van der Leij & Lammes (1997)	Cross-sectional study of 503 asymptomatic women who were undergoing sterilisation	17/503 = 3.4% [2,5%]

There were no studies available that assessed the prevalence of uterine fibroids in women presenting with clinical symptoms.

What is the risk of developing lifestyle-altering symptoms for Australian women with uterine fibroids?

Only one study (DeWaay et al 2002) measured the incidence of uterine fibroids and the point prevalence of uterine fibroids in the same cohort of women (Table 7). The cohort had a mean age of 44 years (range 33–56 years) and consisted of over 90 per cent white women. The risk of uterine fibroids was found to be 13 per cent over 2.5 years, ie an annual incidence of 5.2 per cent. Although subjective assessment of symptoms (ie abnormal uterine bleeding) was undertaken, the proportion of symptomatic women was not made clear in the study. The authors only stated that most uterine fibroids were asymptomatic and not clinically apparent.

Conclusions

Prevalence data on the burden of disease from uterine fibroids varied across the included studies despite the similarity in country demographics. All included studies objectively verified the presence of uterine fibroids although there were possible differences in the sensitivity and specificity of methods used. Despite this, there were similar trends of increases in uterine fibroid prevalence with increasing age towards menopause.

In conclusion, the best available evidence to obtain an estimate of asymptomatic uterine fibroid prevalence indicates a range of 3 to 27 per cent, with a median of 13 per cent. There were no data that provided the prevalence of *symptomatic* uterine fibroids although figures of 10 to 40 per cent are commonly cited (Broder et al 1999; Technology Evaluation Center 2002; Topfer & Hailey 2002). The only available evidence to assess the risk of uterine fibroids was the study conducted by DeWaay et al (2002), which reported 5.2 per cent per year, equivalent to 5,200 per 100,000 persons per year.

Australian census data from 2001 indicates that the total female population in the age range 15–64 years was 6,266,110 (Australian Bureau of Statistics 2002). This, together with

a median prevalence rate of 13 per cent of asymptomatic women with uterine fibroids (derived from the evidence base), means that 814,594 Australian women have the potential for the disease at any one time. As there were no data on the proportion of women developing symptomatic uterine fibroids, the 10 to 40 per cent prevalence estimate cited above has been used to calculate the burden of disease for *symptomatic* uterine fibroids. This indicates an estimated prevalence range of 81,459 to 325,838 Australian women with symptomatic uterine fibroids per year. The range and severity of symptoms experienced by these women, however, will dictate the preferred treatment options.

Is uterine artery embolisation safe?

Studies were included in this assessment of the safety of uterine artery embolisation (UAE) according to the criteria outlined in Box 3.

Box 3 Study selection criteria for safety

Research questions

(1) Is UAE as safe as, or safer than, hysterectomy for the treatment of symptomatic uterine fibroids in women?

(2) Is UAE as safe as, or safer than, other uterine-conserving treatments for the treatment of symptomatic uterine fibroids in women?

Selection criteria	Inclusion criteria
Population	Women with symptomatic uterine fibroids [a].
Intervention	UAE using a vascular occluding agent.
Comparator(s)	(1) Hysterectomy. (2) Uterine-conserving treatments, including myomectomy, hysteroscopic resection, hormone suppression therapy.
Outcomes	*Major complications*, including mortality, septic shock, haemorrhage, early menopause, amenorrhea, miscarriage, serious non-target embolisation [b], uterine perforation, thrombo-embolism, organ damage, idiosyncratic drug reaction, hyponatraemia, rehospitalisation, reoperation, depression. *Minor complications*, including endometritis, post-embolisation syndrome [c], haematoma, uterine adhesions, local infection, minor bleeding.
Study design	Randomised or non-randomised controlled trials, cohort studies, registers, case series, case reports or systematic reviews of these study designs.
Search period	1/1990 [d] – 11/2004
Language	Studies in languages other than English were only translated and included if they represented a higher level of evidence than that available in the English language evidence base.

[a] Fibroids diagnosed clinically and symptoms including menorrhagia, cramping, pelvic pain, pressure or bulk symptoms (frequent urination or incontinence, lower back pain), pain during sexual intercourse, infertility, miscarriage; [b] causing thrombo-embolus, organ damage; [c] pelvic pain, fever, malaise, nausea, vomiting; [d] UAE was first performed for the treatment of symptomatic uterine fibroids in 1994.

This section of the report assesses the safety of UAE in comparison to the existing symptomatic uterine fibroid treatments of hysterectomy and myomectomy. It is inappropriate to compare UAE with the uterine-removing procedure of hysterectomy for the safety outcome of amenorrhea, as amenorrhea is an assured outcome after the latter operation. Similarly, some degree of post-embolisation syndrome is experienced by all UAE patients compared to none who undergo hysterectomy or myomectomy. Only severe post-embolisation syndrome, which requires an escalation of care or readmission to hospital, can therefore be considered as a safety issue.

Procedure related complications have been extracted from the evidence base and separated into major and minor categories. The former category includes life-changing or life-altering adverse events. The following level II and level III-2 studies form the basis for conclusions on the relative safety of UAE compared to hysterectomy and myomectomy.

A high quality level II study (Pinto et al 2003) provided an extensive and detailed list of peri-procedural complications within 30 days of UAE and hysterectomy. This analysis of complications was on a treatment received basis rather than intent to treat. A medium quality level III-2 study (Spies et al 2004b) prospectively followed UAE and hysterectomy patients for 12 months. Adverse events were recorded and categorised into Society for

Cardiovascular and Interventional Radiology (SCVIR) and American College of Gynaecologists categories, which enabled a relatively unbiased assessment of complication severity. Peri-procedural complications were reported as no different between UAE and hysterectomy within 30 days of the procedure; however, 12 months of follow-up revealed a higher occurrence of, and more severe, complications in the hysterectomy group when compared to UAE. A logistic regression analysis showed that only treatment was predictive of peri-procedural complications and that baseline differences between the groups did not influence the complication outcome.

Two medium quality level III-2 studies (Beinfeld et al 2002; Pourrat et al 2003) provided information on relative complications between UAE and hysterectomy, but because their primary comparative foci were costs associated with these procedures they did not provide a detailed interpretation of the complication outcomes. Beinfeld et al (2002) reported that 4 per cent of UAE patients (2/52) and 5 per cent of patients undergoing hysterectomy (12/250) experienced complications within their respective mean hospital stays of 0.95 and 2.6 days. Pourrat et al (2003) reported two cases of peri-operative complication within 6 months of vaginal hysterectomy compared to none after UAE.

A level III-2 medium quality study retrospectively analysed medical records for procedural complications that occurred within 30 days of UAE and myomectomy (Razavi et al 2003). The prevalence of adverse events in the myomectomy group (10/40; 25%) was higher ($p<0.05$) than that in the UAE cohort (7/62; 11%). On this basis they concluded that UAE is safer than abdominal myomectomy. A poor quality level III-2 'brief communication' by McLucas and Adler (2001) reported complication outcomes associated with 32 UAE and 16 myomectomy procedures, respectively.

The evidence provided by aforementioned comparative studies is accompanied by absolute risk estimates derived from 75 pre-test/post-test case series on UAE. These studies provide an estimate of the absolute risk of complications, but not the risk relative to other treatments. Adverse event information is also provided by case reports as a source of evidence in an attempt to capture all possible complications associated with UAE. These data cannot provide measures of the absolute risk of UAE related complications, only the type of complications that are possible.

The following sections will describe the evidence base with respect to each potential complication, be it major or minor. Tables titled 'Other complications' (Tables 19, 20) have also been included to present a more complete view of all reported safety issues. In these tables the categorisation of complications is guided by the authors' classification system. If the authors did not categorise their complications they are simply listed.

Major complications

Mortality

No comparative studies reported a treatment related death in the totals of 415, 416 and 86 patients who underwent UAE, hysterectomy and myomectomy, respectively. Similarly, there were no reports of death in 75 pre-test/post-test case series, except in Vashisht et al (2001), however, this death was previously described in a case report (Vashisht et al 1999). Three case reports described two deaths directly linked to UAE (De Blok et al 2003; Vashisht et al 1999) and another related to undiagnosed leiomyosarcoma (Goldberg et al 2004a). De Blok et al 2003 described septic shock and multiple organ failure as the cause

of death, whereas Vashisht et al (1999), whose patient died after 15 days in intensive care, reported a 'massive haemothorax complicating multi-organ failure'. Further details of these events can be found in Appendix H.

Septic shock

No comparative studies or pre-test/post-test case series reported cases of septic shock in any patients. Four case reports (Aungst et al 2004; Payne & Haney 2003) described septic shock. Two patients recovered with appropriate treatment, while the other two have already been described in the 'mortality' section.

Haemorrhage

Five comparative studies (level II and III-2 evidence) (Beinfeld et al 2002; McLucas & Adler 2001; Pinto et al 2003; Razavi et al 2003; Spies et al 2004b) (Table 8) did not register any haemorrhage complications or blood transfusions in the follow-up of 291 UAE patients. In comparison, 1 to 10 per cent (Pinto et al 2003) of patients undergoing hysterectomy experienced post-procedural haemorrhage or blood transfusion. Pinto et al (2003) also reported that an intra-procedural blood transfusion was necessary in 20 per cent (n = 4) of their hysterectomy patients. The lower value of the range is probably an underestimate of the true population haemorrhage incidence after hysterectomy because Beinfeld et al (2002) only monitored complications, on average, for 2.6 days. According to a retrospective analysis of medical records, abdominal myomectomy was associated with an 8 per cent incidence of blood transfusion within 30 days of the procedure compared to no cases in the UAE cohort (Razavi et al 2003). These data were supported by McLucas and Adler (2001), who reported that 13 per cent of their 16 myomectomy patients underwent a blood transfusion.

Of the substantial amount of level IV evidence available, only Walker et al (1999) reported one patient (out of 200) who haemorrhaged 1 month after UAE and required a three-unit blood transfusion (Walker et al 1999). Four out of 37 case reports also described blood transfusions and haemorrhage as potential complications associated with UAE. Details of these events are contained in Appendix H.

Table 8 Haemorrhage (level II and III-2 evidence)

Study	Quality / Level	Haemorrhage		Number needed to treat [95% CI]
		UAE (n = 38)	HYS (n = 19)	
Pinto et al (2003)	Randomised controlled trial Level – II QS – 24/27 Clin I – 1/4 Rel – 1/5 Stat prec – good	0/40 (0%) underwent a peri-procedural transfusion	6/20 (30%) underwent a peri-procedural transfusion 2/20 (10%) post-procedural 4/20 (20%) intra-procedural	NNTB 3 [NNTB 2 to NNTB 7] p<0.001
		UAE (n = 102)	HYS (n = 50)	

Spies et al (2004b)	Prospective cohort study Level – III-2 QS – 18/27 Clin I – 3/4 Rel – 1/5 Stat prec – average	0/102 (0%) – [0,4] experienced haemorrhage [a]	4/50 (8%) – [2,19] experienced haemorrhage	NNTB 13 [NNTB 6 to NNTB 208] p=0.004
		UAE (n = 57)	HYS (n = 300)	
Beinfeld et al (2002)	Retrospective cohort study Level – III-2 QS – 17/27 Clin I – 4/4 Rel – 1/5 Stat prec – poor	0/52 (0%) experienced haemorrhage	2/250 (1%) experienced haemorrhage	NNTB 125 [NNTB 53 to ∞ to NNTH 329] p=0.52
		UAE (n = 62)	MYO (n = 40)	
Razavi et al (2003)	Retrospective cohort study Level – III-2 QS – 18/27 Clin I – 3/4 Rel – 1/5 Stat prec – average	0/62 (0%) blood transfusion	3/40 (8%) blood transfusion	NNTB 13 [NNTB 6 to∞ to NNTH 151] p=0.03
		UAE (n = 32)	MYO (n = 16)	
McLucas & Adler (2001)	Retrospective cohort study Level – III-2 QS – 9/27 Clin I – 4/4 Rel – 1/5 Stat prec – average	0/32 (0%) blood transfusion	2/16 (13%) blood transfusion	NNTB 8 [NNTB 4 to ∞ to NNTH 27] p=0.04

HYS = hysterectomy; MYO = myomectomy; NNTB = number needed to treat to benefit; NNTH = number needed to treat to harm; Relative risk could not be calculated; 95% CI = 95% confidence interval; Level = level of evidence; QS = quality score; Clin I = clinical importance; Rel relevance of evidence; Stat prec = statistical precision; NA = not applicable; [a] Haemorrhage defined as greater than 2 units of blood loss or post-operative hematocrit level of <24 or post-operative haemoglobin concentration of <8 g/dL

Early menopause and amenorrhea

Although early menopause and amenorrhea are often related outcomes, the former is a more serious complication. Early menopause, which is associated with the initiation of bone mineral density decline, an increased risk of heart disease, hot flushes and sexual dysfunction, is significantly worse than temporary or even permanent amenorrhea. Unfortunately, the majority of studies that reported the incidence of amenorrhea in their follow-up did not confirm, via hormone measurement, whether or not the amenorrheic state reflected early menopause.

Table 9 Amenorrhea (level II and III-2 evidence)

Study	Quality / Level	Amenorrhea			
		UAE (n = 38)			HYS (n = 19)
Pinto et al (2003)	Randomised controlled trial Level – II QS – 24/27	6/38 (17%) amenorrhea at 6 months			17/17 (100%) amenorrhea at 6 months
		UAE (n = 102)			HYS (n = 50)
Spies et al (2004b)	Prospective cohort study Level – III-2 QS – 18/27	7/102 (7%) were amenorrheic at 12 months follow-up			50/50 (100%) were amenorrheic
				Age range	
		3 months	6/102 [a]	38–48 years	
		12 months	6/102	45–47 years	
		Total	7/102		

HYS = hysterectomy; Level = level of evidence; QS = quality score; [a] All, except one 46-year-old, resumed cycles

The level II study by Pinto et al (2003) reported that six UAE patients (17%) suffered from amenorrhea at the 6-month follow-up (Table 9). However, they did not verify whether these patients were sterile or had entered into early menopause via hormone level measurement (eg FSH – follicle stimulating hormone). In fact, they included amenorrheic patients when assessing the positive effectiveness outcome of menstrual bleeding reduction. Only a total hysterectomy with bilateral salpingo-oophorectomy (ie removal of ovaries) is associated with early menopause, whereas subtotal hysterectomy, which leaves at least one functional ovary, is not. It is unclear how many of the 20 hysterectomy patients in Pinto's study entered early menopause because the proportions of women who underwent total or subtotal hysterectomy were not stated. In comparison to Pinto et al (2003), a lower incidence of amenorrhea was reported by Spies et al (2004b), with seven of 102 (7%) UAE patients reporting no menstrual cycle at 12 months.

Furthermore, Spies et al (2004b) reported that the age range of amenorrheic women was 45–47 years, which suggested that they were only 3–5 years away from 'natural' menopause (Table 9). Spies et al (2004b) also reported an interesting trend in transient amenorrhea, where all but one of the six women who were amenorrheic at 3 months had recovered at the 12-month follow-up. This meant that six out of the seven women who were amenorrheic at 12 months developed amenorrhea at least 3 months after their surgery. There is therefore significant potential for short-term studies to underestimate the rate of amenorrhea in their UAE patients. Albeit unlikely, the 45–47 year-old women who developed amenorrhea between 3 and 12 months after the procedure may have undergone 'natural' amenorrhea due to menopause.

Table 10 Rates of amenorrhea after UAE (level IV evidence)

Study	Quality score [a]	Population	Amenorrhea after UAE
Goodwin et al (1999)	3/3	60 consecutive women with symptomatic fibroids	1/60 (2%) with amenorrhea
Pelage et al (2000)	3/3	80 consecutive women with symptomatic uterine fibroids	6/80 (8%) amenorrheic, of these: 2/6 (3%) transient amenorrhea 4/6 (7%) permanent amenorrhea
Razavi et al (2002)	3/3	76 consecutive women with symptomatic uterine fibroids	12/76 (16%) 5/76 (7%) persistent amenorrhea 7/76 (9%) temporary prolonged amenorrhea
Spies et al (2002b) Follow-up study to Spies et al (2001a)	3/3	400 consecutive women with confirmed uterine fibroids	Only 250 patients were available for 12 months follow-up 12/250 (5%) were amenorrheic at 3 months 4/250 (2%) were amenorrheic at 12 months
Joffre et al (2004)	2.5/3	85 women with symptomatic uterine fibroids	83/85 (98%) premenopausal 3/83 (4%) amenorrheic
Spies et al (2004a) Bruno et al (2004)	2.5/3	100 women with symptomatic uterine fibroids	Tri-acryl microspheres 1/54 (2%) were amenorrheic at 3 months PVA particles 1/46 (2%) were amenorrheic at 3 months
Klein & Schwartz (2001)	2/3	35 women with symptomatic uterine fibroids	4/35 (11%) amenorrheic at 6 months
Pron et al (2003b)	2/3	555 consecutive women with confirmed uterine fibroids	494/527 (94%) (28 either menopausal or receiving GnRH) 41/494 (8%) amenorrheic at 3 months 21/494 (4%) amenorrheic at 6 months 3% [1,7] in women <40 years old amenorrhea 41% [26,58] in women >50 years old amenorrhea
Spies et al (2001a)	2/3	200 women with confirmed uterine fibroids	11/200 (6%) amenorrheic at 3 months 4/200 (2%) permanently amenorrheic
Walker & Pelage (2002)	2/3	400 consecutive women with symptomatic fibroids	26/400 (7%) permanent amenorrhoea
Ciraru-Vigneron et al (1999)	1.5/3	184 women with fibroids	20/184 (11%) with amenorrhea 10/20 (50%) 'normal menopause' 5/20 (25%) UAE related 5/20 (25%) transient amenorrhea

[a] Quality score is a reflection of a priori hypotheses, appropriate patient selection and adequate follow-up

Pre-test/post-test case series (level IV evidence) suggest a low prevalence of permanent amenorrhea in UAE patients. On the basis of this type of evidence, effectiveness of UAE compared to other uterine-conserving treatments cannot be determined, but the level of absolute risk of amenorrhea after UAE can be estimated. As in the level III-2 study of Spies et al (2004b), a considerable proportion of studies reported transient amenorrhea, some of which lasted up to 8–10 months (Ahmad et al 2002). The 17 per cent amenorrhea rate reported by Pinto et al (2003) might therefore include women who were transiently amenorrheic at the 6-month follow-up. Some studies have also suggested that older women, or those who are closer to 'natural' menopause, may be less physiologically resilient to the 'insult' of UAE. Pron et al (2003b) reported an amenorrhea rate of 41 per cent in women older than 50 years compared to 3 per cent in women less than 40 years of age. Overall rates of amenorrhea in level IV studies ranged from 1.6 to 11.4 per cent, with a median of 3.8 per cent (Table 10), but none of these studies confirmed whether amenorrhea was a result of ovarian failure (ie early menopause).

Table 11 Early menopause [a] (level III-2 evidence)

Study	Quality / Level	Early menopause [a]		Number needed to treat [95% CI]	Relative Risk [95% CI]
		UAE (n = 62)	MYO (n = 40)		
Razavi et al (2003)	Retrospective cohort study Level – III-2 QS – 18/27 Clin I – 4/4 Rel – 1/5 Stat prec – average	4/62 (6%) Early menopause (all women were >46 years of age)	0/44 (0%) Early menopause	NNTH 16 [NNTH 8 to NNTH 29] p=0.09	NA

MYO = myomectomy; NNTB = number needed to treat to benefit; NNTH = number needed to treat to harm; 95% CI = 95% confidence interval; Level = level of evidence; QS = quality score; Clin I = clinical importance; Rel = relevance of evidence; Stat prec = statistical precision; NA = not applicable; [a] Day 3 serum FSH, hormone levels of above 10 IU/L represent a decline in fertility potential and ovarian reserve, 70% of women with FSH levels >15 IU/L are menopausal.

Healy et al (2004) concluded, based on hormone level measurements at baseline, 3 and 6 months after UAE and hysterectomy, that ovarian function is not affected by UAE or hysterectomy (Healey et al 2004). They suggested that their high UAE success rate (ie no ovarian failure) was due to a 'less aggressive endpoint' when embolising. The slight drop in FSH at 6 months (increase in ovarian reserve) for the hysterectomy group could be due, in part, to inter-assay variability, which was reported as 7 per cent. Even though Pinto et al (2003) and Spies et al (2004b) reported a 17 and 7 per cent prevalence of amenorrhea, respectively, neither study measured whether amenorrhea was associated with the much more serious complication of early menopause. Healy et al (2004) measured serum hormone concentrations and found that UAE did not affect ovarian reserve; however, a substantial loss to follow-up may have biased their results.

When comparing two uterine-conserving treatments, Razavi et al (2003) showed that four UAE patients (6%) suffered early menopause within 30 days of the procedure, compared to none in the myomectomy cohort (Table 11). Early menopause rates are likely to be underestimated in both treatments because of the short follow-up period. Furthermore, Razavi et al (2003) did not outline the procedures that determined whether patients were menopausal because of their reliance on a retrospective review of medical records. It is therefore unknown if menopause was confirmed by hormone levels or whether it was only

characterised by amenorrhea. Albeit biased, the comparison suggests that there might be a higher rate of menopause after UAE compared to myomectomy; however, more comparative studies need to be conducted to confirm this.

Table 12 Early menopause after UAE (level IV evidence)

Study	Quality score [a]	Population	Early menopause after UAE
Huang et al (2004)	3/3	35 symptomatic women	1/35 (3%) early menopause verified by FSH measurement (age = 51 years)
Tropeano et al (2004)	3/3	20 women less than 40 years old, regularly menstruating, normal FSH levels, no history of infertility or ovarian surgery and no desire for further pregnancy	UAE did not affect ovarian reserve in all patients FSH levels Baseline 4.7±1.8 IU/L (3.0–6.9 IU/L) 3 months 5.9±1.6 IU/L (4.1–8.5 IU/L) 6 months 5.4±2.9 IU/L (3.0–8.4 IU/L) 12 months 5.5±2.1 IU/L (3.0–8.1 IU/L)
Ahmad et al (2002)	2.5/3	32 women with symptomatic uterine fibroids	2/32 (6%) women were perimenopausal and with transient amenorrhoea for 3 months FSH levels Baseline 30 and 22 IU/L irregular menses 3 months 48 and 40 IU/L with clinical symptoms 6 months 26 and 27 IU/L Menstrual cycles resumed within 8–10 months post-UAE 30/32 (94%) premenopausal had no disruption to ovarian function FSH levels Baseline 6.8 ± 1.8 IU/L 3 months 7.0 ± 1.7 IU/L (p=0.66) 6 months 6.7 ± 1.2 IU/L (p=0.62) Normal menstrual cycles resumed within 2–3 months
Tulandi et al (2002)	2.5/3	48 women with symptomatic uterine fibroids	FSH levels Baseline 5.7±0.5 IU/L 1 month 9.0±1.1 IU/L (p<0.05) >10 IU/L (n = 7) 3 months 10.7±2.3 IU/L (p<0.01) >10 IU/L (n = 9)
Bradley et al (1998)	2/3	8 women with symptomatic uterine fibroids	1/8 (13%) amenorrheic with elevated FSH (60 IU/L) confirming ovarian failure
Hald et al [b] (2004)	2/3	24 premenopausal women with symptomatic fibroids	1/24 (4%) menopause at 3-month follow-up indicated by elevated FSH levels
Khaund et al (2004)	2/3	50 women with symptomatic uterine fibroids	7/50 (14%) became amenorrheic 6/50 (12%) had menopausal hormone profiles

Chrisman et al (2000)	1.5/3	66 premenopausal women	56/66 (85%) reported resumption of menses after an average of 3.5 weeks (range 1–8 weeks) 10/66 (15%) amenorrheic with an average follow-up of 49 weeks (range 24–76 weeks) 9/10 (90%) (aged >45 years) had elevated FSH levels (range 29.4–100.3 IU/L) 1/10 (10%) (aged <45 years) had non-menopausal FSH levels (10 IU/L)
McLucas et al (2001a)	1.5/3	167 women	4/167 (2%) >45 years of age with premenopausal levels of FSH pre-UAE developed menopausal levels of FSH after 6 months
Walker et al (1999)	1.5/3	200 women	6/200 (3%) developed ovarian failure 3/6 (50%) permanent 3/6 (50%) transient, resolved at 9 months

[a] Quality score is a reflection of a priori hypotheses, appropriate patient selection and adequate follow-up; FSH = follicle stimulating hormone (levels of FSH of menopausal women >50 IU/L); [b] Study by Hald et al (2004) compared UAE with laparoscopy, which is not a comparator in this report; therefore, only the results from the UAE arm are described

Table 12 outlines the level IV studies, which measured serum hormone levels to monitor ovarian function and thus the prevalence of early menopause after UAE. The two largest studies of 167 (McLucas et al 2001a) and 200 (Walker et al 1999) women reported a 2.4 and 1.5 per cent incidence of early menopause, respectively. The highest incidence of early menopause was reported by Chrisman et al (2000), where 10 women out of a sample of 66 (15%) suffered from early menopause; however, nine of these women were over 45 years of age. This suggests that they may have been close to 'natural' menopause anyway. A level IV study (Tropeano et al 2004) which focused on 20 relatively young women (mean age = 35 years) showed that UAE did not affect ovarian reserve in any patients after 12 months of follow-up.

Miscarriage

None of the comparative studies monitored the incidence of miscarriage in successful conceptions after UAE, myomectomy or other uterine-conserving treatments. Hysterectomy is obviously not a relevant comparator for this safety outcome. Pron et al (2005) reported a miscarriage rate of 16.7 per cent (95% CI 5.1,41.9) for 24 pregnancies in 21 women from an original sample of 555 patients (Pron et al 2005). Similarly, Walker and Pelage (2002) reported a miscarriage rate of 15 per cent in 13 pregnancies detected in 400 women. In an extension of their work they reported a miscarriage rate of 27 per cent for 26 post-UAE pregnancies (Carpenter & Walker 2005). Both Pron et al (2005) and Carpenter and Walker (2005) concluded that their miscarriage rates were not different to the background rate of miscarriage in a normal population of a similar age. A higher 40 per cent rate (5/12) of miscarriage was reported by Ravina et al (2000b) but procedures were performed in the years 1995 to 1997, when UAE for this indication was in its infancy. Furthermore, the five cases of miscarriage were attributed to women over the age of 40, which is an age associated with high risk in pregnancy anyway.

Serious non-target embolisation

On rare occasions embolic agents that are injected to occlude the uterine artery can be transported by the vascular system to other areas of the body. In the worst case scenario this can lead to the non-target embolisation and subsequent tissue death of other organs. None of the comparative studies (level II and III-2 evidence) have reported non-target

embolisation complications in their UAE patients. However, comparative evidence is not relevant in this scenario because myomectomy and hysterectomy have zero complication rates for this outcome. Two pre-test/post-test case series (Ciraru-Vigneron et al 1999; Hald et al 2004) reported one case of uterine necrosis each in their respective samples of 24 and 184 women. Both cases required immediate hysterectomy.

Serious non-target embolisation was one of the most common complications reported in case reports (Appendix H). The outcomes of these complications are often serious because presenting symptoms can be confused with post-embolisation syndrome by inexperienced operators. Expert opinion suggests that post-embolisation syndrome occurs within 24 hours after embolisation, whereas symptoms associated with non-target embolisation usually occur later. The time lag between expected symptoms versus those of a serious complication allows the latter to be diagnosed quickly and treated effectively. Eight of 37 case reports described uterine necrosis, buttock necrosis, vaginal vault and cervix necrosis, uterus filled with pus and microspheres, uterus with microspheres throughout the myometrium, and necrotic bladder tissue (De Blok et al 2003; Dietz et al 2004; El-Shalakany et al 2003; Fogt et al 2003; Godfrey & Zbella 2001; Payne et al 2002; Shashoua et al 2002; Sultana et al 2002).

Thrombo-embolism

Pinto et al (2003) reported similar rates of deep vein thrombosis occurring in 2 per cent of UAE and 5 per cent of hysterectomy patients (Table 13). Beinfeld et al (2002) reported that less than 1 per cent of 250 hysterectomy patients experienced pulmonary embolism after their procedure. As previously noted, this study is likely to underestimate complications because it only retrospectively monitored complications within the same hospital stay as the procedure. Further, since the hospital stay was, on average, 0.95 days for UAE and 2.6 days for hysterectomy, hysterectomy patients were effectively 'followed up' for three times as long as UAE patients. The comparison is therefore of questionable validity.

A pre-test/post-test case series by Spies et al (2001a) reported one case of pulmonary embolism and peroneal vein thrombosis in a series of 200 UAE patients. Both complications had only mild consequences. A follow-up study of 400 patients by Spies et al (2002b) may have double reported, but there was one case for each of pulmonary embolism, arterial thrombosis and deep vein thrombosis (Spies et al 2001a, 2002b). Spies et al (2004a) also reported one case of pulmonary embolus (1% of patients) detected 4 days after embolisation.

Table 13 Thrombo-embolism (level II and III-2 evidence)

Study	Quality / Level	Thrombo-embolism		Number needed to treat [95% CI]	Relative risk [95% CI]
		UAE (n = 38)	HYS (n = 19)		
Pinto et al (2003)	Randomised controlled trial Level – II QS – 24/27 Clin I – 4/4 Rel – 1/5 Stat prec – poor	1/40 (2%) deep vein thrombosis	1/20 (5%) deep vein thrombosis	NNTB 40 [NNTH 8 to ∞ to NNTB 12]	0.5 [0.03,7.6] p=0.61

		UAE (n = 57)	HYS (n = 300)		
Beinfeld et al (2002)	Retrospective cohort study Level – III-2 QS – 17/27 Clin I – NA Rel – 1/5 Stat prec – poor	0/57 (0%) pulmonary embolism	2/250 (1%) pulmonary embolism	NNTB 125 [NNTB 53 to ∞ to NNTH 329] p=0.50	NA

HYS = hysterectomy; NNTB = number needed to treat to benefit; NNTH = number needed to treat to harm; 95% CI = 95% confidence interval; Level = level of evidence; QS = quality score; Clin I = clinical importance; Rel = relevance of evidence; Stat prec = statistical precision; NA = not applicable

Organ damage

Organ damage, which can occur from non-target embolisation in the case of UAE and physical damage during surgery in the case of hysterectomy or myomectomy, was reported in two comparative studies (Beinfeld et al 2002; McLucas & Adler 2001). Beinfeld et al (2002) reported that out of 250 patients, three suffered from bowel obstruction and one from bladder injury. This study suggests that physical damage to organs are more prevalent after invasive procedures. McLucas and Adler (2001), in their brief communication, reported one case of small bowel laceration after myomectomy compared to no cases of organ damage in the UAE group.

No pre-test/post-test case series reported organ damage, with the exception of Hald et al (2004) and Ciraru-Vigneron et al (1999), who both reported one case of necrotic uterus (see non-target embolisation). Eight case reports described in the 'serious non-target embolisation' section of this report also highlight the potential of organ damage (mainly of the uterus) associated with UAE.

Idiosyncratic drug reaction

No patients in eight comparative studies were reported to have drug or allergic reactions after UAE, hysterectomy or myomectomy.

Allergic reactions to contrast media and drug reactions have been reported in four pre-test/post-test case series on UAE (level IV evidence). The patient specific consequences were mostly minimal. Ten patients out of 555 (1.8%) were reported by Pron et al (2003a) to have had a reaction to contrast media. Similarly, Spies et al (2002b) reported that 2.5 per cent of 400 UAE patients experienced an allergic reaction and 0.25 per cent a drug reaction (Spies et al 2002b). Spies et al (2004a) in their article comparing two types of embolic agents for UAE reported that 10 per cent of patients suffered from a skin rash or hives, which occurred days and sometimes weeks after embolisation. Andersen et al (2001) reported a slightly higher rate of allergic reaction, with four out of 62 UAE (6.5%) patients suffering a contrast medium reaction, two of whom had to be hospitalised for 2 days, while the remainder suffered from a skin rash.

Rehospitalisation and reoperation

One good quality level II (Pinto et al 2003) and three medium quality level III-2 studies (Pourrat et al 2003; Razavi et al 2003; Spies et al 2004b) reported on rehospitalisation or reoperation attributed to complications within monitoring periods (Table 14).

Pinto et al (2003) recorded complications for 30 days after treatment and reported that 5 per cent of both UAE and hysterectomy patients were rehospitalised. Four (20%) additional hysterectomy patients were reported to have surgical wound and intra-abdominal abscesses. Pinto et al (2003) also presented reoperations due to ineffectiveness of the UAE procedure (see effectiveness section). Spies et al (2004b) reported that hysterectomy patients, compared to UAE, are at an approximately 8 per cent increased risk for both rehospitalisation and reoperation because of complications. These significant differences in risk were only present for the 12-month follow-up period compared to no difference for complications within 30 days of the procedure (Table 14). It therefore seems that monitoring patient complications for 30 days or less (Pinto et al 2003; Razavi et al 2003) may not capture all adverse events. A medium quality level III-2 study conducted by Pourrat et al (2003) retrospectively reviewed medical records of UAE and hysterectomy patients and reported a non-significant difference (p=0.45) for rehospitalisation after 6 months. One UAE patient (3%) was readmitted for fever compared to two hysterectomy patients (6%) for kidney infection and haematoma evacuation.

Razavi et al (2003) reported no significant difference in follow-up hospitalisations for UAE and myomectomy patients based on a 30-day review of post-procedural medical records.

Table 14 Rehospitalisation and/or reoperation (level II and III-2 evidence)

Study	Quality / Level	Rehospitalisation and/or reoperation		Number needed to treat [95% CI]	Relative risk [95% CI]
		UAE (n = 38)	HYS (n = 19)		
Pinto et al (2003)	Randomised controlled trial Level – II QS – 24/27 Clin I – 4/4 Rel – 1/5 Stat prec – poor	2/40 (5%) Readmitted for post-embolisation syndrome and severe pelvic pain	1/20 (5%) Readmitted for anaemia that required blood transfusion	NA	1.0 [0.1,10.4] p=1.0
		UAE (n = 102)	HYS (n = 50)		
Spies et al (2004b)	Prospective cohort study Level – III-2 QS – 18/27 Clin I – 1/4 Rel – 1/5 Stat prec – average	4//102 (4%) Minor therapy, with hospitalisation <48 hours or major therapy with an unplanned increased level of care with hospitalisation >48 hours	6/50 (12%) Required therapy, with hospitalisation <48 hours or major therapy with an unplanned increased level of care with hospitalisation >48 hours	NNTB 12 [NNTB 6 to ∞ to NNTH 59]	0.33 [0.1,1.1] p=0.06
		1/102 (1%) 1 Curettage and hysterectomy subsequent to fibroid passage	4/50 (8%) 1 Bowel injury 1 Vaginal cuff herniation 1 Recurrent bleeding from the vaginal stump 1 Two colonoscopies because of a suspected bowel obstruction	NNTB 14 [NNTB 7 to ∞ to NNTH 135]	0.25 [0.05,1.3] p=0.07
		UAE (n = 37)	HYS (n = 31)		
Pourrat et al (2003)	Retrospective cohort study	1/37 (3%)	2/31 (6%) Readmitted for kidney	NNTB 27 [NNTB 7 to ∞ to NNTH	0.42 [0.04,4.4]

	Level – III-2 QS – 16/27 Clin I – 4/4 Rel – 1/5 Stat prec – poor	Readmitted for fever	infection and haematoma evacuation	15]	p=0.45
		UAE (n = 62)	MYO (n = 40)		
Razavi et al (2003)	Retrospective cohort study Level – III-2 QS – 18/27 Clin I – 4/4 Rel – 1/5 Stat prec – poor	2/62 (4%) Readmitted for endometritis and chronic pelvic pain	1/40 (3%) Readmitted for ileus	NNTH 137 [NNTH 14 to ∞ to NNTB to 17]	1.3 [0.12,13.8] p=0.83

HYS = hysterectomy; MYO = myomectomy; NNTB = number needed to treat to benefit; NNTH = number needed to treat to harm; Level = level of evidence; QS = quality score; Clin I = clinical importance; Rel = relevance of evidence; Stat prec = statistical precision; NA = not applicable

Level II and III-2 evidence (Table 14) suggest a prevalence of rehospitalisation or reoperation associated with UAE of about 4 per cent. This value agrees with the plethora of level IV evidence for this outcome (Table 15). The largest case series of 555 consecutive UAE patients, for which the outcomes were published in six separate manuscripts by Pron et al (2003 a,b,c,d,e; 2005), reported a readmission prevalence of 3 per cent, with half of these undergoing a hysterectomy. Likewise, Spies et al (2002b) reported that 3.8 per cent of 400 UAE patients were readmitted to hospital, of which 1.8 per cent underwent a further procedure. Walker and Pelage (2002) reported that 8 of 400 patients (2%) underwent readmission or other procedures related to complications with UAE. The highest rehospitalisation rate reported in a large case series was 13 per cent (McLucas et al 1999) of 300 UAE patients being readmitted for temperature elevation, pain or nausea, but only 3.7 per cent required further surgical intervention. The largest rehospitalisation rate reported in level IV evidence, regardless of sample size, was 25 per cent, but this value was based on eight UAE patients (Bradley et al 1998).

Table 15 Rehospitalisation and/or reoperation after UAE (level IV evidence)

Study	Quality score [a]	Population	Rehospitalisation and reoperation after UAE	
Brunereau et al (2000)	3/3	58 consecutive women with symptomatic fibroids	1/58 (2%) 1/58 (2%)	required readmission for acute pyelonephritis, treated with antibiotics required hysterectomy within 6 months
Goodwin et al (1999)	3/3	60 consecutive women with symptomatic fibroids	22/60 (37%) 7/60 (12%) 6/60 (10%)	required same day admission for pain management required hysterectomy required readmission for severe post-embolisation syndrome
Pelage et al (2000)	3/3	80 consecutive women with symptomatic uterine fibroids	1/80 (1%)	hysterectomy due to acute septic uterine necrosis

Pron et al (2003c) Same study population as Pron et al (2003a)	3/3	555 consecutive women with confirmed uterine fibroids	57/555 (10%) returned to emergency 16/555 (3%) readmitted to hospital 11/555 (2%) due to pain/nausea/vomiting 2/555 (0.4%) due to fever 1/555 (0.2%) due to urinary tract infection 1/555 (0.2%) due to prolapsed fibroids 1/555 (0.2%) due to hypertension 8/555 (1%), 95% CI [0.6,3] had a hysterectomy
Shan et al (2004)	3/3	100 premenopausal consecutive women	1/100 (1%) severe abdominal pain resulting in hysterectomy after 7 days
Spies et al (2002b) Follow-up study to Spies et al (2001a)	3/3	400 consecutive women with confirmed uterine fibroids	15/400 (4%) required readmission or rehospitalisation: 4/400 (1%) pain 4/400 (1%) leiomyoma passage 2/400 (0.5%) endometritis 1/400 (0.3%) pulmonary embolus 2/400 (0.5%) leiomyoma passage and endometritis 1/400 (0.3%) leiomyoma passage and haemorrhage 1/400 (0.3%) thrombosis Interventions: 4/400 (1.0%) intravenous narcotics 3/400 (0.8%) hysteroscopy 3/400 (0.5%) transfusion 3/400 (0.8%) D&C 1/400 (0.3%) hysterectomy
McLucas et al (1999)	2.5/3	300 women	Rehospitalisation: 12/300 (4%) for increased temperature 21/300 (7%) for pain 6/300 (2%) for nausea Re-treatment: 11/300 (4%) required hysterectomy
Messina et al (2002)	2.5/3	26 women with symptomatic uterine fibroids	3/26 (12%) required hysterectomy due to failure of treatment 1/3 (33%) reported with unremitting pelvic pain and vaginal bleeding 1/3 (33%) developed fever 3 months post-UAE, elevated white blood cell count, progressive pelvic pain, vaginal discharge and expulsion of infected fibroid 1/3 (33%) presented with heavy bleeding
Prollius et al (2004b)	2.5/3	64 consecutive women with symptomatic uterine fibroids	2/64 (3%) required hysterectomy
Spies et al (2004a) Bruno et al (2004)	2.5/3	100 women with symptomatic uterine fibroids	3/100 (3%) readmitted to hospital 1/100 (1%) fibroid passage 1/100 (1%) recurrent pain 1/100 (1%) pulmonary embolus
Bradley et al (1998)	2/3	8 women with symptomatic uterine fibroids	2/8 (25%) readmitted 1/2 (50%) with post-embolisation syndrome treated with antibiotics 1/2 (50%) passed a large necrotic intra-cavity fibroid
Hald et al [b] (2004)	2/3	24 premenopausal women with symptomatic fibroids	1/24 (4%) required dilatation and curettage 1/24 (4%) required hysterectomy

Klein & Schwartz (2001)	2/3	35 women with symptomatic uterine fibroids	3/35 (8.6%) readmitted to hospital 1/3 (33%) for urinary retention – 1-day hospital stay 1/3 (33%) for nausea and vomiting – 2-day hospital stay 1/3 (33%) for pelvic pain, rash and high fever – 4-day hospital stay
Marret et al (2003)	2/3	85 women with symptomatic uterine fibroids	4/85 (5%) required hysterectomy 5/85 (6%) required hysteroscopy resection
McLucas et al (1998)	2/3	25 women with symptomatic uterine fibroid	2/25 (8%) required readmission for management of fever, responded to antibiotics 1/25 (4%) required readmission for management of nausea and vomiting 2 weeks post-UAE
Mehta et al (2002)	2/3	42 women with symptomatic uterine fibroids	7/42 (17%) patients required readmission for infection-like symptoms 2/7 (29%) patients readmitted twice 6/7 (86%) nature and source of infection identified 3/7 (43%) degenerating fibroids requiring manual extraction 3/7 (43%) responded to antibiotic therapy 1/7 (14%) failed to respond and required hysterectomy Median time to readmission = 3 weeks (range 1–29 weeks)
Spies et al (2001b)	2/3	30 women with symptomatic uterine fibroids	1/30 (3%) required readmission for 4 days due to severe constipation causing severe pelvic pain
Spies et al (2001a)	2/3	200 women with confirmed uterine fibroids	21/200 (11%), 95% CI [7,15] required gynaecological intervention and/or readmission in the long term (weeks post-operative) 5/200 (3%) D&C (12–96 weeks) 4/200 (2%) hysteroscopic resection (7–12 weeks) 1/200 (0.5%) abdominal myomectomy (32 weeks) 9/200 (5%) hysterectomy (12–88 weeks) 8/200 (4%) required readmission or rehospitalisation within post-operative period 1/200 (0.5%) required 4 days rehospitalisation for pulmonary embolism, treated with anti-coagulation medication 4/200 (2%) required 1 day rehospitalisation for pain management 3/200 (2%) required readmission to emergency for pain control
Toh et al (2003)	2/3	46 women with symptomatic uterine fibroids	1/46 (2%) rehospitalised for severe pain (2 nights)
Walker & Pelage (2002)	2/3	400 consecutive women with symptomatic fibroids	25/400 (6.3%) required reoperation, of which: 12/25 (48%) hysterectomy (3 for infective complications) 5/25 (20%) hysteroscopic resection for infection and pain associated with infarcted fibroids
Andersen et al (2001)	1.5/3	62 women with symptomatic uterine fibroids	2/62 (3.2%) required reoperation or rehospitalisation 1/62 (2%) contrast reaction, hospitalised for 2 days 1/62 (2%) laparoscopic removal of subserous pedunculated fibroid

Ciraru-Vigneron et al (1999)	1.5/3	184 women	11/184 (6%) required further surgery (not stated) 1/184 (0.5%) with uterine necrosis and small bowel impaction required hysterectomy and resection of small bowel
Hutchins et al (1999)	1.5/3	305 premenopausal women	2/305 (1%) readmitted to hospital due to pain 1/305 (0.4%) discharged after 24 hours 1/305 (0.4%) severe post-embolisation syndrome, hysterectomy performed day 12
McLucas et al (2001a)	1.5/3	167 women	3/167 (2%) experienced fever / post-embolisation syndrome, readmitted to hospital 6/167 (4%) underwent hysterectomy 3/167 (2%) required vaginal myomectomy for removal of necrotic myomas
Siskin et al (2000)	1.5/3	49 women with symptomatic uterine fibroids	1/49 (2%) required hysterectomy due to prolonged pelvic pain
Smith et al (2004)	1.5/3	81 women	11/81 (14%) rehospitalised for pain or fever for a mean of 1.6 nights within a week of UAE procedure 12/81 (15%) underwent hysterectomy Mean time to subsequent treatment was 18.6 months (7–30 months)
Walker et al (1999)	1.5/3	200 women	4/200 (2%) required hysterectomy 1/4 (25%) due to infarcted gas-filled fibroid + tubovarian abscess 1/4 (25%) chronic pain and fever, readmitted after 3 months *E. coli* infection + large necrotic mass prolapsing into cervix 2/200 (1%) required hysteroscopy

[a] Quality score is a reflection of a priori hypotheses, appropriate patient selection and adequate follow-up; D&C = dilation and curettage; [b] Study by Hald et al (2004) compared UAE with laparoscopy which is not a comparator in this report; therefore, only the results from the UAE arm are described

Minor complications

Post-embolisation syndrome

Post-embolisation syndrome, which includes symptoms of pelvic pain, fever, malaise, nausea and vomiting, is a common and anticipated side effect of UAE. These symptoms are said to be associated with fibroid infarction and associated cell death, along with an immune response to foreign embolisation particles. Post-embolisation syndrome, by definition, is not associated with hysterectomy or myomectomy. Comparative studies, in this instance, therefore do not provide a higher level of evidence than pre-test/post-test case series on UAE. Almost all women who undergo UAE experience some form of localised pain, which is usually managed with analgesics; however, the presence of fever, which is usually less severe than that due to a genuine bacterial infection, produces post-embolisation syndrome. Based on 14 level IV studies, it is apparent that a median of ~ 12% (mean = 18%) of women experience post-embolisation syndrome after UAE (Table 16). Substantial between-study variation in the reported prevalence rates of 5 to 40 per cent is probably due to the subjective definition of the condition.

Post-embolisation syndrome should only be classified as a complication when it requires a prolonged hospital stay, readmission to hospital or an escalation of care. Pinto et al (2003) reported that 10 of 40 (25%) patients who received UAE treatment experienced post-embolisation syndrome, which the authors classified as a moderate complication. Of the 10 cases, six were associated with an emergency department visit, and two were serious enough to require rehospitalisation. Three pre-test/post-test case series (Bradley et al 1998; Goodwin et al 1999; McLucas et al 2001a) that reported both post-embolisation syndrome and readmission to hospital because of it reveal that only a small percentage of UAE patients who suffer from post-embolisation syndrome are rehospitalised. Other level IV studies often report that post-embolisation syndrome spontaneously resolves (Table 16).

Table 16 Post-embolisation syndrome after UAE (level IV evidence)

Study	Quality score [a]	Population	Post-embolisation syndrome after UAE
Brunereau et al (2000)	3/3	58 consecutive women with symptomatic fibroids	3/58 (5%) had a fever 48 hours after UAE, resolved without treatment
Goodwin et al (1999)	3/3	60 consecutive women with symptomatic fibroids	20/60 (33%) experienced some post-embolisation syndrome symptoms 6/60 (10%) symptoms were severe enough to require readmission
Pelage et al (2000)	3/3	80 consecutive women with symptomatic uterine fibroids	6/80 (8%) 3–5 days after UAE, resolved with NSAIDs and analgesia
Bapuraj et al (2002)	2.5/3	11 women with symptomatic uterine fibroids	1/11 (10%) treated with analgesics and antibiotics, symptoms resolved within 5 days
Joffre et al (2004)	2.5/3	85 women with symptomatic uterine fibroids	6/85 (7%) with fever and pain within 3–5 days
Park et al [b] (2003)	2.5/3	23 women with clinically confirmed uterine fibroids	3/23 (15%) experienced fever
Prollius et al (2004b)	2.5/3	64 consecutive women with symptomatic uterine fibroids	21/64 (33%) resolved within 7 days with analgesia
Bradley et al (1998)	2/3	8 women with symptomatic uterine fibroids	3/8 (38%) experienced post-embolisation syndrome 1/3 (33%) readmitted 24 hours after discharge with severe pain and fever, treated with antibiotics
Hald et al [b] (2004)	2/3	24 premenopausal women with symptomatic fibroids	3/23 (13%) experienced fever within 3–8 days, with no raised white blood cell count, therefore no additional treatment
Ciraru-Vigneron et al (1999)	1.5/3	184 women	20/184 (11%) experienced fever/post-embolisation syndrome
Hutchins et al (1999)	1.5/3	305 premenopausal women	122/305 (40%) developed post-embolisation syndrome 2 weeks post-UAE 1/305 (0.4%) developed severe post-embolisation syndrome,

			hysterectomy performed day 12
McLucas et al (2001a)	1.5/3	167 women	12/167 (7%) experienced fever/post-embolisation syndrome 3/167 (2%) readmitted to hospital
Siskin et al (2000)	1.5/3	49 women with symptomatic uterine fibroids	1/49 (2%) reported prolonged fever (6 weeks) post-UAE Symptoms resolved at 12 weeks
Al Muzrakchi & Szmigielski (2003)	1/3	4 women with severe fibroid related menorrhagia	1/4 (25%) abdominal pain, sweating, vomiting high blood pressure

[a] Quality score is a reflection of a priori hypotheses, appropriate patient selection and adequate follow-up; NSAIDs = non-steroidal anti-inflammatory drugs; [b] Studies by Hald et al (2004) and (Park et al (2003) compared UAE with laparoscopy which is not a comparator in this report; therefore, only the results from the UAE arm are described

Severe pelvic pain was included in this category because it is a major symptomatic constituent of post-embolisation syndrome. Pinto et al (2003) reported that three (8%) UAE patients visited the emergency department with severe pelvic pain but none were readmitted to hospital (Table 17). In their study severe pelvic pain was classified as a moderate complication. Beinfeld et al (2002) reported that only one patient out of 52 (2%) treated with UAE experienced severe pelvic pain. This prevalence may be an underestimate because they only assessed complications during the patient's hospital stay (a mean of 0.95 days) and complications data were missing for 15 per cent of patients. Razavi et al (2003) reported that one UAE patient (1/62; 2%) was readmitted to hospital for pelvic pain compared to two myomectomy patients (2/40; 5%) who had chronic pelvic and incisional pain.

Seventeen pre-test/post-test case series have reported patient-perceived pain during and after UAE. As with post-embolisation syndrome, the range (20–100%) in the proportion of patients who report pain is large because of the varying definitions and subjective scales used to define and assess pain. The effectiveness of pain management also contributes to the variation. The largest case series of 555 women (Pron et al 2003c) reported that 16, 19, 35 and 22 per cent of 548 women interviewed 2 weeks after UAE experienced post-procedural pain which they classified as minor, uncomfortable, very uncomfortable and unbearable, respectively. They also assessed the same patients via a continuous pain scale spanning 1 to 10, the lower extreme representing minimal pain and the upper, the worst pain imaginable. The median value reported was 7.5, with a majority (58%) of patients selecting numbers between 7 and 10. However, pain should only be classified as a safety issue when it requires an increased level of care or readmission to hospital. Of the larger case series (Hutchins Jr et al 1999; Spies et al 2001a), only 0.7 per cent (2/305) and 3.5 per cent (7/200), respectively, of UAE patients were rehospitalised for pain associated with UAE.

Table 17 Pain after UAE (level IV evidence)

Study	Quality score [a]	Population	Pain after UAE
Pelage et al (2003)	3/3	20 women with symptomatic uterine fibroids who did not desire pregnancy	5/20 (25%) no post-procedural pain 11/20 (55%) moderate post-procedural pain 4/20 (20%) intense post-procedural pain 1/20 (5%) delayed intense pain 3 days post-UAE, which required readmission for intravenous narcotics
Pelage et al (2000)	3/3	80 consecutive women with symptomatic uterine fibroids	68/80 (85%) intense pelvic pain immediately post-UAE, controlled by patient-administered analgesia
Pron et al (2003c) Same study population as Pron et al (2003a)	3/3	555 consecutive women with confirmed uterine fibroids	2 weeks follow-up (n = 548) Post-procedural pain, category rating n (%) None Minor Uncom V Uncom Unbearable 44 (8) 86 (16) 103 (19) 188 (35) 116 (22) Post-procedural pain, numeric rating [b] n (%) 0 1–2 3–4 5–6 7–10 44 (8) 25 (5) 63 (12) 95 (18) 313 (58) Mean pain rating = 7.0 Median pain rating = 7.5 Ineffective post-procedural pain management based on patient report = 57/548 (10%)
Shan et al (2004)	3/3	100 premenopausal consecutive women	Mean time for resolution of post-procedural pain = 7 days 1/100 (1%) severe abdominal pain resulting in hysterectomy 83/100 (83%) complete cessation of pain within 7 days 15/100 (15%) cessation of pain within 7–14 days 1/100 (1%) discomfort for 40 days
Spies et al (2002b) Follow-up study to Spies et al (2001a)	3/3	400 consecutive women with confirmed uterine fibroids	5/400 (1%) recurrent prolonged pain
Bapuraj et al (2002)	2.5/3	11 women with symptomatic uterine fibroids	11/11 (100%) experienced post-operative pain, treated with NSAIDs 1/11 (9%) experienced severe abdominal pain treated with morphine
Joffre et al (2004)	2.5/3	85 women with symptomatic uterine fibroids	17/85 (20%) severe pelvic pain 3/85 (4%) persistent pain after 1 week
Goodwin et al (1999)	2.5/3	60 consecutive women with symptomatic fibroids	22/60 (37%) required same-day admission for pain management
Park et al [c] (2003)	2.5/3	23 women with clinically confirmed uterine fibroids	7/23 (30%) experienced pain

Spies et al (2004a) Bruno et al (2004)	2.5/3	100 women with symptomatic uterine fibroids	Mean maximum VAS score in first week n = 99 4.89±0.26 [4.4,5.5] Mean number of patient-controlled analgesia doses attempted n = 96 71±7 [57,84] Mean number of patient-controlled analgesia doses given n = 97 28±2 [26,32]
Bradley et al (1998)	2/3	8 women with symptomatic uterine fibroids	5/8 (63%) experienced intermittent pain 3–8 weeks post-UAE, treated with diclofenac
Sena-Martins et al (2003)	2/3	32 women with symptomatic uterine fibroids	32/32 (100%) experienced post-procedural pain
Spies et al (2001a)	2/3	200 women with confirmed uterine fibroids	8/200 (4%) 4/200 (2%) required 1 day rehospitalisation for pain management 3/200 (2%) required readmission to emergency for pain control 1/200 (0.5%) haematoma, causing pain, resolved spontaneously in 10 days
Toh et al (2003)	2/3	46 women with symptomatic uterine fibroids	6/46 (13%) experienced severe abdominal pain, resolved in 1 week
Andersen et al (2001)	1.5/3	62 women with symptomatic uterine fibroids	Majority of patients experienced severe pain for 12–24 hours post-UAE, treated with NSAIDs
Hutchins et al (1999)	1.5/3	305 premenopausal women	2/305 (1%) experienced pain and were readmitted
Smith et al (2004)	1.5/3	81 women	11/81 (14%) rehospitalised for pain or fever for a mean of 1.6 nights within a week of UAE procedure

[a] Quality score is a reflection of a priori hypotheses, appropriate patient selection and adequate follow-up; Uncom = uncomfortable, V Uncom = very uncomfortable; NSAIDs = non-steroidal anti-inflammatory drugs; VAS = visual analogue scale; [b] numeric rating ranging from 1 = minimum pain to 10 = worst pain imaginable; [c] Study by Park et al (2003) compared UAE with laparoscopy, which is not a comparator in this report; therefore, only the results from the UAE arm are described

Endometritis

Endometritis is defined as an inflammation or irritation of the endometrium. In the context of this report, endometritis is probably associated with infection due to necrotic fibroids after UAE or irritation of the uterine lining due to insertion of medical instruments after myomectomy. This safety outcome is not associated with hysterectomy for obvious reasons. Razavi et al (2003) reported one case of endometritis in 62 UAE patients that required rehospitalisation for intravenous antibiotics, compared to no cases in the myomectomy cohort (n = 40).

The prevalence of endometritis in UAE patients estimated by three level IV studies (Andersen et al 2001; Huang et al 2004; Spies et al 2002b) is 1.6 (1/62), 0.5 (2/400) and 6 (2/35) per cent, respectively. This complication is therefore rarely encountered after UAE.

Haematoma

Pinto et al (2003) reported that 20 per cent of UAE (8/40) patients experienced a post-puncture haematoma as compared to 10 per cent of hysterectomy (2/20) patients who had a surgical wound haematoma. Our analysis showed that the apparent difference between the treatment arms was not statistically significant (p=0.33) because the study was underpowered to detect differences of this magnitude. Pourrat et al (2003) also reported haematoma as a post-procedural complication in their cost-effectiveness study. Only one out of 31 hysterectomy patients experienced a surgical wound haematoma. The highest level study in this review (level II; Pinto et al 2003) reported a higher incidence of haematoma in UAE patients compared to hysterectomy. No comparative studies reported on the prevalence of haematoma after UAE in comparison to myomectomy.

Ten level IV studies show that the median prevalence of puncture wound haematoma in UAE patients is 1.5 per cent, ranging from 0.25 per cent (Spies et al 2002a) to 7 per cent (Burn et al 1999). Four studies reported that puncture wound haematomas did not require any further treatment or intervention.

Uterine adhesions

A level III-2 study, which retrospectively analysed complications associated with UAE and myomectomy within 30 days of the procedure, reported that 5 per cent of myomectomy patients suffered from uterine adhesions compared to none treated with UAE (Razavi et al 2003). No pre-test/post-test level IV case series reported uterine adhesions as a complication associated with UAE.

Local infection

Two prospective (Pinto et al 2003; Spies et al 2004b) and three retrospective (Beinfeld et al 2002; McLucas & Adler 2001; Razavi et al 2003) studies reported on rates of local infection or symptoms related to infection (Table 18). All studies reported higher infection rates or symptoms in myomectomy and hysterectomy compared to the minimally invasive technique of UAE, although the wide confidence intervals indicate that the studies were largely underpowered. With the exception of Prollius et al (2004b), who reported an 11 per cent prevalence in 64 UAE patients, six level IV studies confirm a low rate of infection associated with UAE, with the prevalence of local infection not exceeding 1.7 per cent (Goodwin et al 1999).

Table 18 Local infection (level II and III-2 evidence)

Study	Quality / Level	Local infection		Number needed to treat [95% CI]	Relative Risk [95% CI]
		UAE (n = 38)	HYS (n = 19)		
Pinto et al (2003)	Randomised controlled trial Level – II QS – 24/27 Clin I – 3/4 Rel – 2/5 Stat prec – poor	2/40 (5%) Urinary tract infection	2/20 (10%) Urinary tract infection	NNTB 20 [NNTB 5 to ∞ to NNTH 10]	0.5 [0.08,3.3] p=0.46

		UAE (n = 102)	HYS (n = 50)		
Spies et al (2004b)	Prospective cohort study Level – III-2 QS – 18/27 Clin I – 2/4 Rel – 2/5 Stat prec – poor	13/102 (13%) – 95%CI [7,28] Occurrence of infection not present on admission or initiation of antibiotics >24 hours after surgery	12/50 (24%) – 95%CI [13,38] Occurrence of infection not present on admission or initiation of antibiotics >24 hours after surgery	NNTB 9 [NNTB 4 to ∞ to NNTH 46]	0.53 [0.26,1.01] p=0.08
		UAE (n = 57)	HYS (n = 300)		
Beinfeld et al (2002)	Retrospective cohort study Level – III-2 QS – 17/27 Clin I – 4/4 Rel – 2/5 Stat prec – poor	0/52 (0%)	1/250 (0.3%) Wound infection 1/250 (0.3%) Respiratory infection	NNTB 125 [NNTB 53 to ∞ to NNTH 329] p=0.52	NA
		UAE (n = 62)	MYO (n = 40)		
Razavi et al (2003)	Retrospective cohort study Level – III-2 QS – 18/27 Clin I – 2/4 Rel – 2/5 Stat prec – poor	0/62 (0%) Wound infection	2/40 (5%) Wound infection	NNTB 20 [NNTB 9 to ∞ to NNTH 57] p=0.08	NA
		UAE (n = 32)	MYO (n = 16)		
McLucas & Adler (2001)	Retrospective cohort study Level – III-2 QS – 9/27 Clin I – x/4 Rel – x/5 Stat prec – poor	7/32 (22%) Temperature elevation over 38.1 degrees	5/16 (31%) Temperature elevation over 38.1 degrees	NNTB 11 [NNTB 3 to ∞ to NNTH 8]	0.7 [0.26,1.9] p=0.48

HYS = hysterectomy; MYO = myomectomy; Level = level of evidence; QS = quality score; Clin I = clinical importance; Rel = relevance of evidence; Stat prec = statistical precision

Minor bleeding

Minor bleeding was not reported by most comparative studies, with the exception of Razavi et al (2003), who described blood loss associated with UAE as minimal. In comparison, blood loss during abdominal myomectomy was quantified at a mean of 376 ml and a range of 50–2,000 ml. No level IV studies reported blood loss as a complication associated with UAE.

Other complications

Overall morbidity, which encompasses all adverse events recorded within the 12 months following the procedure, was reported by Spies et al (2004b) (Table 19). This study found that a significantly greater percentage of hysterectomy patients suffered from overall morbidity compared to UAE. A high quality level II study conducted by Pinto et al (2002)

reported that vaginal discharge was more prevalent after UAE when compared to hysterectomy. Twenty-two per cent of UAE patients complained of vaginal discharge after UAE.

Rarer post-procedural complications reported by the highest level study (Pinto et al 2003), but isolated to UAE patients, included two (5%) with renoureteral colic, two with thigh paraesthesia, one (2%) with anal fissure and one with vulvovaginitis. None of the aforementioned were categorised as major complications. Razavi et al (2003) reported that one UAE patient suffered from transient paraesthesia over the groin area, compared to no such complications in the myomectomy cohort. McLucas and Adler (2001) reported two cases of ileus (non-mechanical blockage of the intestine caused by the cessation of peristalsis) in 16 myomectomy patients. A case of ileus after myomectomy was also reported by Razavi et al (2003) but was included in the rehospitalisation section of this report. Beinfeld et al (2002) reported one incidence of urinary retention out of 250 hysterectomy cases compared to no cases in the UAE patients. The assortment of complications above is not of great consequence because their prevalence is low. However, one case of respiratory arrest reported by Beinfeld et al (2002) is a notable exception. Even though only one case has been reported, it is the most severe adverse event associated with UAE reported by the comparative studies.

Table 19 Other complications (level II and III-2 evidence)

Study	Quality / Level	Other complications				Number needed to treat [95% CI]	Relative Risk [95% CI]
		UAE (n = 38)		HYS (n = 19)			
Pinto et al (2003)	Randomised controlled trial Level – II QS – 24/27 Clin I – 2/4 Rel – 2/5 Stat prec – good	Intra-procedural		Intra-procedural			
		7/40 (18%)	arterial spasm	0/20 (0%)	arterial spasm		
		2/40 (5%)	uterine artery dissection	0/20 (0%)	uterine artery dissection		
		2/40 (5%)	gluteal artery perforation	0/20 (0%)	gluteal artery perforation		
		0/40 (0%)	vesicle fissure	1/20 (5%)	vesicle fissure	NNTH 4 [NNTH 3 to NNTH 18]	5.5 [0.76,40] p=0.04
		TOTAL	11/40 (28%)	TOTAL	1/20 (5%)		
		Post-procedural		Post-procedural			
		Minor		Minor			
		9/40 (22%)	vaginal discharge	0/20 (0%)	vaginal discharge		
		1/40 (2%)	urinary retention	1/20 (10%)	urinary retention		
		2/40 (5%)	thigh paraesthesia	1/20 (0%)	thigh paraesthesia		
		TOTAL	12/40 (30%)	TOTAL	2/20 (10%)	NNTH 5 [NNTH 2 to NNTH 155]	3 [0.74,12] p=0.07
		Moderate		Moderate			
		2/40 (5%)	renoureteral colic	0/20 (0%)	renoureteral colic		
		1/40 (2%)	vulvovaginitis	0/20 (0%)	vulvovaginitis		
		1/40 (2%)	anal fissure				
		TOTAL	4/40 (10%)	TOTAL	0/20 (0%)	NNTH 10 [NNTH 5 to NNTH 142] p=0.14	NA

		UAE (n = 102)		HYS (n = 50)				
Spies et al (2004b)	Prospective cohort study Level – III-2 QS – 18/27 Clin I – 1/4 Rel – 1/5 Stat prec – good	Overall morbidity n = 15/102 (15%) 95%CI [9,23] Infection or readmission or unintended surgery or haemorrhage, or life-threatening complications (American College of Gynaecologists standards)		Overall morbidity n = 17/50 (34%) 95%CI [21,49] Infection or readmission or unintended surgery or haemorrhage, or life-threatening complications (American College of Gynaecologists standards)		NNTB 5 [NNTH 3 to NNTH 23]	0.43 [0.24,0.79] p<0.01
		UAE (n = 57)		HYS (n = 300)			
Beinfeld et al (2002)	Retrospective cohort study Level-III – 2 QS – 17/27 Clin I – 4/4 Rel – 1/5 Stat prec – NA	1/52 (2%)	Respiratory arrest	0/250 (0%)	Respiratory arrest	NNTH 52 [NNTH 18 to ∞ to NNTB 55] p=0.03	NA
		0/52 (0%)	Urinary retention	1/250 (0.3%)	Urinary retention	NNTH 250 [NNTH 85 to ∞ to NNTB 262] p=0.64	NA
		0/52 (0%)	Dehiscence	1/250 (0.3%)	Dehiscence	NNTH 250 [NNTH 85 to ∞ to NNTB 262] p=0.64	NA
		UAE (n = 62)		MYO (n = 40)			
Razavi et al (2003)	Retrospective cohort study Level – III-2 QS – 18/27 Clin I – 4/4 Rel – 2/5 Stat prec – poor	1/62 (2%)	Transient numbness over groin access site	0/40 (0%)	Transient numbness over groin access site	NNTH 62 [NNTH 21 to ∞ to NNTB 66] p=0.42	NA
		UAE (n = 32)		MYO (n = 16)			
McLucas & Adler (2001)	Retrospective cohort study Level – III-2 QS – 9/27 Clin I – 4/4 Rel – 2/5 Stat prec – poor	0/32 (0%) Ileus		2/16 (13%) Ileus		NNTB 8 [NNTB 4 to ∞ to NNTH 27] p=0.04	NA
		0/32 (0%) Phlebitis		1/16 (6%) Phlebitis (inflammation of vein)		NNTB 16 [NNTB 6 to ∞ to NNTH 18] p=0.15	NA

HYS = hysterectomy; MYO = myomectomy; NNTB = number needed to treat to benefit; NNTH = number needed to treat to harm; Level = level of evidence; QS = quality score; Clin I = clinical importance; Rel = relevance of evidence; Stat prec = statistical precision; NA = not applicable

The most common 'other' complication in level IV studies is that of fibroid passage. This report did not focus on the complications arising from the vaginal expulsion of necrotic fibroids; however, seven of nine level IV studies reported this outcome in 0.5 to 6.7 per cent of their cohorts. Complications arising from fibroid passage, or lack thereof, are also described in nine case reports (Appendix H). The consequences of fibroid necrosis in situ are as far reaching as death, as reported by Vashisht et al (2000); however, the majority of necrotic fibroids are passed successfully without further complications. This type of complication can be avoided via careful selection of patients with the appropriate type of fibroid (ie pedunculated fibroids are most likely to cause problems). Most other complications listed in Table 20 are relatively minor. The more concerning complications are anaphylactic responses in two of 555 UAE patients, seizure in one of 555 patients (Pron et al 2003a) and femoral nerve injury in three of 400 patients (Spies et al 2002b).

Table 20 Other complications after UAE (level IV evidence)

Study	Quality score [a]	Population	Other complications
Pelage et al (2000)	3/3	80 consecutive women with symptomatic uterine fibroids	4/80 (5.0%) expelled necrotic fragments through cervix in first month 1/80 (1.25%) partial dissection of uterine artery, with no clinical consequences
Pron et al (2003a)	3/3	555 consecutive women with confirmed uterine fibroids	2/555 (0.4%) anaphylactoid response 5/555 (0.9%) vasovagal response 1/555 (0.2%) pseudoaneurysm 1/555 (0.2%) hypertension 1/555 (0.2%) arthritic flare 1/555 (0.2%) seizure, requiring hospitalisation for 3 days 1/555 (0.2%) leg numbness
Shan et al (2004)	3/3	100 premenopausal consecutive women	1/100 (1.0%) persistent urinary irritation symptoms and intermittent heamaturia for 40 days post-UAE
Spies et al (2002b) Follow-up study to Spies et al (2001a)	3/3	400 consecutive women with confirmed uterine fibroids	10/400 (2.5%) leiomyoma passage 4/400 (1%) urinary tract infection 3/400 (0.8%) femoral nerve injury 2/400 (0.5%) vessel injury 2/400 (0.5%) urinary retention 1/400 (0.3%) vaginal discharge 1/400 (0.3%) thrush 1/400 (0.3%) phlebitis
Goodwin et al (1999)	2.5/3	60 consecutive women with symptomatic fibroids	4/60 (6.7%) passed submucosal fibroid via vagina
Prollius et al (2004b)	2.5/3	64 consecutive women with symptomatic uterine fibroids	2/64 (3.1%) presented with fibroid slough, then secondary infection treated with oral antibiotics
Spies et al (2004a) Bruno et al (2004)	2.5/3	100 symptomatic women	1/100 (1%) fibroid passage which required readmission 1/100 (1%) urinary retention

Sena-Martins et al (2003)	2/3	32 women with symptomatic uterine fibroids	2/32 (6%)	myoma elimination
Spies et al (2001b)	2/3	30 women with symptomatic uterine fibroids	1/30 (3.3%)	fibroid expulsion
Spies et al (2001a)	2/3	200 consecutive women with confirmed uterine fibroids	4/200 (2.0%) 1/200 (0.5%) leiomyoma passage, removed during office visit 2/200 (1.0%) urinary retention requiring recatheterisation 1/200 (0.5%) phlebitis	
Ciraru-Vigneron et al (1999)	1.5/3	184 women	6/184 (3.3%) expulsion of submucosal myomata 2/184 (1.1%) uterine artery dissection observed 3/184 (1.6%) urinary tract infection	
McLucas et al (2001a)	1.5/3	167 women	8/167 (5.0%) passing necrotic myomas 3/8 (37.5%) required vaginal myomectomy to remove necrotic myoma	

[a] Quality score is a reflection of a priori hypotheses, appropriate patient selection and adequate follow-up

Case reports

Case reports, by definition, present the worst outcomes associated with a procedure because an uneventful outcome is rarely worthwhile reporting. Thirty-seven case reports are listed in Appendix H. Three deaths are reported, two through multi-organ failure related to complications after UAE (Baker et al 2002; De Blok et al 2003; Vashisht et al 1999) and one associated with progression of cancer because of an undiagnosed leiomyosarcoma (Goldberg et al 2004a). Joyce et al (2001) also reported un-diagnosed leiomyosarcoma. Septic shock was reported by Aungst et al (2004) and Payne & Haney (2003) but both patients recovered after appropriate treatment and hysterectomies. The majority of case reports described issues with non-target embolisation and infection complications associated with tissue or fibroid necrosis. This section of safety attempts to encompass all possible adverse events associated with UAE.

Summary

Is uterine artery embolisation as safe as, or safer than, hysterectomy for the treatment of symptomatic uterine fibroids in women?

The evidence base for the safety of UAE in comparison to hysterectomy includes one good quality level II study and three level III-2 studies. None of the comparative studies reported deaths, septic shock, miscarriage, serious non-target embolisation, uterine perforation, idiosyncratic drug reaction, hyponatremia, depression, endometritis, uterine adhesions or minor bleeding after UAE or hysterectomy.

One level II and two level III-2 studies did not report any cases of peri-procedural haemorrhage in UAE patients. In comparison, 10, 8 and 1 per cent, respectively, of hysterectomy patients in the three comparative studies either underwent a post-procedural blood transfusion or experienced haemorrhage.

The prevalence of amenorrhea after UAE has been estimated by one level II and one level III-2 study to be 17 and 7 per cent, respectively. These studies did not confirm whether amenorrhea was related to the more serious complication of ovarian failure. Level III-2 evidence suggests that both UAE and subtotal *laparoscopic* hysterectomy do not affect ovarian function. There was no comparative data on UAE versus subtotal *abdominal* hysterectomy for ovarian function.

A level II study reported a slightly increased rate of deep vein thrombosis after hysterectomy when compared to UAE. Furthermore, a level III-2 study described five instances of organ damage in 250 hysterectomy patients compared to no cases in the UAE group.

It is evident from level II and III-2 studies that there are no statistically significant differences in reoperation or rehospitalisation rates due to complications between UAE and hysterectomy. The highest level II study reported that the same percentage (5%) of UAE and hysterectomy patients were rehospitalised because of procedural complications. A medium quality level III-2 study reported less rehospitalisations and reoperations after UAE compared to hysterectomy.

Other peri-procedural complications reported in a level II study which were isolated to UAE included vaginal discharge, thigh paraesthesia, renoureteral colic, vulvovaginitis and anal fissure. Conversely, in this study, urinary retention and vesicle fissure were complications only reported after hysterectomy.

UAE appears to be as safe as, or safer than, abdominal hysterectomy.

Is uterine artery embolisation as safe as, or safer than, other uterine-conserving treatments for the treatment of symptomatic uterine fibroids in women?

The highest level of evidence available to draw conclusions on the relative safety of UAE in comparison to another uterine-conserving treatment (myomectomy) was level III-2 evidence. One medium and one poor quality study reported on safety outcomes for UAE and abdominal myomectomy.

Mortality, septic shock, miscarriage, serious non-target embolisation, uterine perforation, thrombo-embolism, idiosyncratic drug reaction, hyponatremia and depression were not reported in either comparative study for UAE or abdominal myomectomy.

Two level III-2 studies reported zero prevalence of blood transfusion associated with UAE compared to 8 and 13 per cent, respectively, for their myomectomy cohorts.

One medium level III-2 study reported a 6 per cent prevalence of early menopause after UAE compared to zero prevalence after myomectomy. Conversely, this study reported a higher rate of wound infection, chronic pelvic pain, uterine adhesions and intra-procedural bleeding in abdominal myomectomy patients compared to the UAE group.

A poor quality level III-2 study reported two cases of ileus, one of phlebitis and one of small bowel laceration from 16 abdominal myomectomy patients, compared to no reported incidence in the UAE group.

Based on medium quality level III-2 evidence, the rate of rehospitalisation for complications is equivalent for both UAE and myomectomy. The reason for

rehospitalisation for two UAE patients was endometritis and pelvic pain, while one myomectomy patient was readmitted for ileus.

Based on the limited evidence, UAE appears to be as safe as, or safer than, abdominal myomectomy.

Is uterine artery embolisation effective?

Studies were included in this assessment of the effectiveness of uterine artery embolisation (UAE) according to the criteria outlined in Box 4.

Box 4 Study selection criteria for effectiveness

Research questions	
(1) Is UAE as, or more, effective at treating symptomatic uterine fibroids in women compared to hysterectomy?	
(2) Is UAE as, or more, effective at treating symptomatic uterine fibroids in women compared to other uterine-conserving treatments?	
Selection criteria	**Inclusion criteria**
Population	Women with symptomatic uterine fibroids [a].
Intervention	UAE using a vascular occluding agent
Comparator(s)	(1) Hysterectomy.
	(2) Uterine-conserving treatments, including myomectomy, hysteroscopic resection, hormone suppression therapy.
Outcomes	Primary – menstrual blood loss [b], occurrence of pressure or bulk symptoms, patient-assessed pelvic pain, patient-assessed quality of life, sexual function.
	Secondary – convalescence (duration of hospital stay, return to normal activities/work), analgesia usage, pregnancy outcome [c], fibroid recurrence, further treatment, uterine size, time to relief of symptoms.
Study design	Randomised or non-randomised controlled trials or cohort studies, uncontrolled pre-test/post-test case series or systematic reviews of these study designs.
Search period	1/1990 [d] – 3/2005
Language	Studies in languages other than English will only be translated and included if they represent a higher level of evidence than is available in the English language evidence base.

[a] Fibroids diagnosed clinically and symptoms including menorrhagia, cramping, pelvic pain, pressure or bulk symptoms (frequent urination or incontinence, lower back pain), pain during sexual intercourse, infertility, miscarriage; [b] bleeding cessation, reduction in menorrhagia and consequent anaemia; [c] Only applies to women seeking pregnancy; [d] UAE was first performed for the treatment of symptomatic uterine fibroids in 1994

This section of the report assesses the effectiveness of UAE compared to existing uterine-conserving (abdominal myomectomy) and removal (hysterectomy) procedures. There were no studies that compared UAE with other uterine-conserving treatments such as hysteroscopic resection or hormone therapy.

One level II and four level III-2 studies comparing UAE with hysterectomy, three level III-2 studies retrospectively assessing UAE against myomectomy, and 75 pre-test/post-test case series of women receiving UAE (level IV evidence) formed the evidence base for the assessment of UAE effectiveness. All patient-relevant outcomes, with the exception of women seeking pregnancy, time to relief of symptoms and fibroid recurrence were assessed by at least one comparative study. The outcomes that were missing in the comparative analysis were assessed using the next highest level of evidence (level IV; pre-test/post-test case series), but no conclusive recommendations can be made on the basis of these studies alone. It is essential to examine the effectiveness of UAE in the context of existing practice, and therefore the conclusions of the effectiveness section will be based primarily on the comparative studies (level II and III-2 evidence) described here. Greater weight or importance will be given to effectiveness outcomes classified as primary, namely symptom control and quality of life.

The highest level of evidence available for this report was a good quality randomised controlled trial comparing UAE against hysterectomy. Conducted in Spain, this trial followed 38 UAE and 19 hysterectomy patients for 6 months assessing patient-relevant outcomes including menstrual bleeding, duration of hospital stay, time taken to return to normal activities and further treatment (level II evidence) (Pinto et al 2003). Seventy-nine per cent of both the UAE and hysterectomy groups were classified as premenopausal or menopausal, with respective average ages of 46 and 45 years.

Four level III-2 studies, two of which were prospective (Healy et al 2004; Spies et al 2004b) and two retrospective (Beinfeld et al 2002; Pouratt et al 2003), assessed UAE against hysterectomy. Spies et al (2004b) followed a cohort of 152 women (UAE: n = 102; hysterectomy: n = 52) who received treatment for symptomatic fibroids in 11 different centres within the United States. They prospectively assessed patient-relevant outcomes such as menstrual bleeding, pressure or bulk symptoms, pelvic pain, quality of life, duration of hospital stay, time taken to return to normal activities, further treatment and uterine size for 12 months following the procedures. Healey et al (2004) followed 68 UAE and 16 laparoscopic hysterectomy patients for 6 months, assessing uterine volume and ovarian reserve outcomes. This medium quality Canadian study recruited healthy premenopausal women aged 39 to 50 years who were regularly menstruating to examine the effect of UAE and hysterectomy (without oophorectomy) on ovarian reserve. The primary focus of the level III-2 retrospective medium quality studies of Beinfeld et al (2002) and Pouratt et al (2003) were cost or cost-effectiveness analysis for UAE compared to hysterectomy. The only effectiveness outcomes of interest in these studies were hospital stay and complication rate, with the latter being summarised in the safety section of this report.

Three retrospective level III-2 studies (Broder et al 2002; McLucas & Adler 2001; Razavi et al 2003) provided data on the relative effectiveness of UAE compared to another uterine-conserving treatment (myomectomy). Razavi et al (2003), who interviewed 40 UAE and 62 myomectomy patients at approximately 14 months post-procedure, reported on outcomes such as menstrual bleeding, pressure or bulk symptoms, pelvic pain, duration of hospital stay, return to normal activities and work, analgesia use and further treatment. Conducted in the United States, the main limitations of this medium quality study included a significantly older UAE group and the reliance on patient recall for outcomes such as pain medication use and resumption of normal activities. Broder and colleagues (Broder et al 2002) mailed surveys to 59 UAE and 38 myomectomy patients approximately 3.8 years after their respective procedures. Of the 50 UAE and 30 myomectomy patients who completed the questionnaire in this medium quality study, data were collected on outcomes such as overall satisfaction, symptomatic improvement and additional invasive treatment. Unfortunately, only *overall* symptom improvement was reported, which combined components of menorrhagia, dysmenorrhea, bulk and pelvic/abdominal pain, and therefore symptom data could not be included as an effectiveness outcome in this report. McLucas and Alder (2001) presented a poor quality study (primarily because of lack of reporting), in which all women who underwent UAE and myomectomy in a community hospital in 1999 were retrospectively assessed for complications and hospital stay.

The evidence provided by the aforementioned comparative studies is accompanied by absolute risk estimates derived from 75 pre-test/post-test case series (level IV evidence) on UAE.

Primary outcomes

Menstrual blood loss

One level II (Pinto et al 2003) and two level III-2 studies (Razavi et al 2003; Spies et al 2004b) have assessed the effectiveness of UAE for the resolution of menorrhagia in comparison to hysterectomy or myomectomy (Table 21).

Table 21 Menstrual blood loss (level II and III-2 evidence)

Study	Quality / Level	Reduction in blood loss				Number needed to treat [95% CI]	Relative benefit [a] [95% CI]
		UAE (n = 38)			HYS (n = 19)		
Pinto et al (2003)	Randomised controlled trial Level – II QS – 24/27 Clin I – 2/4 Rel – 1/5 Stat prec – good	31/36 (86%) reported bleeding cessation at 6 months follow-up [b] 20/36 (56%) full recovery 5/36 (14%) partial recovery 6/36 (17%) amenorrhea			NR but assumed to be 100%	NNTH 7 [NNTH 4 to NNTH 39]	0.86 [0.75,0.98] p=0.09
		UAE (n = 102)			HYS (n = 50)		
Spies et al (2004b)	Prospective cohort study Level – III-2 QS – 18/27 Clin I – NA Rel – 1/5 Stat prec – NA		PBAC [c]	% redn [d]	NR	NA	NA
		Baseline	436±287				
		3 months	161±133 [e]	56±35			
		6 months	141±110 [e]	58±37			
			Self-reported menorr-hagia score	% redn [d]			
		Baseline	47±14				
		3 months	23±11 [e]	47±31			
		6 months	19±8 [e]	57±20			
		12 months	17±10 [e]	61±21			
		UAE (n = 62)			MYO (n = 40)		
Razavi et al (2003)	Retrospective cohort study Level – III-2 QS – 18/27 Clin I – 1/4 Rel – 1/5 Stat prec – good	48/52 (92%) reported completely or significantly resolved menorrhagic symptoms at mean 14.3 months follow-up [f] 31/52 (60%) reported complete resolution			14/22 (64%) of the sample reported completely or significantly resolved menorrhagic symptoms at mean 14.6 months follow-up 6/22 (27%) reported complete resolution	NNTB 4 [NNTB 2 to 14]	1.45 [1.05, 2.01] p<0.05

HYS = hysterectomy; MYO = myomectomy; [a] Therefore, if outcome favours UAE, RB >1.0; if it favours HYS or MYO, RB <1.0; 95% CI = 95% confidence interval; Level = level of evidence; QS = quality score; Clin I = clinical importance; Rel = relevance of evidence; Stat prec = Statistical precision; NA = not applicable; [b] Assessed using self-report of the 'number of menstruation days and/or bleeding between menses and the number of tampons and/or sanitary napkins used; [c] PBAC = Pictorial blood loss assessment chart; [d] Mean per cent reduction from baseline; [e] p<0.001 for baseline comparison; [f] 6-point scale – completely, significantly moderately resolved, no change, moderately or significantly worse

A randomised controlled trial comparing UAE and abdominal hysterectomy was conducted in the University Hospital of Getafe, Spain (Pinto et al 2003). Sixty-four eligible consecutive patients were recruited between April 1999 and June 2001, but seven were excluded because they refused to participate or did not meet the selection criteria. The remainder were randomised via computer, with concealed allocation to either treatment group (hysterectomy: n = 19: UAE: n = 38). The UAE cohort was informed of the study and the alternative treatment options (namely hysterectomy), whereas the hysterectomy patients were not informed of the study or of the possible alternative treatment. Statistical analyses for baseline characteristics were not presented but it is apparent from the tabulated baseline characteristics that the groups did not differ significantly for age, gynaecological history and menopausal status. However, there was a trend toward a larger dominant fibroid volume in the hysterectomy group (hysterectomy = 113±138 ml; UAE = 72±86 ml), with a greater proportion of mural (hysterectomy = 68%, UAE = 42%) and lesser proportion of submucosal (hysterectomy = 11%, UAE = 40%) fibroids. It is unclear whether these results indicate that concealment of allocation has been subverted and patient selection is a factor; or whether they are due to chance. Either way it appears that hysterectomy patients may have had a more serious fibroid disease compared to the UAE group. It is worthwhile noting that almost 80 per cent of UAE and hysterectomy patients were classified as premenopausal or menopausal before their procedures.

This trial report occurs at 6 months but the authors will continue to follow the patients for 2 years. Menorrhagia was assessed in the UAE group via self-report of the 'number of menstruation days and/or bleeding between menses and the number of tampons and/or sanitary napkins used', and whether these variables had reduced by 1/3, 2/3, stayed the same or increased. Eighty-six per cent (31/36) of the participants that underwent UAE reported bleeding cessation at 6 months, of which 20 had a full recovery and five a partial recovery, and six had amenorrhea. The analysis did not include four additional patients who underwent UAE but had clinical failure and subsequent hysterectomy. An intent-to-treat analysis would have therefore reduced the relative menorrhagia effectiveness of UAE to 78 per cent (ie 31/40). The authors made a reasonable assumption that hysterectomy was 100 per cent effective at resolving menorrhagia. The absolute risk difference between the procedures suggests that for every seven women successfully treated with UAE (95% CI 4,39), one woman's menorrhagia will not resolve at 6 months when compared to hysterectomy. The gain in effectiveness from undergoing hysterectomy would, of course, need to be placed in the context of a woman's desire to retain her uterus.

Spies et al (2004b) conducted a multicentre (11 treatment centres) cohort study in the United States, for which 102 women underwent UAE and 50 women underwent hysterectomy (80% abdominal, 16% laparoscopic and 4% laparoscopically assisted vaginal), and were followed up prospectively at 3, 6 and 12 months. At baseline, UAE patients had more severe disease (ie larger uterine volume), and were more likely to be Black, have undergone previous treatment for their fibroids, have more numerous fibroids and have experienced more self-assessed moderately or extremely heavy menstrual bleeding. These confounders were adjusted for via logistic regression for the peri-operative complication outcomes, pelvic pain and bulk symptoms. Mean baseline pictorial blood loss assessment chart (PBAC) scores, age, previous pregnancies and type of dominant fibroid were no different between the groups. PBAC and self-reported menorrhagia scores were assessed in the UAE cohort at 3 and 6 months and 3, 6 and 12 months post-operation, respectively. The aforementioned surveys are valid assessment tools for women with menstrual bleeding; however, hysterectomy patients were not assessed post-operatively because the surveys had not been validated in women without menstrual bleeding.

Nevertheless, Spies et al (2004b) reported an average 56 per cent reduction in PBAC at 3 months and a 58 per cent reduction at 6 months follow-up in UAE patients. Similarly, self-reported menorrhagia scores reduced by a mean of 47, 57 and 61 per cent at 3, 6 and 12 months follow-up, respectively. These data demonstrate that UAE significantly affects menorrhagic symptoms, but it is difficult to draw conclusions without comparing these results to other uterine-conserving treatments.

Razavi et al (2003) compared UAE with another uterine-conserving treatment, abdominal myomectomy, and found that UAE was more effective in controlling menorrhagic symptoms. They retrospectively analysed the medical records of 111 consecutive patients that underwent either UAE (n = 67) or abdominal myomectomy (n = 44) between July 1998 and December 2000. Five patients were excluded from the UAE group because their procedure was an adjunct to myomectomy, and four patients were excluded from the myomectomy cohort because they were asymptomatic and were undergoing the procedure because of fertility issues. Baseline characteristics of age, presenting symptoms and hematocrit were reported, with statistical tests showing that UAE patients were older (UAE = 44 years, myomectomy = 38 years) and more often reported menorrhagic symptoms compared to patients undergoing myomectomy. Mean follow-up periods of 14.3 months for UAE patients and 14.6 months for myomectomy patients were not significantly different. Ninety-two per cent of the UAE group with menorrhagic symptoms at baseline (48/52) reported either completely or significantly resolved menorrhagic symptoms, compared to 64 per cent (14/22) in the myomectomy group.

Abdominal myomectomy therefore presents a 45 per cent (RR 1.45, 95% CI 1.05,2.01) greater risk for not completely or significantly resolving menorrhagic symptoms compared to UAE. Furthermore, 3/22 (14%) myomectomy patients compared to 1/52 (2%) UAE patients reported, in their telephone questionnaire at follow-up, that there was no change or a moderate worsening of their menorrhagic symptoms. It is unclear whether age differences at baseline reported for the complete sample extend to the subsets (ie only those who presented with menorrhagic symptoms at baseline were assessed for improvements). This separation of outcome assessment also led to a significant reduction in effective sample size. The results comparing two uterine-conserving treatments should therefore be interpreted with caution.

Level IV evidence (Appendix I) consistently shows that there is a significant reduction in menorrhagia post-UAE. Unfortunately, menorrhagia was only objectively assessed in two studies (Hald et al 2004; Park et al 2003; using pictorial blood loss assessment score or menstrual flow diary). Other assessment methods used patient-assessed improvement in menorrhagia with descriptive terms such as complete resolution, markedly improved, great improvement, moderate improvement or slight improvement. The descriptive term classified as a 'success' varied between studies so it is difficult to summarise the varied results, other than to say it is clear that at least 79 per cent (with the exception of Andersen et al (2001) who reported only 47%) of UAE patients report an improvement in menorrhagia. Whether an improvement, rather than menorrhagia resolution, can be classified as a success is debatable.

Occurrence of pressure or bulk symptoms

An enlarged fibroid uterus can cause symptoms similar to those seen in pregnancy, including urinary frequency, constipation, lower back pain and painful sexual intercourse. Improvements in pressure and bulk symptoms were assessed by two level III-2 studies

(Razavi et al 2003; Spies et al 2004b), one of which compared UAE with hysterectomy while the other compared UAE with myomectomy (Table 22).

Table 22 Occurrence of pressure or bulk symptoms (level III-2 evidence)

Study	Quality / Level	Reduction in pressure or bulk symptoms		Number needed to treat [95% CI]	Relative benefit [a] [95% CI]
		UAE (n = 102)	HYS (n = 50)		
Spies et al (2004b)	Prospective cohort study Level – III-2 QS – 18/27 Clin I – 2/4 Rel – 1/5 Stat prec – good	78/98 (80%) reported an improvement in pelvic discomfort/pressure at 6 months [b]	35/44 (80%) reported an improvement in pelvic discomfort/pressure at 6 months	NA	1.0 [0.84,1.20] p=0.99
		81/98 (83%) [c] reported an improvement in pelvic discomfort/pressure at 12 months [b]	42/44 (94%) reported an improvement in pelvic discomfort/pressure at 12 months	NNTH 8 [NNTH 4 to NNTH 32]	0.87 [0.77,0.97] p=0.06 Authors reported p value based on Fisher's exact test[e]
		UAE (n = 62)	MYO (n = 40)		
Razavi et al (2003)	Retrospective cohort study Level – III-2 QS – 18/27 Clin I – 4/4 Rel – 1/5 Stat prec – poor	28/37 (76%) reported completely or significantly resolved mass effect symptoms at mean 14.3 months follow-up [d]	21/23 (91%) reported completely or significantly resolved mass effect symptoms at mean 14.6 months follow-up	NA	0.83 [0.66, 1.03] p=0.13
		7/37 (19%) reported complete resolution	15/23 (65%) reported complete resolution		

HYS = hysterectomy; MYO = myomectomy; [a] Therefore, if outcome favours UAE, RB >1.0; if it favours HYS or MYO, RB <1.0; Level = level of evidence; QS = quality score; Clin I = clinical importance; Rel = relevance of evidence; Stat prec = statistical precision; [b] 7-point symptom improvement scale (no details); [c] p=0.06 (Fisher's exact test between UAE and HYS); [d] 6-point symptom improvement scale (completely, significantly moderately resolved, no change, moderately or significantly worse); [e] Relative benefit calculated on raw data whereas p value is adjusted for difference in baseline characteristics

Spies et al (2004b) reported that hysterectomy was 13 per cent more effective at controlling pelvic discomfort/pressure symptoms than UAE at a 12-month follow-up. There was no difference at the 6 month follow-up. The 7-point symptom assessment scale used by Spies and colleagues (Spies et al 2004b) is not a validated instrument and it is unclear what levels of the scale (ie mild, moderate or significant improvement) qualified as symptom improvement. Results indicate that for every eight women treated with UAE (95% CI 4,32), one additional patient would have no improvement in their pressure and bulk symptoms when compared to hysterectomy. Even though the UAE cohort had a significantly larger baseline uterine volume (689±466 ml) compared to the hysterectomy group (389±521 ml), logistic regression revealed that none of the baseline differences influenced this outcome.

Of 37 UAE and 23 myomectomy patients who presented with mass effect symptoms, Razavi et al (2003) found that 76 and 91 per cent, respectively, reported completely or significantly resolved mass effect symptoms during a telephone questionnaire approximately 14 months after treatment. Razavi et al (2003) argued that myomectomy,

which surgically removes fibroids, is logically more effective ($p<0.05$) at controlling mass effect symptoms. However, calculations in the current report did not support the analysis by Razavi et al (2003), with the 95% CI surrounding the relative risk point estimate of 0.83, including unity (ie no effect; chi-squared $p=0.13$). When a stricter success criteria is applied (ie resolution of symptoms), it is apparent that myomectomy resolves symptoms (65% of patients) more often than UAE (19% of patients).

Level IV evidence reinforces that UAE is effective at improving bulk symptoms in a majority of patients (Appendix I). The subjective and unblinded assessment of this outcome, combined with high dropout rates during follow-up in some studies, may have presented a more optimistic outcome than what would be observed in the treated population. As with menorrhagia, and again with the exception of data from Andersen et al (2001), greater than 80 per cent of UAE patients subjectively reported an improvement in pressure or bulk symptoms after their procedure. For studies that reported both, it is clear that only approximately half of those who report improvement in symptoms experience complete resolution.

Pelvic pain

Two level III-2 studies (Razavi et al 2003; Spies et al 2004b) have assessed pelvic pain at follow-up intervals of 6 and 14 months after treatment (Table 23).

Table 23 Pelvic pain (level III-2 evidence)

Study	Quality / Level	Improvement in pelvic/menstrual pain		Number needed to treat [95% CI]	Relative benefit [a] [95% CI]
		UAE (n = 102)	HYS (n = 50)		
Spies et al (2004b)	Prospective cohort study Level – III-2 QS – 18/27 Clin I – 2/4 Rel – 1/5 Stat prec – good	78/94 (83%) reported an improvement in pelvic pain at 6 months follow-up [b]	41/47 (88%) reported an improvement in pelvic pain at 6 months follow-up	NA	0.95 [0.82, 1.1] p=0.51
		79/94 (84%) reported an improvement in pelvic pain at 12 months follow-up [b]	46/47 (98%) reported an improvement in pelvic pain at 12 months follow-up	NNTH 7 [NNTH 4 to NNTH 19]	0.86 [0.78,0.95] p=0.02 [d]
		UAE (n = 62)	MYO (n = 40)		
Razavi et al (2003)	Retrospective cohort study Level – III-2 QS – 18/27 Clin I – 4/4 Rel – 1/5 Stat prec – poor	25/34 (74%) reported completely or significantly resolved pain symptoms at mean 14.3 months follow-up [c]	14/26 (54%) reported completely or significantly resolved pain symptoms at mean 14.6 months follow-up	NA	1.36 [0.91, 2.06] p=0.11
		10/34 (29%) reported complete resolution	10/26 (38%) reported complete resolution		

HYS = hysterectomy; MYO = myomectomy; [a] Therefore, if outcome favours UAE, RB >1.0; if it favours HYS or MYO, RB <1.0; Level = level of evidence; QS = quality score; Clin I = clinical importance; Rel = relevance of evidence; Stat prec = statistical precision; [b] 7-point symptom improvement scale (no details); [c] 6-point symptom improvement scale (completely, significantly moderately resolved, no change, moderately or significantly worse); [d] Relative risk is calculated on unadjusted data

In their prospective follow-ups of UAE and hysterectomy patients treated in 11 participating hospitals, Spies et al (2004b) reported that 79 of the 94 UAE patients (84%) presenting with pelvic pain symptoms at baseline reported an improvement at their 12-month interview. In comparison, a significantly greater proportion (98%; p=0.02) of the hysterectomy group reported an improvement in pelvic pain symptoms. The same instrument that was used for pressure or bulk symptomatic outcome was used to assess pelvic pain (ie the degree of symptom change on a 7-point scale). This is not a validated instrument. Regardless, there was a higher incidence of pain symptom improvement in the hysterectomy cohort at 12 months. Again, when logistic analysis adjusted for the clinically more severe baseline disease in UAE patients, the trend did not change.

Razavi et al (2003) compared the incidence of complete or significant pain resolution (on a 6-point scale) for mean follow-up periods of 14.3 and 14.6 months in UAE and myomectomy cohorts, respectively. Seventy-four per cent of patients treated with UAE, compared to 54 per cent of patients treated with myomectomy, reported completely or significantly resolved pain symptoms; however, this comparison did not reach statistical significance (chi-squared p=0.11) because of the relatively small sample size on which the estimates were based. Improvements in pain outcomes were based on 34 of 62 UAE patients and 26 of 40 myomectomy patients who presented with pain symptoms. When imposing stricter success criteria (ie symptom resolution), the trend was reversed (Table 23) but statistical significance was, again, not achieved.

The effectiveness of UAE for controlling pain symptoms compared to the existing surgical procedures is somewhat equivocal. Data suggest that UAE is less effective than hysterectomy for controlling pain symptoms (Spies et al 2004b). In comparison to myomectomy, UAE displayed a trend toward resolved or improved pain outcomes, but the opposite trend was apparent when analysing symptom resolution only (Razavi et al 2003).

Level IV evidence (Appendix I) on either chronic pelvic pain or pain during menstruation (ie dysmenorrhea) shows that, as with other symptomatic changes, a majority of UAE patients experience improvement in either or both of the aforementioned symptoms. When subjectively quantified on a scale of 1 to 10, Prollius et al (2004b) reported median improvement of 4 points following UAE in their 64 consecutive UAE patients. In the largest sample of 555 UAE patients, 75 per cent of the 322 followed up at 3 months reported an improvement in dysmenorrhea. Walker and Pelage (2002) reported that 79 per cent of 255 women (out of 400 at baseline) reported an improvement in menstrual pain at a mean follow-up of 16.7 months. Other level IV studies also report improvements in pain symptoms after UAE. Again, it is worthwhile noting that basing procedural success on symptomatic improvements (rather than the stricter criteria of symptom resolution) is open to interpretation.

Quality of life

One level III-2 study compared the quality of life of 76 UAE (out of a potential 102) and 30 hysterectomy (out of a potential 50) patients (Spies et al 2004b; Table 24). Short form-12 (SF-12) scores were measured at baseline and then at 3, 6 and 12 months after treatment in both groups to assess subjective overall health status and quality of life. Baseline physical and mental SF-12 scores did not reflect the significantly greater number of fibroids, larger uterine volume and greater likelihood of experiencing extremely or moderately heavy menstrual bleeding in the UAE group. In fact, there was a statistically significant difference for baseline mental SF-12 in the opposite to expected direction (ie

the UAE group scored better than the hysterectomy group). It is unclear as to whether quality of life was adjusted for baseline differences between the groups.

Table 24 Quality of life (level III-2 evidence)

Study	Quality / Level	Improvement in quality of life					Relative change
		UAE (n = 102)			HYS (n = 50)		
Spies et al (2004b)	Prospective cohort study Level – III-2 QS – 18/27 Clin I – NA Rel – 1/5 Stat prec – NA		SF-12 (physical)	% inc	SF-12 (physical)	% inc	
		Baseline	45±8		43±10		
		3 months	52±6 [a]	20±26	51±7 [a]	22±26	0.91
		6 months	53±5 [a]	22±26	52±5 [a]	26±34	0.85
		12 months	54±6 [a]	23±27	51±7 [a]	25±33	0.92
			SF-12 (mental)	% inc	SF-12 (mental)	% inc	
		Baseline	45±12		41±11[b]		
		3 months	52±8 [a]	21±35	52±11 [a]	38±53	0.55
		6 months	53±8 [a]	25±38	50±12 [a]	32±51	0.78
		12 months	53±8 [a]	23±38	51±11 [a]	39±60	0.59

HYS = hysterectomy; Level = level of evidence; QS = quality score; Clin I = clinical importance; Rel = relevance of evidence; Stat prec = statistical precision; % inc = mean per cent increase from baseline; [a] Significant within-group difference compared to baseline, no significant differences between UAE and HYS at 3, 6 and 12 months; [b] Significant baseline difference between UAE and HYS (p=0.03)

Spies et al (2004b) reported similar increases in the physical component of the SF-12 scores in both UAE and hysterectomy groups, with no significant differences in SF-12 score at any of the follow-up periods. Mental SF-12 scores were not different between the treatments at follow-up, but the percentage increase from baseline was greater in the hysterectomy group because their baseline mental SF-12 values were significantly lower than the UAE group. A large amount of variation, described by large standard deviations around the means, is inherent in repeated measures of subjective health assessment, and it is evident that some patients in both the UAE and hysterectomy groups perceived their physical and mental quality of life as worse after their operations. In summary, it is clear that both hysterectomy and UAE improve physical and mental SF-12 scores, with significant improvements being reported at 3 months and remaining stable at 6 and 12 months follow-up. Absolute improvements in mental and physical components of SF-12 are comparable for both UAE and hysterectomy, with larger relative improvements in mental SF-12 after hysterectomy (relative change = 0.59 at 12 months) because of their significantly lower baseline score compared to UAE.

Level IV evidence (Pron et al 2003b; Smith et al 2004; Spies et al 2004a) supports significant improvements in quality of life after UAE. Pron et al (2003b) used an unvalidated scale of 1 to 10, with 1 being minimal interference with daily activities and 10 being complete interference. They showed that the mean score in 555 UAE patients before their procedure was 8, whereas 3 months after UAE it was 3. Similarly, Smith et al (2004) reported a significant ($p<0.05$) 36 per cent improvement in the validated health related

quality of life score. Spies et al (2004a) used a fibroid-specific symptom and quality of life questionnaire to assess quality of life 3 months after UAE. Out of a score of 100 (higher numbers reflecting a better score), they reported a significant mean improvement from 48±21 at baseline to 82±16 at 3 months for 54 patients embolised with microspheres. Similar improvements were reported for 46 patients embolised with PVA particles. The aforementioned improvements in quality of life are a subjective and personally weighted (ie what the individual perceives as an important outcome) estimate of overall satisfaction and physiological functioning. It is therefore reassuring to see that at least one comparative (level III-2 evidence) and three pre-test/post-test case series (level IV) show a consistent trend towards positive changes in quality of life after UAE.

Sexual function

Two pre-test/post-test case series (Huang et al 2004; Vashisht et al 2000) have reported patient-perceived sex life after UAE. Vashisht et al (2000) only followed up 50 per cent of their patients, but of the 11 patients, 18, 73 and 9 per cent reported a better, the same and worse sex life, respectively. Similarly, in the study of Huang et al (2004), a majority (86%) of 35 UAE patients rated their sexual function as unchanged, with 8 per cent reporting slightly worse sexual function.

Secondary outcomes

Duration of hospital stay

A relatively large amount of comparative information was available on the duration of hospital stay for women who received treatment for symptomatic uterine fibroids. One level II (Pinto et al 2003) and four level III-2 studies (Beinfeld et al 2002; Pourrat et al 2003; Razavi et al 2003; Spies et al 2004b) compared the hospital stay for UAE with that of hysterectomy or myomectomy (Table 25).

Table 25 Duration of hospital stay (level II and III-2 evidence)

Study	Quality / Level	Duration of hospital stay	
		UAE (n = 38)	HYS (n = 19)
Pinto et al (2003)	Randomised controlled trial Level – II QS – 24/27 Clin I – 2/4 Rel – 2/5 Stat prec – good	Mean = 1.7±1.6 days p<0.001 for UAE and HYS comparison	Mean = 5.9±2.5 days
		UAE (n = 102)	HYS (n = 50)
Spies et al (2004b)	Prospective cohort study Level – III-2 QS – 18/27 Clin I – 2/4 Rel – 2/5 Stat prec – good	Mean = 0.8 days p<0.001 for UAE and HYS comparison	Mean = 2.3 days

		UAE (n = 57)	HYS (n = 300)
Beinfeld et al (2002)	Retrospective cohort study Level – III-2 QS – 17/27 Clin I – 3/4 Rel – 2/5 Stat prec – good	Mean = 1.0±0.4 days p<0.001 for UAE and HYS comparison	Mean = 2.6±1.0 days
		UAE (n = 37)	HYS (n = 31)
Pourrat et al (2003)	Retrospective cohort study Level – III-2 QS – 16/27 Clin I – 2/4 Rel – 2/5 Stat prec – NA	Mean = 3.6 days (range 2–7 days) statistical result not reported	Mean = 7.3 days (range 5–21 days)
		UAE (n = 62)	MYO (n = 40)
Razavi et al (2003)	Retrospective cohort study Level – III-2 QS – 18/27 Clin I – 2/4 Rel – 2/5 Stat prec – average	Mean = 0 days (outpatient procedure) p <0.05 for UAE and MYO comparison	Mean = 2.9 days (range 2–7 days)
		UAE (n = 32)	MYO (n = 16)
McLucas & Adler (2001)	Retrospective cohort study Level – III-2 QS – 9/27 Clin I – 2/4 Rel – 2/5 Stat Prec – NA	Mean = 1.1 days (range 1–2 days) statistical result not reported	Mean = 3.6 days (range 2–7 days)

HYS = hysterectomy; MYO = myomectomy; Level = level of evidence; QS = quality score; Clin I = clinical importance; Rel = relevance of evidence; Stat prec = statistical precision; NR = not reported; NA = not applicable

One level II study performed an intent-to-treat analysis of hospital stay (Pinto et al 2003) because of crossover between the two treatment arms for hysterectomy and UAE. Their analysis of hospital stay, which included rehospitalisations, revealed a significantly ($p<0.001$) shorter mean stay for UAE patients compared to abdominal hysterectomy patients. Likewise, Spies et al (2004b) reported a significantly shorter ($p<0.001$) mean hospital stay for UAE compared to hysterectomy (80% of which were abdominal), but they did not report associated ranges or variance statistics. A retrospective review (Pourrat et al 2003) on the cost-effectiveness of UAE and vaginal hysterectomy reported a clinically significant average 3.7-day difference. The level III-2 medium quality study by Beinfeld et al (2002) reported a shorter hospital stay, even though UAE patients had a clinically more severe disease at baseline and six high-cost (presumably associated with a long hospital stay) outliers were removed from the hysterectomy group.

A level III-2 study conducted by Razavi et al (2003) retrospectively compared hospital stay of UAE to abdominal myomectomy, which is another uterine-conserving treatment. UAE was performed as an outpatient procedure; hence, a zero-day hospital stay for UAE was significantly shorter than the mean 2.9-day stay for abdominal myomectomy. This trend was supported by the data of McLucas and Adler (2001), who also reported a significantly shorter hospital stay for UAE compared to myomectomy.

Based on comparative data of level II and level III-2 evidence, it is unequivocal that mean hospital stay associated with UAE is shorter than that attributed to hysterectomy. The comparator, which was predominantly abdominal hysterectomy, is an invasive procedure and would therefore be expected to result in a longer hospital stay compared to UAE. Two studies (Pinto et al 2003; Pourrat et al 2003) included rehospitalisations in their total estimate but a significantly shorter stay for UAE still prevailed. Data reported in retrospective level III-2 studies of Razavi et al (2003) and McLucas and Adler (2001) showed that UAE was also associated with a shorter hospital stay compared to myomectomy.

Short hospital stays were also reported in pre-test/post-test case series (level IV evidence) ranging from means of 0.8 days (Klein & Schwartz 2001) to 2.9 days (Bapuraj et al 2002). The longest hospital stay associated with UAE for any one individual was 11 days, reported in the large case series of Pron et al (2003c), presumably because of post-intervention complications.

Return to normal activities/work

As with hospital stay, there is a consistent trend towards a shorter duration required for return to normal activities and work after UAE compared to myomectomy and hysterectomy, based on level II (Pinto et al 2003) and III-2 evidence (Razavi et al 2003; Spies et al 2004b) (Table 26).

Table 26 Return to normal activities/work (level II and III-2 evidence)

Study	Quality / Level	Time taken to return to normal activities/work	
		UAE (n = 38)	HYS (n = 19)
Pinto et al (2003)	Randomised controlled trial Level – II QS – 24/27 Clin I –1/4 Rel – 2/5 Stat prec – good	Mean = 10±7 days to resumption of normal activities p<0.001 for UAE and HYS comparison	Mean = 36±21 days to resumption of normal activities
		UAE (n = 102)	HYS (n = 50)
Spies et al (2004b)	Prospective cohort study Level – III-2 QS – 18/27 Clin I – 1/4 Rel – 2/5 Stat prec – good	Mean = 11 days return to work p<0.001 for UAE and HYS comparison	Mean = 33 days return to work
		UAE (n = 62)	MYO (n = 40)
Razavi et al (2003)	Retrospective cohort study Level – III-2 QS – 18/27 Clin I – 1/4 Rel – 2/5 Stat prec – average	Mean = 8 days (range 1–49 days) to resumption of normal activities p<0.05 for UAE and MYO comparison	Mean = 36 days (range 7–120 days) to resumption of normal activities

HYS = hysterectomy; MYO = myomectomy; Level = level of evidence; QS = quality score; Clin I = clinical importance; Rel = relevance of evidence; Stat prec = statistical precision

The highest level study (Pinto et al 2003) showed that UAE patients resumed normal activities within a mean of 10 days compared to over a month for hysterectomy ($p<0.001$). Spies et al (2004b) reported similar mean values of 11 and 33 days, respectively, for return to work after UAE and hysterectomy ($p<0.001$). This statistically significant and clinically important difference was present even though the UAE group had a more severe disease at baseline. A comparison of the time required to resume normal activities after UAE and myomectomy conducted by Razavi et al (2003) also found that UAE was associated with a shorter convalescence ($p<0.05$). Even though there is some overlap, denoted by the large ranges and standard deviations, on average UAE is associated with a shorter period of convalescence compared to either myomectomy or hysterectomy.

Mean convalescence days reported by eight level IV pre-test/post-test case series are also remarkably consistent and relate well to the means reported in the UAE treatment arms of level II and III-2 comparative studies. Spies et al (2001a) reported the lowest return to normal activities at an average of 8 days for 200 UAE patients, compared to a mean 17-day return to work reported by Walker and Pelage (2002). Most studies reported wide ranges associated with the means, suggesting that not every patient enjoys a short convalescence time. Some of the extreme individual values include 60 days reported by Hutchins et al (1999), 75 days reported by Delaney et al (1999) and 90 days reported by Walker and Pelage (2002). Conversely, individual convalescence times of zero days have also been reported (Hutchins et al 1999; Walker & Pelage 2002).

Pregnancy outcome

Pregnancy outcome after UAE is not well researched because the primary aim of UAE is to treat uterine fibroids minimally invasively while conserving a woman's uterus. Women who seek further childbearing are usually counselled into other uterine-conserving treatments because of the lack of data available for pregnancy outcome. Hence, no comparative studies examined pregnancy rates after non–uterine-removing surgery in women who were actively trying to achieve pregnancy. Some level IV studies (Bradley et al 1998; Ciraru-Vigneron et al 1999; Hutchins et al 1999; McLucas et al 2001b) reported the rate of pregnancies in a cohort but it was not stated what percentage of the sample were attempting to conceive. Other studies have reported on pregnancy outcomes after successful conception (Carpenter & Walker 2005) by patients who have previously undergone UAE. Even though these studies provide evidence of uterine viability after UAE, they do not provide information on how UAE affects fertility. A level III-2 study conducted by Healy et al (2004) examined ovarian function after UAE in comparison to laparoscopic hysterectomy without oophorectomy. Ovarian function was assessed via follicle stimulating hormone (FSH) and verified with luteinising hormone and estradiol both before and 3 and 6 months after UAE and hysterectomy. They found that no patient developed premature ovarian failure following UAE or hysterectomy in the 6 months follow-up. Furthermore, there was only a slight increase in the percentage of women with a lower ovarian reserve 6 months after UAE (baseline: 71%; 6 months: 68% had FSH <10 IU/L). A 30 and 20 per cent dropout rate for UAE and hysterectomy patients, respectively, may have skewed results towards a more positive outcome in both groups.

Two level IV studies reported that only 12 per cent (Forman et al 1999) and 42 per cent (Walker & Pelage 2002) of women attempting to conceive after UAE achieved pregnancy. However, in both cases it was unclear whether the women had subfertility at baseline and were therefore unlikely to achieve pregnancy anyway. The effect of UAE on fertility as compared to other uterine-conserving techniques is yet to be established. The debate on

pregnancy outcome after UAE is unlikely to be resolved in the near future, as the desire for future childbearing is a relative contraindication for this minimally invasive procedure.

Analgesia usage

One medium quality level III-2 study (Razavi et al 2003) assessed analgesia use in UAE patients compared to myomectomy patients. However, the estimates of 'days taking pain mediation' were derived from patient recall approximately 14 months after patients' operations, so the estimates are likely to contain significant random error. An unbiased comparative analysis of analgesia use between UAE and a comparator remains to be conducted.

Data from a pre-test/post-test case series (level IV evidence; Appendix I) on 555 women who underwent UAE also showed that 26, 44 and 26 per cent of their sample took pain medication for 0–3, 4–7 and 8–14 days, respectively (Pron et al 2003c). Other level IV evidence (Bradley et al 1998; Bruno et al 2004; Delaney et al 1999; Hald et al 2004) reported on morphine or other analgesic use, but little can be inferred from this information due to the lack of comparator.

Fibroid recurrence

No comparative studies reported on fibroid recurrence for the uterine-conserving treatments of UAE and myomectomy. A level IV study by Marret et al (2003; quality score 2/3), prospectively followed 85 women for 2 years. Symptom recurrence in eight women revealed seven cases of new fibroids and one case of fibroid progression. A 10 per cent rate of fibroid symptom recurrence within 2 years would be placed into context if compared to recurrence rates of other uterine-conserving treatments such as myomectomy.

No further treatment

Further treatment, as an effectiveness outcome, is defined in this report as the failure of the intervention to resolve symptoms associated with fibroids to such a degree that further intervention is required. This is distinct from rehospitalisation and reoperation due to procedural complications as presented in the safety section of this report. One level II (Pinto et al 2003) and four level III-2 (Broder et al 2002; Pourrat et al 2003; Razavi et al 2003; Spies et al 2004b) studies reported follow-up surgical interventions within their monitoring period (Table 27) because of procedure ineffectiveness.

Theoretically, UAE is a less definitive solution to uterine fibroids compared to hysterectomy and would therefore be expected to have a higher rate of further treatment. Of the four comparative studies (Table 27; level II and III-2 evidence) which reported further treatment after UAE in comparison to hysterectomy, none reported a statistically significant difference. The highest level study by Pinto et al (2003), however, did report an increase in risk of further treatment with UAE compared to hysterectomy, with a confidence interval that did not include unity. On average, for every eight patients (95% CI 4,44) treated with UAE, one more would have to undergo subsequent surgery because of clinical failure (ie failure to relieve symptoms associated with fibroids) in comparison to hysterectomy.

Table 27 No further treatment (level II and III-2 evidence)

Study	Quality / Level	No further treatment		Number needed to treat [95% CI]	Relative benefit [a] [95% CI]
		UAE (n = 40)	HYS (n = 17)		
Pinto et al (2003)	Randomised controlled trial Level – II QS – 24/27 Clin I – 1/4 Rel – 1/5 Stat prec – average	35/40 (88%) No further treatment Further treatment due to clinical failure 3 HYS 2 awaiting surgery	17/17 (100%) No further treatment	NNTH 8 [NNTH 4 to NNTH 44]	0.88 [0.78,0.98] p=0.13
		UAE (n = 102)	HYS (n = 50)		
Spies et al (2004b)	Prospective cohort study Level – III-2 QS – 18/27 Clin I – 4/4 Rel – 1/5 Stat prec – poor	101/102 (99%) No further treatment Further treatment due to clinical failure 1 UAE reoperation	50/50 (100%) No further treatment	NA	0.99 [0.97,1.01] p=0.48
		UAE (n = 37)	HYS (n = 31)		
Pourrat et al (2003)	Retrospective cohort study Level – III-2 QS – 16/27 Clin I – 4/4 Rel – 1/5 Stat prec – poor	35/37 (95%) No further treatment Clinical failure 1 no clinical improvement 1 no echographic improvement	31/31 (100%) Effectiveness of vaginal HYS was assumed to be 100%	NA	0.95 [0.88,1.02] p=0.19
		UAE (n = 62)	MYO (n = 40)		
Razavi et al (2003)	Retrospective cohort study Level – III-2 QS – 18/27 Clin I – 4/4 Rel – 1/5 Stat prec – poor	57/62 (92%) No further treatment Further treatment due to clinical failure 3 MYO 2 HYS	36/40 (90%) No further treatment Further treatment due to clinical failure 3 MYO 1 HYS	NA	1.02 [0.90,1.16] p=0.74
		UAE (n = 51)	MYO (n = 30)		
Broder et al (2002)	Retrospective cohort study Level – III-2 QS – 16/27 Clin I – 1/4 Rel – 1/5 Stat prec – good	36/51 (71%) No further treatment Further treatment [a b] 6 HYS 8 MYO 1 UAE	29/30 (99%) No further treatment Further treatment [c] 1 HYS	NNTH 4 [NNTH 3 to NNTH 8]	0.73 [0.60,0.88] p=0.004

HYS = hysterectomy; MYO = myomectomy; [a] Therefore if outcome favours UAE, RB >1.0; if it favours HYS or MYO, RB <1.0; Level = level of evidence; QS = quality score; Clin I = clinical importance; Rel = relevance of evidence; Stat prec = statistical precision; [b] Patients having UAE have an adjusted odds ratio of 12.5 (95% CI = 1,110; p=0.02) for requiring further invasive treatment; [c] The authors did not note whether the reoperations were because of clinical failure or safety issues.

Medium quality comparative studies on UAE and myomectomy were conducted by Razavi et al (2003) and Broder et al (2002). Razavi et al (2003) found no difference in follow-up treatments between the UAE and myomectomy patients within 1 month of their index procedure. The limitation of this study is that only successful myomectomy procedures were reported because the intra-operative conversion of myomectomy to hysterectomy was not assessed. Broder et al (2002) circulated a postal questionnaire ~47 months after treatment to 59 and 38 women who had undergone UAE and myomectomy, respectively. Data on contactable patients (UAE – n = 53: myomectomy – n = 32) suggests that the adjusted odds (for age and follow-up) of further treatment with UAE were 12.5 times that of myomectomy. However, their results are confounded by the fact that 80 per cent of UAE patients compared to 3 per cent of myomectomy patients had already undergone a myomectomy. The large difference in baseline prior gynaecological surgery means that no weight can be given to the highly significant, yet confounded, results of this study.

The highest rate of further treatment for UAE patients reported in 12 pre-test/post-test case series (level IV evidence) was reported as 9/60 (15%) by Goodwin et al (1999), which is similar to that reported by Pinto et al (2003; level II evidence). The majority of level III-2 and level IV evidence report that clinical failures occur in less than 8 per cent of UAE patients.

In conclusion, the highest level study (Pinto et al 2003) indicates that there is a 12 per cent increase in risk for further treatment due to clinical failure with UAE compared to hysterectomy. Conflicting results exist on the rate of follow-up treatment after UAE compared to myomectomy (Broder et al 2002; Razavi et al 2003). However, the results of Broder et al (2002) are discounted by the fact that extreme baseline differences in previous gynaecological intervention between UAE and myomectomy groups were not adjusted for. The evidence appears to show no difference in follow-up treatment between the two uterine-conserving procedures (Razavi et al 2003).

Uterine size

When comparing the effectiveness of UAE against hysterectomy, reduction in uterine size cannot be compared as the latter procedure completely removes the uterus. Spies et al (2004b) and Healey et al (2004) both reported mean uterine size reductions of 33 per cent at their 6-month follow-up of UAE patients. These studies provide the highest level of evidence for pre-test/post-test case series analysis. Two studies (Broder et al 2002; Razavi et al 2003) which retrospectively compared UAE against myomectomy did not compare uterine size reduction because myomectomy patient data were unavailable. Standard post-procedural care for myomectomy often does not involve imaging.

In contrast to comparative studies, uterine size is one of the most well researched outcomes of UAE in pre-test/post-test case series, probably because it is one of the few objective measures of clinical success. Twenty-one level IV studies reported on uterine size or volume (Appendix I), measured via ultrasound, MRI (enhanced or non-enhanced) or computed tomography. The mean reductions from baseline ranged from 27 per cent (Park

et al 2003) to 69 per cent (Walker et al 1999), with a median of 41 per cent (Smith et al 2004). It is clear that UAE has a significant impact on uterine size. Whether or not uterine size reductions of 41 per cent relate to significant patient-relevant outcomes (ie symptoms) remains to be seen.

Summary

Is uterine artery embolisation as, or more, effective at treating symptomatic uterine fibroids in women compared to hysterectomy?

One level II study and four level III-2 studies have reported on the effectiveness of UAE in comparison to hysterectomy. The majority of comparative effectiveness outcomes are reported in two key studies by Pinto et al (2003; level II) and Spies et al (2004b; level III-2). No comparative studies reported on uterine size, sexual function, fibroid recurrence or time to relief of symptoms.

Primary outcomes

Level II evidence shows that UAE is inferior at resolving menorrhagic symptoms compared to hysterectomy. Nevertheless, 86 per cent of UAE patients reported cessation of bleeding. A level III-2 study reported that UAE patients were 13 and 14 per cent less likely to report improvements in pelvic discomfort/pressure and pelvic pain, respectively, compared to hysterectomy patients. The authors (Spies et al 2004b) reported that these outcomes were unaffected by the fact that the UAE group had a significantly more severe baseline disease. The same level III-2 study reported equivalent improvements in quality of life for UAE and hysterectomy patients 12 months after treatment.

Secondary outcomes

Level II (one study) and III-2 (three studies) evidence indicates that convalescence, which includes hospital stay and return to normal activities, is shorter after UAE when compared to hysterectomy. The highest level of evidence (level II) reported an increased rate of further treatment after UAE compared to abdominal hysterectomy. In contrast, two level III-2 studies reported no difference between UAE and hysterectomy for further treatment. A level III-2 study showed that neither UAE nor subtotal laparoscopic hysterectomy affected ovarian function. Level IV studies that report on coincidental successful pregnancies show that further childbearing is possible after UAE; however, the rate of pregnancy success in women seeking further childbearing is unlikely to be resolved as pregnancy is a relative contraindication to UAE treatment.

As symptom control is the primary outcome to assess the effectiveness of uterine fibroid treatments, it appears that UAE is less effective than abdominal hysterectomy.

Is uterine artery embolisation as, or more, effective at treating symptomatic uterine fibroids in women compared to other uterine-conserving treatments?

Three retrospective level III-2 studies provided data on the effectiveness of UAE compared to myomectomy. However, only one medium quality study of Razavi et al (2003) thoroughly reported effectiveness outcomes and therefore provides the evidence base for most of the conclusions.

Primary outcomes

Based on one level III-2 study there is a 45 per cent greater probability that a UAE patient will report improved or resolved menorrhagic symptoms compared to a myomectomy patient. A trend towards better pain outcomes after UAE compared to myomectomy is also reported. Conversely, this level III-2 study suggests that fewer UAE patients experience improved mass effect symptoms compared to myomectomy patients.

Secondary outcomes

Level III-2 evidence (two studies) consistently reported a shorter convalescence period associated with UAE compared to abdominal myomectomy. The best quality level III-2 evidence suggests that the follow-up treatment rate was equivalent for both procedures.

Based on the limited data available, UAE appears to be as, or more, effective than abdominal myomectomy.

What are the economic considerations?

The purpose of an economic evaluation is to assist decision-makers in ensuring that society's ultimately scarce resources are allocated to those activities from which we will get the most value. That is, it seeks to enhance economic efficiency.

Economic evaluation under the MSAC process focuses on the scarce resources available within the Australian health system. It asks whether these scarce resources would be better spent on producing the amount of health gain obtainable through the intervention in question or through the identified comparator intervention(s).

UAE appears to be safer, but is less effective at controlling fibroid related symptoms, when compared to abdominal hysterectomy. However, this comparison is confounded by the fact that the latter procedure removes the uterus, whereas the former does not. Compared to uterine-removing hysterectomy, the benefit or value of uterine preservation associated with UAE is currently unquantified, and therefore the extent to which it may offset less effective symptom control in an economic model is uncertain. The more relevant comparator is therefore abdominal myomectomy, which is also a uterine-conserving procedure. Based primarily on one level III-2 study, UAE appears to be safer and at least as effective as abdominal myomectomy.

Proceeding with a cost-effectiveness analysis based on the results of one small study could result in large confidence intervals around estimates, reflecting a large element of random error which might not be resolvable by sensitivity analysis. Until more data are published that reinforce the effectiveness equivalence or superiority of UAE compared to myomectomy (abdominal or otherwise), a cost-effectiveness analysis is unlikely to provide much guidance for policy makers. A cost-comparison analysis has therefore been undertaken for UAE and its comparators, abdominal hysterectomy and abdominal myomectomy.

Objective

The aim of the present economic evaluation was to review the costs of UAE compared to both abdominal hysterectomy and abdominal myomectomy when these interventions are provided under Australian conditions, and to provide an indication of the extent of uncertainty entailed. The type of investigation chosen was a cost-comparison analysis. The perspective of the analysis was that of all third-party payers, henceforth described as the Australian health system overall, rather than a societal approach. Cost data therefore covered all non-trivial health system resources directly used in providing the intervention. Neither direct costs of informal care, nor indirect costs (also known as productivity costs) were considered due to the paucity of information in the literature for UAE. Following the economic evaluation, a financial incidence analysis was conducted to identify which costs would be borne by which funding agents (Commonwealth, State or private sector).

Unit costs of relevant items

Table 28 presents the Medicare Benefit Schedule item numbers associated with UAE and its comparators abdominal myomectomy and hysterectomy. The magnetic resonance imaging (MRI) item (MBS item number 63470) is currently only listed for the indication of

staging cervical cancer. However, because MRI provides a clearer picture of uterine architecture, it can assist in visualisation of the fibroid type and location, which is important with a minimally invasive technique such as UAE. Hence, the analysis allows for the possibility that the listing of MBS item number 63470 may be broadened to acknowledge this.

Table 28 Definition of MBS item numbers associated with abdominal hysterectomy, myomectomy and UAE (potentially)

MBS item no.	Schedule fee (100%) ($)	Definition
23	30.85	Level B general practitioner consult
104	72.60	Professional attendance at consulting rooms or hospital by a specialist
105	36.40	Subsequent attendances during a single course of treatment
63470	403.20	MRI for the pelvis for staging of cervical cancer
55731	98.00	Ultrasound scan of pelvis
65090	11.25	Blood grouping (including back-grouping if performed) – ABO and Rh (D antigen)
65099	113.40	Blood compatibility tests by cross-match
65060	7.95	Haemoglobin, erythrocyte sedimentation rate, blood viscosity
65070	17.20	Erythrocyte count, haematocrit, haemoglobin, calculation or measurement of red cell index or indices, platelet count, leucocyte count and manual or instrument generated differential count
72816	87.10	Tissue pathology of a sample from the uterus – endometrium – polyp; level 3 complexity level. Examination of complexity level 3 biopsy material with 1 or more tissue blocks, including specimen dissection, all tissue processing, staining, light microscopy and professional opinion or opinions – 1 separately identified specimen
73527	10.20	Detection of human chorionic gonadotrophin for diagnosis of pregnancy
66695	30.70	Quantitation in blood or urine of hormones and hormone binding proteins
35653	572.45	Hysterectomy, abdominal, subtotal or total, with or without removal of uterine adnexae
35649	454.80	Hysterectomy or uterine myomectomy, abdominal
35321	690.05	Peripheral arterial or venous catheterisation to administer agents to occlude arteries
51303	20% of proc. fee	Assistance at any operation for which the fee exceeds $473.75
51300	73.25	Assistance at any operation for which the fee does not exceed $473.75
17603	36.40	Examination of a patient in preparation for the administration of an anaesthetic relating to a clinically relevant service, being an examination carried out at a place other than an operating theatre or an anaesthetic induction room
20846	168.50	Initiation of management of anaesthesia for radical hysterectomy
23083	134.80	Time unit cost for anaesthesia for a 1:56 to 2:00 hour duration
60075	96.10	Selective arteriography by digital subtraction angiography (2 vessels)
60030	1176.10	Digital subtraction angiography of the abdomen – 7 to 9 data acquisition runs

proc. = procedure; MRI = magnetic resonance imaging

Costs per patient

Table 29 derives the pre- and post-hospital costs per patient for each of the three procedures from the MBS items in Table 28. Inpatient MBS costs, which are only applicable to the private sector, are also presented. Table 29 also presents a weighted UAE cost estimate, which assumes that 8 per cent of UAE patients will require a post-hospital investigative MRI scan because of continuing symptoms. This estimate could vary significantly, as the UAE failure rate can be associated with clinician experience and the type/size of embolic particles selected. Nevertheless, comparative studies (levels II and III-2 evidence) reported a median 8 per cent re-treatment rate for lack of symptom resolution (see 'No further treatment' section). A majority of case series (level IV evidence) also reported re-treatment rates of less than 8 per cent. This value is therefore a conservative (ie high) estimate. If MRI scans are not reimbursed for pre- and post-hospital patient imaging (ie 2 x $403), then the cost to the Commonwealth would be $2,682 for both those patients who have their symptoms resolved by UAE (asymptomatic) and those who do not (symptomatic).

Table 29 MBS unit costs ($) associated with abdominal hysterectomy, myomectomy and UAE

	Abdominal hysterectomy	Abdominal myomectomy	UAE
Pre-hospital MBS costs ($)			
GP consult	31 (23)	31 (23)	31 (23)
Gynaecologist consult	73 (104)	73 (104)	73 (104)
IR consult	---	---	73 (104)
Ultrasound imaging	98 (55731)	98 (55731)	98 (55731)
MR imaging	---	403 (63470) a	403 (63470) a
Histopathology	87 (72816)	87 (72816)	87 (72816)
Blood tests			
Blood group	11 (65090)	11 (65090)	---
Hold serum	113 (65099)	113 (65099)	---
Hb level	---	---	8 (65060)
Pregnancy test	10 (73527)	10 (73527)	10 (73527)
Full blood exam	17 (65070)	17 (65070)	---
Luteinising hormone level	31 (66695)	31 (66695)	31 (66695)
Subtotal (pre-hospital)	*471*	*874*	*814*
Inpatient MBS costs (private patients) ($)			
Procedure fee	572 (35653)	455 (35649)	690 (35321)
Assistant fee	115 (51303)	73 (51300)	138 (51303)
Anaesthetist fee–pre-med	36 (17603)	36 (17603)	--- g
Anaesthetist fee–initiation and management	169 (20846)	169 (20846)	--- g
Anaesthetist fee–time component	135 (23083)	135	--- g
DSA procedure fee	---	---	1,176 (60030)
Selective arteriography procedure fee	---	---	96 (60075)
Subtotal (inpatient)	*1,027*	*868*	*2,100*
Post-hospital MBS costs			
Gynaecologist consult	---	---	73 (105)
Imaging b	0	98 (55731) h	98 (55731) h
MR imaging c	0 d	403 (63470) a,e	403 (63470) a,e
Subtotal (post-hospital; asymptomatic)	*0*	*98*	*171*

	(post-hospital; symptomatic)	*NA [d]*	*403*	*476*
	(post-hospital weighted average) [f]	*NA*	*NA*	*195*
Total cost	(post-hospital; asymptomatic)	1,498	1,840	3,085
	(post-hospital; symptomatic)	NA [d]	2,145	3,390
	(post-hospital weighted average) [f]	NA	NA	3,109

Parentheses enclose the MBS item number used to estimate the cost; Pre- and post-hospital costs are estimated at 100 per cent of the MBS schedule fee – costs associated with treatment via public hospital outpatient departments could not be obtained; IR = interventional radiologist; MR = magnetic resonance; DSA = digital subtraction angiography; [a] MRI scans are not currently reimbursed for this indication, however this item number approximates the cost associated with this procedure; [b] asymptomatic patient; [c] symptomatic patient; [d] assuming that HYS patients always have their fibroid related symptoms resolved; [e] assuming that an MRI scan is necessary to establish the cause of continuing symptoms; [f] assuming that 8 per cent of UAE patients have continuing symptoms after operation and therefore require a follow-up scan; [g] Expert opinion suggests that the anaesthetist fee is not likely to be claimed for embolisation; [h] An ultrasound was assumed to be sufficient for assessment of treatment success in an asymptomatic patient

An alternative estimate of the inpatient costs for UAE has been obtained from private patient data provided by a Victorian public hospital (Table 30). In addition, UAE hospital stay costs were approximated using a gynaecological AR-DRG item that was similarly non-invasive (curettage and hysteroscopy, N10Z) and hospital stay duration from the comparative evidence base. An attempt was made to align the aforementioned costs to the AR-DRG cost buckets that are used for hysterectomy and myomectomy. It is clear that the cost of embolic material is the primary contributor to procedural cost (Table 30; patient consumables). Even though this component significantly affects the total UAE cost to the health system, it does not alter costs to the Commonwealth, as the cost associated with embolic material is the responsibility of the private patient and/or the private health insurer.

Table 30 Non-MBS private hospital inpatient unit cost estimates for UAE by source

Unit cost estimate ($)	Allocated cost bucket	Components	Source
7	Ward medical	1.8-day hospital stay x private sector estimated daily medical cost for another non-invasive procedure (curettage and hysteroscopy, N10Z)	Hospital stay is the average reported by one level II, five level III-2 and seven level IV studies
175	Ward nursing	1.8-day hospital stay x private sector estimated daily nursing cost for another non-invasive procedure (curettage and hysteroscopy, N10Z)	Hospital stay is the average reported by one level II, five level III-2 and seven level IV studies
0	Non-clinical salaries	NA	NA
0	Pathology	NA (assuming that pre-op work-up/imaging is thorough)	NA
84	Imaging	Radiographer fee Film cost Contrast medium cost	Based on private patient data sourced from a Victorian public hospital
0	Allied	NA	NA
58	Pharmacy	1500 mg paracetamol, Voltaren 100 mg suppository, Oxytocin 20 mg oral, 2 mg Midazolam iv, 25 µg Fentanyl iv, 1 g cephazolin and 4 mg Odansetron	Estimated medication use via expert opinion
0	Critical care	NA	NA (or insignificant)
0	Operating rooms	NA	NA
0	Emergency departments	NA	NA (or insignificant)

66	Supplies	Equipment lease Equipment maintenance	Based on private patient data sourced from a Victorian public hospital
198	Specialist procedure suite	Radiology suite cost Interventional radiologist fee Procedural nursing fee	Based on private patient data sourced from a Victorian public hospital [a]
1,547	Prostheses [b]	Patient related consumables	Based on private patient data sourced from a Victorian public hospital
46	On-costs	Salaries and wages overheads	Based on private patient data sourced from a Victorian public hospital
153	Accommodation 'hotel'	1.8-day hospital stay x (mean daily hotel cost for NO7Z and NO4Z in the private system)	Hospital stay is the average reported by one level II, five level III-2 and seven level IV studies
271	Depreciation	Equipment depreciation value	Based on private patient data sourced from a Victorian public hospital
17	Unspecified	Clerical cost Patient transport cost Administration cost	Based on private patient data sourced from a Victorian public hospital
2,622	TOTAL		

[a] likely underestimate; [b] embolic particles

Total health system costs of hysterectomy, myomectomy and UAE for private and public patients are presented in Table 31. The total health system cost of hysterectomy in the public hospital system was calculated as the sum of the public sector AR-DRG cost and the pre- and post-hospital MBS cost estimates (ie outpatient costs). The cost of hysterectomy in the private hospital system was calculated in the same way, except that inpatient MBS item numbers were also added to the total. It is worthwhile noting that cost data were able to be retrieved specifically for abdominal hysterectomy for the public sector AR-DRG estimate, whereas only the broader category of 'hysterectomy for non-malignancy', which includes 16 surgical variants of hysterectomy, was available for the private sector AR-DRG. The private hospital AR-DRG cost estimate is therefore not specific to abdominal hysterectomy and should be interpreted with caution.

The total health system cost of myomectomy was calculated in a similar fashion to that for hysterectomy. Again, the private sector AR-DRG data are provided only for the broad category of 'other uterine and adnexa procedures', for which uterine myomectomy is a component. This broader category is a composite of myomectomy and 63 other uterine and adnexa procedures, which casts considerable doubt on the use of the private sector cost weight for this AR-DRG item as an estimate of myomectomy costs. The possibility of a significant underestimation of private sector cost using this broad category is evidenced by a mean hospital stay of 1.04 days compared to the mean 3.3-day hospital stay for myomectomy reported by two comparative studies in this report. It is evident that the private sector cost data would incorporate many simpler, and thus cheaper, procedures compared to myomectomy. In contrast, public sector AR-DRG estimates are specific to uterine myomectomy and should therefore approximate costs, relative to other procedures, with tolerable accuracy.

When performed in a private hospital, the total cost of UAE is equivalent to the cost of hysterectomy for non-malignancy (NO4Z) at the limit of accuracy for the available data, which, because it is averaged across multiple procedures, should be interpreted with caution. The cost of UAE is considerably greater than the cost of 'other uterine and adnexa procedures for non-malignancy'. However, as previously highlighted, the cost of the latter is subject to considerable uncertainty given that the available data do not distinguish between myomectomy and 63 other uterine and adnexa procedures.

When performed in a public hospital, procedure specific data for abdominal hysterectomy and myomectomy (Casemix Data and Reporting Section of the Department of Health and Ageing) suggests there is not a substantial difference in cost between the two comparators. This again highlights the substantial possibility for error in using the private hospital AR-DRG (NO7Z) to estimate the cost of myomectomy. No cost estimate for UAE is available for the public sector.

Reliable cost estimates per patient were calculated for UAE in the *private* sector. Conversely, the costs per patient for the comparators abdominal hysterectomy and myomectomy could only be reliably obtained for the *public* sector. The costs per patient calculated for UAE (private sector, weighted estimate), abdominal hysterectomy for non-malignancy (public sector, asymptomatic patient) and myomectomy (public sector, asymptomatic patient) were $5,731, $6,195 and $6,331, respectively. It was not possible to estimate the cost per patient for all three procedures within either one or other of the private or public health sectors. Thus, because of the limitations of the available data, it is not yet possible to determine if there are substantial differences in the cost per patient to the Australian health system overall of abdominal hysterectomy, myomectomy and UAE (Table 31).

Table 31 Total cost per patient to the Australian health system using AR-DRG cost weights and MBS item numbers for abdominal hysterectomy, myomectomy and UAE

	PUBLIC SECTOR			PRIVATE SECTOR		
Component cost for DRG ($)						
AR-DRG	Procedure level data [a]	Procedure level data [b]	NA	N04Z	N07Z	NA
AR-DRG description	Abdominal HYS 35653-01	Uterine MYO 35649-03	UAE	HYS for non-malignancy	Other uterine and adnexa procedures for non-malignancy	UAE (from Table 30)
Ward medical	753	749	NI	22	5	7
Ward nursing	1,626	1,525	NI	707	135	175
Non-clinical salaries	226	253	NI	104	20	0
Pathology	182	177	NI	1	0	0
Imaging	40	34	NI	6	1	84
Allied	34	33	NI	18	5	0
Pharmacy	131	98	NI	53	23	58
Critical care	8	0	NI	23	4	0
Operating rooms	2,101	1,879	NI	1,598	518	0
Emergency departments	4	4	NI	5	3	0
Supplies	184	167	NI	260	68	66
Specialist procedure suite	5	0	NI	27	8	198
Prostheses	35	24	NI	367	6	1,547
On-costs	176	182	NI	362	94	46

Hotel	125	135	NI	446	78	153
Depreciation	94	99	NI	270	68	271
Unspecified	0	0	NI	0	0	17
Subtotal	*5,724*	*5,359*	*NA*	*4,269*	*1,036*	*2,622*
Inpatient cost for MBS (from Table 28) ($)						
Inpatient costs	NA [c]	NA [c]	NA [c]	1,027	868	2,100
Ambulatory care cost for MBS (from Table 28) ($)						
Pre-hospital costs	471 [g]	874 [g]	814	471	874	814
Post-hospital costs						
Asymptomatic patient [d]	0	98	171	0	98	171
Symptomatic patient [e]	NA	403	476	NA	403	476
Weighted average [f]	NA	NA	195	NA	NA	195
Total cost per procedure ($)						
Asymptomatic patient [d]	6,195	6,331	NA	5,596	2,705	5,707
Symptomatic patient [e]	6,195	6,636	NA	5,596	3,010	6,012
Weighted average [f]	NA	NA	NA	NA	NA	5,731

HYS = hysterectomy; MYO = myomectomy; Australian refined diagnosis related groups (AR-DRGs) cost estimates are from round 7 cost report (2002–03) available on the Department of Health and Ageing website http://www.health.gov.au/internet/wcms/publishing.nsf/Content/health-casemix-costing-fc_r7.htm (accessed 11/5/05); all component costs are presented as the sum of direct and overhead costs; [a] procedure level data for abdominal HYS represent data from 47 hospitals; [b] procedure level data for uterine MYO are based on data from 38 hospitals; [c] inpatient MBS item numbers are not claimable when a procedure is performed on a public patient in a public hospital; [d] patient whose fibroid symptoms are resolved by the index procedure; [e] patients whose symptoms are unresolved or unsatisfactorily resolved, necessitating follow-up imaging each on one occasion for MYO and UAE; [f] assuming that 8 per cent of UAE patients have continuing symptoms after operation and therefore require follow-up scans; [g] assuming that work-up imaging and pathology occurs prior to inpatient admission; NA = not applicable; NI = no information

Implications for the Australian health system

An estimate of the total number of women eligible for an intervention due to uterine fibroids was obtained by applying a median evidence-based asymptomatic prevalence rate of 13 per cent to the total female population aged 15–64 years (n = 6,266,110) (Australian Bureau of Statistics 2002). The estimate implied that 814,594 women could potentially have the disease at any one time. As there are no data on the proportion of women developing symptomatic uterine fibroids, the commonly cited rate of 10 to 40 per cent has been used to calculate the prevalence of the disease. This indicates a range of possible candidates for an intervention due to fibroids at 81,459 to 325,838 per year. However, not all cases of symptomatic uterine fibroids will go on to receive surgical or radiological intervention such as hysterectomy, myomectomy or UAE. The decision to undergo such treatments will depend on the age of the woman, the severity of the problem and the type of intervention she is willing to undergo. There are also non-invasive or adjunctive treatment options available, such as hormone therapy, and some women will simply deal with symptoms, knowing that they are likely to be resolved at menopause. No estimates have been obtained regarding the proportion of women with symptomatic uterine fibroids who will decide to undergo hysterectomy, myomectomy or UAE.

Financial implications for the Commonwealth

At rebates of 75% for inpatient services and 85% for out of hospital services, and ignoring safety net issues, the additional Commonwealth expenditure per patient for UAE compared to abdominal hysterectomy is $1,262, and compared to myomectomy is $956, in

the private sector. The corresponding figures for the public sector are $538 compared to abdominal hysterectomy and $37 compared to myomectomy (Table 32)

Table 32 Additional Commonwealth expenditures and copayments per patient [a]

Location of service		Additional expenditure per patient ($) Commonwealth expenditure: MBS rebate [b]	MBS copayment	Total = 100% MBS schedule fee [c]
PRIVATE SECTOR				
UAE versus HYS	Inpatient	805	268	1,073
	Out of hospital [d]	457	81	538
	Total	1,262	349	1,611
UAE versus MYO	Inpatient	924	308	1,232
	Out of hospital [d]	32	5	37
	Total	956	313	1,269
PUBLIC SECTOR				
UAE versus HYS	Out of hospital [d]	457	81	538
UAE versus MYO	Out of hospital [d]	32	5	37

[a] ignoring safety net issues [b] MBS rebate at 75% of schedule fee for inpatient services and at 85% for out of hospital services; [c] from Table 31; [d] pre-hospital costs and weighted average post-hospital costs

The Health Insurance Commission statistics on MBS item number usage (Table 6) indicate that there were a total of 2,424 services that can be reliably determined as being associated with uterine fibroid removal by uterine-conserving procedures. There were also 16,612 services that were non-discriminatory for uterine fibroid removal, which are likely to have been one of several patient indications associated with the usage of those Medicare items. These are private sector estimates.

For the private sector a maximum estimate of the likely service usage and costs to the Commonwealth associated with UAE, under the extreme assumption that all these procedures are replaced by UAE, can be obtained by multiplying the total annual number of Medicare services associated with symptomatic uterine fibroid treatments (19,036; Table 6) by the maximum additional Commonwealth expenditure for a UAE procedure ($1,262 compared to hysterectomy; Table 32). This suggests a maximum additional Commonwealth expenditure of $24.0 million.

An alternative expenditure estimate can be calculated on the premise that all private sector uterine-conserving treatments currently reimbursed by the Commonwealth (n = 2,424 in 2002–03) are replaced by UAE. This would result in a substantially lower additional Commonwealth expenditure of $3.1 million.

Limitations of the economic analysis

It is worthwhile noting that cost estimates in Tables 29 and 31 are approximations that require several arbitrary assumptions, which may or may not hold true. However, without these assumptions final cost estimates cannot be calculated. It is important to note that cost estimates for UAE, hysterectomy and myomectomy are not intended to be accurate

total health system costs, but instead provide a measure of relative cost when compared to each other. Finally, indirect cost savings due to UAE having a convalescence time approximately one-third that of its comparators (see 'Return to normal activities/work') are not presented in this analysis because it is unclear which method should be used to place a value on this, indirect costs and cost savings being a controversial topic in the literature.

The MBS item numbers for all three procedures are probably the most reliable cost estimates in the economic analysis; however, these only represent costs attributable to the Commonwealth (and associated patient copayments) and not the total cost to the health system.

The total health system costs estimated for the comparators are based on ambulatory care and inpatient MBS costs added to AR-DRG cost estimates. The AR-DRG estimates are based on a sample of Australian hospitals that can provide patient-level data in the public sector but only modelled data for private sector estimates. Table 31 contains procedure specific costs for total abdominal hysterectomy and myomectomy, which are based on data from 47 hospitals with 1,032 separations and 38 hospitals with 175 separations, respectively. Although public hospital procedure-level data are more specific and relevant than the broader AR-DRG classifications used for private hospital data, they are based on smaller samples and therefore are susceptible to greater random variation. Furthermore, public sector AR-DRG estimates also contain the costs to the hospital of private patients being treated within the public hospital. This decreases calculated overall health system costs because MBS item numbers (used for private patients) are not added to public sector AR-DRG subtotals. Finally, AR-DRG cost estimates are biased towards larger hospitals with extensive accounting systems, which may therefore also spuriously decrease the overall cost estimate because these larger hospitals assumedly benefit from economies of scale.

The majority of assumptions for this cost comparison analysis are required for UAE, which is a procedure that (to date) does not have any AR-DRG cost estimates associated with it. The cost information was derived from limited data provided by a Victorian public hospital. In order to compare UAE with hysterectomy and myomectomy, data from the hospital were separated into cost buckets. It is possible that costs have been misclassified; however, this does not affect the overall health system UAE cost estimate, on which the economic conclusions are based. The weighted average cost of UAE should provide a worst case scenario, assuming that 8 per cent of UAE patients do not have their symptoms controlled and therefore require follow-up investigative MR imaging. It has been assumed that one scan would be sufficient to establish the reason for clinical failure; however, some expert opinion suggests that up to three post-procedure scans could be performed, although these are more likely to be performed for the purpose of clinical data collection. Costs of follow-up procedures required for failed UAE have not been modelled because it is impossible to determine which treatment path the patient is likely to select (ie hysterectomy, myomectomy or re-UAE). Furthermore, if these costs were modelled then the costs of follow-up interventions for abdominal hysterectomy and myomectomy should also be modelled. There are no reliable data in the report for the rate of follow-up interventions for these two procedures. The total costs therefore apply, in all cases, to uncomplicated hysterectomy, myomectomy and UAE.

The biggest limitation to estimating the potential cost of UAE to the Commonwealth Government and health system is that the number of patients who would potentially consider UAE in Australia is difficult to estimate. Total cost estimates have been based on

the extreme scenario of all uterine removal and conservation procedures (n = 19,036) being replaced with UAE. In reality, this would not occur, but the proportion of women who currently undergo hysterectomies and myomectomies who would alternatively use UAE is unknown. It is also unknown how many women with symptomatic fibroids would not have a hysterectomy or myomectomy but would seek a UAE procedure because of its non-invasive nature and relatively short convalescence. Because it is currently best practice to involve a gynaecologist in the assessment of a UAE patient, the rate of UAE uptake in the Australian community would also depend on the proportion of gynaecologists who are willing to inform their patients of an alternative procedure that would be performed by another specialist. Again, this proportion is conjectural. Therefore, although extreme scenario expenditure estimates have been provided, they are unlikely to be realised.

Expert opinion

Fertility and pregnancy outcome

The desire to maintain fertility represents a relative contraindication to UAE as preservation of fertility cannot be assured on the basis of current literature. There is also no good evidence on whether embolisation and subsequent mummification of moderate to large leiomyomas predisposes to uterine rupture during labour.

There are numerous case reports of uncomplicated pregnancies and normal deliveries following UAE. However, the quality of data on the effect of UAE on fertility and pregnancy outcomes is poor.

UAE may sometimes remain a preferred option in patients who wish to maintain their childbearing potential and are not candidates for other uterine-conserving procedures. As for all fibroid embolisations, it is recommended that these decisions be made in conjunction with the obstetrician/gynaecologist and the interventionalist, and be based on a detailed explanation of risks and alternative treatments.

Discussion and conclusions

Safety

Is uterine artery embolisation as safe as, or safer than, hysterectomy for the treatment of symptomatic uterine fibroids in women?

The relative safety of uterine artery embolisation (UAE) in comparison to hysterectomy was assessed by one good quality level II study (Pinto et al 2003), one medium quality level III-2 prospective study (Spies et al 2004b) and two medium quality level III-2 retrospective studies (Beinfeld et al 2002; Pourrat et al 2003). The highest level of evidence for each outcome is used to draw conclusions on UAE safety relative to hysterectomy. The thorough review of safety issues provided by the highest level study means that it provides the evidence for most of the conclusions.

None of the comparative studies reported cases of death, septic shock, miscarriage, serious non-target embolisation, uterine perforation, idiosyncratic drug reaction, hyponatremia, depression, endometritis, uterine adhesions or minor bleeding associated with either UAE or hysterectomy.

The level II study by Pinto et al (2003) reported that no UAE patients suffered from haemorrhage whereas 10 per cent of hysterectomy patients required post-procedural blood transfusions. An additional four hysterectomy patients (20%) required a blood transfusion during their procedure.

The prevalence of amenorrhea after UAE has been estimated by one level II and one level III-2 study to be 17 and 7 per cent, respectively. Neither study measured hormone levels to confirm whether amenorrhea was indicative of the much more serious complication of ovarian failure and early menopause. Healey et al 2004 (level III-2 evidence) showed that UAE and subtotal hysterectomy did not affect ovarian function.

Level II evidence indicates a slightly increased rate of deep vein thrombosis after abdominal hysterectomy compared to UAE. However, prevalence was low for both procedures (Pinto et al 2003).

The highest level study to report organ damage (level III-2 evidence; Beinfeld et al 2002) described three cases of bowel obstruction and two of bladder injury after hysterectomy (87% abdominal; 8% vaginal; 5% laparoscopic) compared to no cases associated with UAE.

Readmission to hospital as a consequence of complications was recorded in an equal proportion of UAE and abdominal hysterectomy patients in the level II study (Pinto et al 2003). Admissions were for post-embolisation syndrome and severe pelvic pain for UAE patients, and anaemia that required a blood transfusion for a hysterectomy patient. No reoperations for complications associated with either procedure were reported. A medium quality level III-2 study reported a lower rate of rehospitalisation and reoperation after UAE in comparison to hysterectomy within 12 months of the index procedure (Spies et al 2004b).

Pinto et al (2003; level II evidence) reported that 25 per cent of UAE patients experience post-embolisation syndrome, 15 per cent requiring emergency department visits and 5 per cent rehospitalisation. As the name suggests, post-embolisation syndrome is a safety issue isolated to UAE.

Similarly, Pinto et al (2003) suggest that twice the proportion of UAE patients suffer from a haematoma (post-puncture) compared to abdominal hysterectomy patients (surgical wound haematomas). This study reports a converse trend for urinary tract infection, with twice the proportion of hysterectomy patients experiencing this complication compared to UAE patients. Spies et al (2004b) (level III-2 evidence) also found a lower rate of minor infection in UAE, compared to hysterectomy, patients.

Other procedural complications reported in the highest level study (level II) by Pinto et al (2003) included a higher rate of vaginal discharge, thigh paraesthesia, renoureteral colic, vulvovaginitis and anal fissure after UAE in comparison to hysterectomy. The converse applied for complications of urinary retention and vesicle fissure.

It is essential to note that, although high-level comparative studies report that UAE on the whole is a safer procedure than abdominal hysterectomy, case reports highlight the possibility of more major complications associated with UAE. This report acknowledges the bias associated with commenting on rare adverse events based on case reports which have been presented for UAE and not its comparator; however, to enhance the safety of UAE in the future, two issues need to be highlighted. Although major complications after UAE are rare, it is apparent from the literature that a reasonable percentage of adverse events originate either from the infarction of non-target organs (mainly the uterus) or the detachment of the infarcted target fibroid from the uterine wall. These events can often lead to infection. Unfortunately, symptoms associated with serious infection and non-target embolisation often mimic the common, minor complications of post-embolisation syndrome. As a consequence, they may be left untreated. Even though expert opinion suggests that the timing of fever and pain associated with post-embolisation syndrome and serious infection are distinctly different, there is still a need for diligent post-operative care of the UAE patient. Another major complication associated with UAE, which can be reduced via a thorough preclinical work-up, is the incorrect embolisation of a leiomyosarcoma, as opposed to a uterine fibroid. Without a thorough preclinical work-up, the disease is left undetected until symptoms reappear, which is often too late.

In conclusion, the highest level studies do not report death, septic shock or non-target embolisation for either UAE or hysterectomy. A greater proportion of hysterectomy patients suffered from haemorrhage, deep vein thrombosis, organ damage, urinary retention and minor infection. Level II evidence found no difference in rehospitalisation or reoperation due to complications although a level III-2 study showed that UAE rehospitalisation and reoperation rates were lower than those for hysterectomy. Minor complications such as post-embolisation syndrome, vaginal discharge, post-puncture haematoma and thigh paraesthesia are more common in UAE patients. Overall, UAE appears to be as safe as, or safer than, abdominal hysterectomy with fewer major complications. Further research comparing the relative safety of UAE with the less invasive treatment of laparoscopic hysterectomy would provide some interesting comparisons.

Is uterine artery embolisation as safe as, or safer than, other uterine-conserving treatments for the treatment of symptomatic uterine fibroids in women?

A medium quality retrospective level III-2 study by Razavi et al (2003) reported on the safety of UAE in comparison to abdominal myomectomy. A poor quality retrospective level III-2 study (McLucas & Adler 2001) provided a brief overview of complications associated with UAE and myomectomy. The two aforementioned studies provided the evidence base for the safety of UAE relative to abdominal myomectomy.

Mortality, septic shock, miscarriage, serious non-target embolisation, uterine perforation, thrombo-embolism, idiosyncratic drug reaction, hyponatremia and depression were not reported in either comparative study for UAE or abdominal myomectomy.

No blood transfusions were reported for UAE patients in these studies compared to a prevalence of 8 and 13 per cent for the respective myomectomy groups. Similarly, Razavi et al (2003) reported a higher rate of wound infection, chronic pelvic pain, uterine adhesions and intra-procedural bleeding in myomectomy patients compared to the UAE group. McLucas and Adler (2001) reported that the prevalence of ileus, phlebitis and organ damage (one case of small bowel laceration) was also comparatively higher in myomectomy patients. The rate of rehospitalisation for complications was equivalent for both UAE and myomectomy (Razavi et al 2003). The reason for rehospitalisation for two UAE patients was endometritis and pelvic pain, while one myomectomy patient was readmitted for ileus. The rate of early menopause appears to be higher after UAE compared to myomectomy (Razavi et al 2003). There is also a higher prevalence of transient numbness over the groin access site after UAE.

In conclusion and based on the limited data, it appears that UAE is probably as safe as, or safer than, abdominal myomectomy. The higher rate of early menopause after UAE compared to myomectomy is the most concerning safety outcome. The reason for a higher rate of menopause could be because the collateral arteries of the ovaries are compromised during embolisation of the uterine artery feeding the fibroid, whereas during myomectomy the fibroid is surgically removed in an open technique with better visualisation. Further comparative research needs to be conducted on the safety of UAE compared to *other* uterine-conserving fibroid treatments.

Effectiveness

Is uterine artery embolisation as, or more, effective at treating symptomatic uterine fibroids in women compared to hysterectomy?

The evidence base for the effectiveness of UAE in comparison to hysterectomy includes one good quality level II study (Pinto et al 2003), two prospective medium quality level III-2 studies (Healy et al 2004; Spies et al 2004b;) and two retrospective medium quality level III-2 studies (Beinfeld et al 2002; Pourrat et al 2003). The highest level studies for each outcome, on which these conclusions are based, used abdominal hysterectomy (Pinto et al 2003); laparoscopic hysterectomy (Healy et al 2004); and 80 per cent abdominal, 16 per cent laparoscopic and 4 per cent combined laparoscopic and vaginal hysterectomy (Spies et al 2004b) as their comparators. There were no comparative studies that assessed sexual function, analgesia use, fibroid recurrence or time to relief of symptoms for either UAE or hysterectomy.

Primary outcomes

Not surprisingly, when comparing UAE against the uterine-removing treatment of hysterectomy, the highest level of evidence (level II; Pinto et al 2003) available indicates that UAE is less effective at controlling menorrhagic symptoms. Nevertheless, 86 per cent of UAE patients still reported bleeding resolution. The highest level of evidence for improvements in bulk/pressure symptoms was a level III-2 study, which indicated that fewer UAE patients compared to hysterectomy patients reported improvements in pelvic discomfort/pressure. Similar trends for pelvic/menstrual pain were also reported. Even though the UAE group had a clinically more severe baseline disease in this study, none of these differences were reported to affect the pelvic discomfort/pressure and pelvic/menstrual pain outcomes. Spies et al (2004b) was also the only comparative study to assess quality of life, finding that there were equivalent improvements in SF-12 questionnaire scores one year after UAE and hysterectomy.

Secondary outcomes

The good quality level II study by Pinto et al (2004) found that both hospital stay and the time taken to return to normal activities were significantly shorter after UAE compared to hysterectomy. However, they also reported that 13 per cent of UAE patients underwent further surgical intervention because of clinical failure compared to none of the 20 hysterectomy patients. Medium quality level III-2 evidence shows that neither UAE nor subtotal hysterectomy affect ovarian function (Healey et al 2004). Pregnancy outcome is not a relevant measure when comparing UAE with hysterectomy as the latter procedure, by definition, removes the uterus and childbearing potential. Furthermore, pregnancy outcome data for UAE patients are sparse because pregnancy is a relative contraindication for this procedure.

Therefore, based on the highest levels of evidence available, UAE appears to be less effective at resolving the primary symptoms (menorrhagia, pain and bulk) associated with uterine fibroids, and is associated with equivalent improvements in quality of life, when compared to abdominal hysterectomy. UAE patients are more likely to need further treatment, but this minimally invasive procedure is associated with a significantly reduced

convalescence time, when compared to hysterectomy. UAE is unlikely to affect ovarian function. Overall, the minimally invasive, uterine-conserving treatment of UAE appears to be less effective than hysterectomy.

It is possible to estimate the self-perceived benefit a woman gains by retaining her uterus; however, to integrate this benefit into a model in such a way that it offsets the lesser degree of symptom control offered by UAE is virtually impossible. Further research comparing UAE and hysterectomy is therefore of limited value, because comparisons between uterine-conserving and -removing surgery are always conditional on the different aims of the procedures. The primary aim of hysterectomy is to resolve the symptomatic problems by removing the offending organ entirely, whereas UAE attempts to resolve or improve symptoms while maintaining the overall physiological function of the patient. It should be noted that, in the current context of practice in both Australia and overseas, many women are not eligible for uterine-conserving surgery as a treatment for their fibroid disease. However, many of these women are eligible for UAE as a non-invasive uterine-conserving procedure. Any differences in the effectiveness and safety of these procedures must therefore be placed in the context of disease severity and the patient's desire for uterine conservation.

In the Australian context a non-randomised controlled trial is currently (2005) being undertaken at the Wesley Hospital in Brisbane, Queensland, and funded by the Wesley Research Institute. Personal communication with the group has revealed that they are several years away from publishing data. Their assessment of symptom control, quality of life and sexual function in proposed sample groups of 75 UAE patients and 15–20 hysterectomy and myomectomy patients may provide useful additional data. However, still more research needs to be conducted with regards to comparing UAE with, primarily, other uterine-conserving options available to Australian women.

Is uterine artery embolisation as, or more, effective at treating symptomatic uterine fibroids in women compared to other uterine-conserving treatments?

The evidence base for the effectiveness of UAE compared to other uterine-conserving treatments included three retrospective level III-2 studies that compared UAE against abdominal myomectomy (Broder et al 2002; McLucas & Adler 2001; Razavi et al 2003). No other uterine-conserving procedures were comparatively assessed against UAE. Furthermore, the medium quality study by Broder et al (2002) and poor quality study by McLucas and Adler (2001) were only included for those effectiveness outcomes related to further treatment and hospital stay, respectively. The majority of UAE effectiveness conclusions are therefore based on the data provided by Razavi et al (2003). No comparative evidence is available for quality of life, sexual function, fibroid recurrence, uterine size and time to relief of symptoms.

Primary outcomes

The highest available evidence reported that UAE patients were more likely to report completely or significantly resolved menorrhagic and pain symptoms compared to abdominal myomectomy. The converse trend applied for mass effect symptoms (level III-2; Razavi et al 2003).

Secondary outcomes

Razavi et al (2003) reported a shorter return time to normal activities and less days taking pain medication for UAE patients compared to abdominal myomectomy patients. Both the medium quality level III-2 study of Razavi et al (2003) and the poor quality level III-2 study of McLucas and Adler (2001) reported a significantly shorter hospital stay after UAE compared to abdominal myomectomy.

Razavi et al (2003) reported no difference in the likelihood of further treatment after UAE compared to myomectomy. In contrast, another medium quality level III-2 study (Broder et al 2002) reported a higher rate of follow-up treatment after UAE compared to myomectomy, but their results were confounded by extreme baseline differences between the treatment arms.

The effect of UAE on pregnancy outcome is debatable, and is likely to remain that way because further childbearing is a relative contraindication for UAE. Pregnancies in UAE cohorts therefore comprise a very small percentage of total sample size (Carpenter & Walker 2005; Pron et al 2005) because they are usually coincidental or unintended. It is worthwhile clarifying that the primary aim of UAE is not to maintain uterine viability for pregnancy but to treat fibroid symptoms in situ, via a minimally invasive technique that retains the uterus.

Based on the limited data available, UAE appears to be as, or more, effective than abdominal myomectomy.

There is a paucity of comparative information on UAE and other uterine-conserving treatments, and further research comparing various interventions with the same goals needs to be conducted. Important areas that are currently under-researched include determination of fibroid or symptom recurrence and the rate of follow-up treatments for UAE compared to other uterine-conserving fibroid treatments.

Cost-effectiveness

Although UAE appears to be as safe as, or safer than, abdominal myomectomy and just as effective, the study on which these conclusions are predominately based has a small sample size. Proceeding with a cost-effectiveness analysis based on the results of one small study could result in large confidence intervals around estimates, introducing a significant element of random error which might not be resolvable by sensitivity analysis. Until more data are published that reinforce the effectiveness equivalence or superiority of UAE compared to myomectomy (abdominal or otherwise), a cost-effectiveness analysis is unlikely to provide much guidance for policy makers. A cost-comparison analysis was therefore conducted for UAE and its comparators, abdominal hysterectomy and abdominal myomectomy.

Reliable cost estimates per patient were only able to be calculated for UAE in the private sector. Conversely, total health system costs per patient for the comparators abdominal hysterectomy and abdominal myomectomy could only be reliably determined for the public sector. The total costs calculated for UAE (private sector), abdominal hysterectomy for non-malignancy (public sector) and myomectomy (public sector) were $5,731, $6,195 and $6,331, respectively. However, because of the inability to estimate the total health system cost for all three procedures within either one or other of the private or public health sectors specifically, it is not yet possible to determine if there are substantial differences in cost to the Australian health system overall between abdominal hysterectomy, myomectomy and UAE.

Financial implications for the Commonwealth

Currently, the private patient MBS reimbursement for discriminatory item numbers related specifically to uterine fibroids stands at 2,424 procedures in 2002–03. Other procedures such as hysterectomy, for which the indications are not specifically defined, were claimed for 16,612 times in 2002–03. The most extreme case scenario is that 100 per cent of the aforementioned uterine-conserving and -removing procedures (n = 19,036) could be replaced with UAE. It is also possible that a proportion of women who would not have undergone either hysterectomy or myomectomy may choose the non-invasive UAE procedure, but these are not included in these calculations. The MBS item numbers claimed for ambulatory and inpatient costs for a private patient undergoing UAE sum to a total of $3,109. The maximum additional Commonwealth expenditure on private sector procedures would therefore be $24.0 million if all hysterectomy and myomectomy procedures were replaced with UAE. An alternative expenditure estimate can be calculated on the premise that only the private sector uterine-conserving treatments currently reimbursed by the Commonwealth (n = 2,424 in 2002–03) are replaced by UAE, which would result in a substantially lower estimate of additional Commonwealth expenditure of $3.1 million.

Recommendation

The MSAC recommended that on the strength of evidence pertaining to uterine artery embolisation for the treatment of symptomatic uterine fibroids, public funding *should* be supported for this procedure.

'The evidence suggests that UAE is safe, clinically effective and potentially cost-effective for the treatment of symptomatic uterine fibroids. It appears to be more effective than myomectomy for the control of menorrhagia and pain but less effective in controlling pressure symptoms.

It is safer but less effective in controlling symptoms compared with hysterectomy.

The MSAC recommends that UAE be funded on an interim basis for the treatment of women with symptomatic uterine fibroids with a review within 5 years. The MSAC recommends that patients be referred by a specialist gynaecologist.'

The Minister for Health and Ageing accepted this recommendation on 28th of March 2006.

Appendix A MSAC terms of reference and membership

The MSAC's terms of reference are to:

- advise the Minister for Health and Ageing on the strength of evidence pertaining to new and emerging medical technologies and procedures in relation to their safety, effectiveness and cost-effectiveness, and under what circumstances public funding should be supported;
- advise the Minister for Health and Ageing on which new medical technologies and procedures should be funded on an interim basis to allow data to be assembled to determine their safety, effectiveness and cost-effectiveness;
- advise the Minister for Health and Ageing on references related either to new and/or existing medical technologies and procedures; and
- undertake health technology assessment work referred by the Australian Health Ministers' Advisory Council (AHMAC) and report its findings to AHMAC.

Membership of the MSAC comprises a mix of clinical expertise covering pathology, nuclear medicine, surgery, specialist medicine and general practice, plus clinical epidemiology and clinical trials, health economics, consumers, and health administration and planning:

Member	**Expertise or Affiliation**
Dr Stephen Blamey (Chair)	general surgery
Associate Professor John Atherton	cardiology
Professor Syd Bell	pathology
Dr Michael Cleary	emergency medicine
Dr Paul Craft	clinical epidemiology and oncology
Dr Gerry FitzGerald	Australian Health Ministers' Advisory Council representative
Dr Kwun Fong	thoracic medicine
Dr Debra Graves	medical administrator
Professor Jane Hall	health economics
Professor John Horvath	Chief Medical Officer, Department of Health and Ageing
Ms Samantha Robertson	Department representative
Dr Terri Jackson	health economics
Professor Brendon Kearney	health administration and planning
Associate Professor Donald Perry-Keene	endocrinology
Dr Ray Kirk	health research
Dr Michael Kitchener	nuclear medicine
Professor Alan Lopez	medical statistics and population health

Dr Ewa Piejko	general practice
Ms Sheila Rimmer	consumer health issues
Professor Jeffrey Robinson	obstetrics and gynaecology
Professor Michael Solomon	colorectal surgery, clinical epidemiology
Professor Ken Thomson	radiology
Dr Douglas Travis	urology

Appendix B Advisory panel

Advisory panel for MSAC application 1081
Uterine artery embolisation (UAE)

Dr Ray Kirk (Chair) BSc, MSc, PhD Health Sciences Centre, College of Science University of Canterbury, Christchurch, NZ	Member of the MSAC Deputy-Director and Senior Lecturer in Health Sciences
Dr Stuart Lyon MBBS FRANZCR Department of Radiology The Alfred, Melbourne, VIC	Nominated by the Royal Australian & New Zealand College of Radiologists Interventional Radiologist
Dr Geoffrey Reid Suite 4, 70 Bowral Street, Bowral, NSW	Nominated by the Australian Gynaecological Endoscopic Society
Professor Jeffrey Robinson BSC, MB BCh BAO, FRCOG, FRANZCOG Dept Obstetrics & Gynaecology, University of Adelaide, Adelaide, SA	Member of the MSAC Professor Obstetrics and Gynaecology
Ms Jo-Anne Tamlyn BA Chronic Illness Alliance Camberwell, VIC	Nominated by the Consumers' Health Forum of Australia

Appendix C Search strategies

Bibliographic databases used to identify literature

Electronic database	Time period
AustHealth	1997 – 11/2004
Cinahl	1990 – 11/2004
Cochrane Library – including, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, the Cochrane Central Register of Controlled Trials (CENTRAL), the Health Technology Assessment Database, the NHS Economic Evaluation Database	1990 – 11/2004
Current Contents	1993 – 11/2004
Embase.com (including Embase and Medline)	1990 – 3/2005
Pre-Medline	2004
ProceedingsFirst	1993 – 11/2004
PsycInfo	1990 – 11/2004
Web of Science – Science Citation Index Expanded	1995 – 11/2004
EconLit	1990 – 11/2004

Other sources of evidence

Additional sources of literature – peer-reviewed, unpublished and grey literature – were sought from the sources outlined below.

Source	Location
Internet	
NHMRC- National Health and Medical Research Council (Australia)	http://www.health.gov.au/nhmrc/
Australian Department of Health and Ageing	http://www.health.gov.au/
US Department of Health and Human Services (reports and publications)	http://www.os.dhhs.gov/
New York Academy of Medicine Grey Literature Report	http://www.nyam.org/library/greylit/index.shtml
Trip database	http://www.tripdatabase.com
Current Controlled Trials metaRegister	http://controlled-trials.com/
Health Technology Assessment International (HTAi)	http://www.htai.org/
International Network for Agencies for Health Technology Assessment	http://www.inahta.org/
National Library of Medicine Health Services/Technology Assessment Text	http://text.nlm.nih.gov/
National Library of Medicine Locator Plus database	http://locatorplus.gov
U.K. National Research Register	http://www.update-software.com/National/
Websites of Health Technology Agencies	See Appendix D
Websites of Specialty Organisations	See Appendix D
Hand searching (journals from 2003–04)	
Applied Radiology	Internet table of contents
Australian and New Zealand Journal of Obstetrics and Gynaecology	Library or electronic access
BJOG: an International Journal of Obstetrics and Gynaecology	Library or electronic access
British Journal of Radiology	Library or electronic access
Cardiovascular and Interventional Radiology	Library or electronic access
Clinical Radiology	Library or electronic access
Fertility and Sterility	Library or electronic access
Gynaecological Endoscopy	Library or electronic access
Human Reproduction	Internet table of contents
Journal of the American Association of Gynecological Laparoscopists	Internet table of contents
Journal of Vascular and Interventional Radiology	Internet table of contents
Obstetrics and Gynecology	Library or electronic access
Obstetrical and Gynecological Survey	Library or electronic access
Radiology	Library or electronic access
Seminars in Interventional Radiology	Internet table of contents
Expert clinicians	
Studies other than those found in regular searches	MSAC Advisory Panel
Pearling	
All included articles had their reference lists searched for additional relevant source material	

Search terms used

Area of inquiry	Search terms
Burden of disease	EmTree 'uterus'/exp AND 'benign tumor'/exp 'prevalence'/exp OR 'epidemiology'/exp OR 'cohort analysis'/exp OR 'incidence'/exp Text words leiomyo?ma* OR lyomyo?ma* OR fibromyoma* OR myoma* OR (fibroma* AND uter*) OR (fibroid* AND uter*) inciden* OR prevalen* OR cohort OR cross?section* OR registry OR register Limits [1990–2005]/py [english]/lim
Safety	EmTree 'uterine artery embolization'/exp OR 'myomectomy'/exp OR 'hysterectomy'/exp 'uterus'/exp AND 'benign tumor'/exp Text words safe* OR injur* OR morbid* OR mortal* OR complication* OR (adverse AND event*) emboli* OR block* OR occlu* OR voa OR microsphere* OR embosphere* OR particle* OR myomect* OR hysterect* OR progesterone OR (hysteroscop* AND resect*) leiomyo?ma* OR lyomyo?ma* OR fibromyoma* OR myoma* OR (fibroma* AND uter*) OR (fibroid* AND uter*) Limits [1990–2005]/py
Effectiveness and cost-effectiveness	EmTree 'uterine artery embolization'/exp 'uterus'/exp AND 'benign tumor'/exp Text words emboli* OR block* OR occlu* OR voa OR microsphere* OR embosphere* OR particle* leiomyo?ma* OR lyomyo?ma* OR fibromyoma* OR myoma* OR (fibroma* AND uter*) OR (fibroid* AND uter*) Limits [1990–2005]/py

Appendix D Internet sites searched

General sites

Australia

- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S) http://www.surgeons.org/open/asernip-s.htm
- Centre for Clinical Effectiveness, Monash University http://www.med.monash.edu.au/healthservices/cce/evidence/
- Health Economics Unit, Monash University http://chpe.buseco.monash.edu.au

Austria

- Institute of Technology Assessment / HTA unit http://www.oeaw.ac.at/ita/e1-3.htm

Canada

- Agence d'Evaluation des Technologies et des Modes d'Intervention en Santé (AETMIS) http://www.aetmis.gouv.qc.ca/en/index.htm
- Alberta Heritage Foundation for Medical Research (AHFMR) http://www.ahfmr.ab.ca/publications.html
- Canadian Coordinating Office for Health Technology Assessment (CCOHTA) http://www.ccohta.ca/entry_e.html
- Canadian Health Economics Research Association (CHERA/ACRES) – Cabot database http://www.mycabot.ca
- Centre for Health Economics and Policy Analysis (CHEPA), McMaster University http://www.chepa.org
- Centre for Health Services and Policy Research (CHSPR), University of British Columbia http://www.chspr.ubc.ca
- Health Utilities Index (HUI) http://www.fhs.mcmaster.ca/hug/index.htm
- Institute for Clinical and Evaluative Studies (ICES) http://www.ices.on.ca

Denmark

- Danish Institute for Health Technology Assessment (DIHTA) http://www.dihta.dk/publikationer/index_uk.asp
- Danish Institute for Health Services Research (DSI) http://www.dsi.dk/engelsk.html

Finland

- FINOHTA http://www.stakes.fi/finohta/e/

France

- L'Agence Nationale d'Accréditation et d'Evaluation en Santé (ANAES) http://www.anaes.fr/

Germany

- German Institute for Medical Documentation and Information (DIMDI) / HTA http://www.dimdi.de/en/hta/index.html

The Netherlands

- Health Council of the Netherlands Gezondheidsraad http://www.gr.nl/adviezen.php

New Zealand

- New Zealand Health Technology Assessment (NZHTA) http://nzhta.chmeds.ac.nz/

Norway

- Norwegian Centre for Health Technology Assessment (SMM) http://www.oslo.sintef.no/smm/Publications/Engsmdrag/FramesetPublications.htm

Spain

- Agencia de Evaluación de Tecnologias Sanitarias, Instituto de Salud "Carlos III"I/Health Technology Assessment Agency (AETS) http://www.isciii.es/aets/cdoc.htm

- Catalan Agency for Health Technology Assessment (CAHTA) http://www.aatm.es/cgi-bin/frame.pl/ang/pu.html

Sweden

- Swedish Council on Technology Assessment in Health Care (SBU) http://www.sbu.se/admin/index.asp

- Center for Medical Health Technology Assessment http://www.cmt.liu.se/English/Engstartsida.html

Switzerland

- Swiss Network on Health Technology Assessment (SNHTA) http://www.snhta.ch/

United Kingdom

- Health Technology Board for Scotland http://www.htbs.org.uk/
- National Health Service Health Technology Assessment (UK) / National Coordinating Centre for Health Technology Assessment (NCCHTA) http://www.hta.nhsweb.nhs.uk/
- University of York NHS Centre for Reviews and Dissemination (NHS CRD) http://www.york.ac.uk/inst/crd/
- National Institute for Clinical Excellence (NICE) http://www.nice.org.uk/index.htm

United States

- Agency for Healthcare Research and Quality (AHRQ) http://www.ahrq.gov/clinic/techix.htm
- Harvard School of Public Health – Cost-Utility Analysis Registry http://www.hsph.harvard.edu/cearegistry/
- U.S. Blue Cross/ Blue Shield Association Technology Evaluation Center (TEC) http://www.bcbs.com/consumertec/index.html

Speciality sites

Radiological

- American College of Radiology http://www.acr.org/s_acr/index.asp
- American Society of Interventional & Therapeutic Neuroradiology http://www.asitn.org/
- British Institute of Radiology http://www.bir.org.uk
- British Society of Interventional Radiology http://www.bsir.org/
- Canadian Association of Radiologists http://www.car.ca/
- Canadian Interventional Radiology Association http://www.car.ca/cira/
- CIRSE: Cardiovascular and Interventional Radiological Society of Europe http://www.cirse.org/master_01.php?pp=1,0,0,0,0
- Mid-American Interventional Radiological Society http://www.mirs.org/
- Radiological society of North America http://www.rsna.org/
- Royal College of Radiologists http://www.rcr.ac.uk/
- Society of Cardiovascular angiography and Interventions http://www.scai.org/

- Society of Interventional Radiology http://www.sirweb.org/
- The Royal Australian & New Zealand College of Radiologists http://www.ranzcr.edu.au/index.htm

Gynaecological

- American Association of Gynecologic Laparoscopists http://www.aagl.com/
- European Association of Gynaecologists and Obstetricians http://www.obgyn.net/eago/eago.htm
- European Society of Gynecology http://www.seg-web.org/
- International Federation of Gynecology and Obstetrics (FIGO) http://www.figo.org/
- International Pelvic Pain Society http://www.pelvicpain.org/
- International Society for Gynecologic Endoscopy http://www.isge.org/
- Royal Australian and New Zealand College of Obstetricians and Gynaecologists http://www.ranzcog.edu.au
- Royal College of Obstetricians and Gynaecologists http://www.rcog.org.uk/
- Society of Obstetricians and Gynaecologists of Canada http://sogc.medical.org/sogcnet/index_e.shtml
- The American College of Obstetricians and Gynecologists http://www.acog.com/

Appendix E Critical appraisal checklists

Systematic review critical appraisal checklist

Source: (Khan et al 2001)

Title of assessment:
Title of systematic review:
Author(s):
Year:
Comparators:
Score : /6 (0=not stated; 1=stated)

1. **What is the review's objective? /1**

   What were the population/participants, interventions, outcomes and study designs?

2. **What sources were searched to identify primary studies? /1**

   What sources (eg databases) were searched and were any restrictions by date, language and type of publication used? Were other strategies used to identify research?

3. **What were the inclusion criteria and how were they applied? /1**

4. **What criteria were used to assess the quality of primary studies and how were they applied? /1**

5. **How were the data extracted from the primary studies? /1**

6. **How were the data synthesised? /1**

   How were differences between studies investigated?

   How were the data combined? Was it reasonable to combine the studies?

   What were the summary results of the review?

   Do the conclusions flow from the evidence reviewed?

Checklist for appraising the quality of intervention studies

THE UNIVERSITY OF ADELAIDE AUSTRALIA

STUDY QUALITY ASSESSMENT CHECKLIST

Suitable for trials, cohorts and case-control studies assessing interventions

(Downs and Black (1998)–adapted for this MSAC assessment)

Uterine artery embolisation for symptomatic uterine fibroids

Author(s):
Institution(s):
Year:
Study Design:
Comparators:

Reporting

1. *Is the hypothesis/aim/objective of the study clearly described?*

yes	1
no	0

2. *Are the main outcomes to be measured clearly described in the Introduction or Methods section?*
   If the main outcomes are first mentioned in the Results section, the question should be answered 'no'.

yes	1
no	0

3. *Are the characteristics of the patients included in the study clearly described?*
   In cohort studies and trials, inclusion and/or exclusion criteria should be given.

yes	1
no	0

4. *Are the interventions of interest clearly described?*
   Interventions that are to be compared should be clearly described.

yes	1
no	0

5. *Are the distributions of principal confounders in each group of subjects to be compared clearly described?*
   Possible confounders = age, ethnic group, menopausal status, disease severity (location and size of fibroids), gynaecological history

yes	2
partially	1
no	0

6. *Are the main findings of the study clearly described?*
   Simple outcome data (including denominators and numerators) should be reported for all major findings so that the reader can check the major analyses and conclusions (This question does not cover statistical tests which are considered below).

yes	1
no	0

7. *Does the study provide estimates of the random variability in the data for the main outcomes?*
   In non-normally distributed data the inter-quartile range of results should be reported. In normally distributed data the standard error, standard deviation or confidence intervals should be reported. If the distribution of the data is not described, it must be assumed that the estimates used were appropriate and the question should be answered 'yes'.

yes	1
no	0

8. *Have all important adverse events that may be a consequence of the intervention been reported?*
   This should be answered 'yes' if the study demonstrates that there was a comprehensive attempt to measure adverse events.

   Adverse events = Major complications – including mortality, septic shock, haemorrhage, endometritis, post-embolisation syndrome, early menopause, amenorrhea, infertility, miscarriage, serious non-target embolisation, uterine perforation, thrombo-embolism, organ damage, idiosyncratic drug reaction, hyponatraemia, rehospitalisation, reoperation, depression. Minor complications – including haematoma, uterine adhesions, local infection, minor bleeding.

yes	1
no	0

9. *Have the characteristics of patients lost to follow-up been described?*
   This should be answered 'yes' where there were no losses to follow-up or where losses to follow-up were so small that findings would be unaffected by their inclusion. This should be answered 'no' where a study does not report the number of patients lost to follow-up.

yes	1
no	0

10. *Have the actual probability values been reported (eg 0.035 rather than <0.05) for the main outcomes, except where the probability value is less than 0.001?*

yes	1
no	0

External validity

All the following criteria attempt to address the representativeness of the findings of the study and whether they may be generalised to the population from which the study subjects were derived.

11. *Were the subjects asked to participate in the study representative of the entire population from which they were recruited?*
    The study must identify the source population for patients and describe how the patients were selected. Patients would be representative if they comprised the entire source population, an unselected sample of consecutive patients, or a random sample. Random sampling is only feasible where a list of all members of the relevant population exists. Where a study does not report the proportion of the source population from which the patients are derived, the question should be answered as 'unable to determine'.

yes	1
no	0
unable to determine	0

12. *Were those subjects who were prepared to participate representative of the entire population from which they were recruited?*
    The proportion of those asked who agreed should be stated. Validation that the sample was representative would include demonstrating that the distribution of the main confounding factors was the same in the study sample and the source population.

yes	1
no	0
unable to determine	0

13. *Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive?*
    For the question to be answered 'yes' the study should demonstrate that the intervention was representative of that in use in the source population. The question should be answered 'no' if, for example, the intervention was undertaken in a specialist centre unrepresentative of the hospitals most of the source population would attend.

yes	1
no	0
unable to determine	0

Internal validity - Bias

14. *Was an attempt made to blind study subjects to the intervention they have received?*
    For studies where the patients would have no way of knowing which intervention they received, this should be answered 'yes'.

yes	1
no	0
unable to determine	0

15. *Was an attempt made to blind those measuring the main outcomes of the intervention?*

yes	1
no	0
unable to determine	0

16. *If any of the results of the study were based on "data dredging", was this made clear?*
    Any analyses that had not been planned at the outset of the study should be clearly indicated. If no retrospective unplanned subgroup analyses were reported, then answer 'yes'.

yes	1
no	0
unable to determine	0

17. *In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients?*
    Where follow-up was the same for all study patients the answer should be 'yes'. If different lengths of follow-up were adjusted for by, for example, survival analysis the answer should be 'yes'. Studies where differences in follow-up are ignored should be answered 'no'.

yes	1
no	0
unable to determine	0

18. *Were the statistical tests used to assess the main outcomes appropriate?*
    The statistical techniques used must be appropriate to the data. For example non-parametric methods should be used for small sample sizes. Where little statistical analysis has been undertaken but where there is no evidence of bias, the question should be answered 'yes'. If the distribution of the data (normal or not) is not described it must be assumed that the estimates used were appropriate and the question should be answered 'yes'.

yes	1
no	0
unable to determine	0

19. *Was compliance with the intervention/s reliable?*
    Where there was non-compliance with the allocated treatment or where there was contamination of one group, the question should be answered 'no'. For studies where the effect of any misclassification was likely to bias any association to the null, the question should be answered 'yes'.

yes	1
no	0
unable to determine	0

20. *Were the main outcome measures used accurate (valid and reliable)?*
    For studies where the outcome measures are clearly described, the question should be answered 'yes'. For studies which refer to other work or that demonstrates the outcome measures are accurate, the question should be answered 'yes'.

yes	1
no	0
unable to determine	0

Internal validity – Confounding (selection bias)

21. *Were the patients in different intervention groups (trials and cohort studies) recruited from the same population?*
    For example, patients for all comparison groups should be selected from the same hospital. The question should be answered 'unable to determine' where there is no information concerning the source of patients included in the study.

yes	1
no	0
unable to determine	0

22. *Were study subjects in different intervention groups (trials and cohort studies) recruited over the same period of time?*
    For a study which does not specify the time period over which the patients were recruited, the question should be answered as 'unable to determine'.

yes	1
no	0
unable to determine	0

23. *Were study subjects randomised to intervention groups?*
    Studies which state that subjects were randomised should be answered 'yes' except where method of randomisation is unknown or would not ensure random allocation. For example, alternate allocation would score 'no' because it is predictable.

yes	1
no	0
unable to determine	0

24. *Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?*
    All non-randomised studies should be answered 'no'. If assignment was concealed from patients but not from staff, it should be answered 'no'.

yes	1
no	0
unable to determine	0

25. *Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?*
    This question should be answered 'no' for trials if: the main conclusions of the study were based on analyses of treatment rather than intention-to-treat; the distribution of known confounders in the different treatment groups was not described; or the distribution of known confounders differed between the treatment groups but was not taken into account in the analyses. In non-randomised studies if the effect of the main confounders was not investigated or confounding was demonstrated but no adjustment was made in the final analyses the question should be answered as 'no'.

yes	1
no	0
unable to determine	0

26. *Were losses of patients to follow-up taken into account?*
    If the number of patients lost to follow-up are not reported, the question should be answered as 'unable to determine'. If the proportion lost to follow-up was too small to affect the main findings, the question should be answered 'yes'.

yes	1
no	0
unable to determine	0

Subscale Scores

Reporting = /11
External validity = /3
Bias = /7
Confounding = /6

Total Quality Index Score = /27

Power

27. *Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%?*

    a. Was there enough power to detect a difference of ..%, in the outcome "…."?

    sample sizes – n_1 = n_2 =
    p

Checklist for the critical appraisal of case series

Source: (Young et al 1999)

Title of review:
Title of study:
Author(s):
Year:
Comparators:
Score: /3

1. **Was the study conducted prospectively?**
   /1

- Were the key outcomes measured before and after the intervention, using clear criteria defined *a priori*?

2. **Was the method of selection of cases identified and appropriate?**
   /1

- Were patients selected consecutively or in an unbiased manner?
- Was there evidence that the characteristics of the included cases were not significantly different from those of the treated population?

3. **Was the duration and completeness of follow-up reported and was it adequate?**

- Are the number and characteristics of losses to follow-up presented? [#]
  /0.5
- Are losses to follow-up managed by performing sensitivity analysis and/or including them in the final analysis?
  /0.5

[#] Losses to follow-up >20% are unacceptable, particularly if unaccounted for.

Checklist for appraising economic evaluation studies

Source: (NHMRC 2001)

Title of assessment:
Title of study:
Author(s):
Year:
Comparators:
Score : **/16**

Appraisal items for internal validity

1. Was the study question well defined?
2. Were appropriate health care options chosen and clearly described?
3. Was an appropriate study type used?
4. Was the effectiveness of the health care options established?
5. Were the cost estimates related to baseline population risk?
6. Were all the relevant costs and consequences identified for each health care option?
7. Was differential timing considered?
8. Was an incremental analysis performed?
9. Was a sensitivity analysis performed?
10. Were modelling techniques used in a clear and reasonable way?

Criteria for assessing the generalisability of economic evaluation studies

11. Patient group
12. Health system setting
13. Health care option
14. Resource costs
15. Marginal versus average cost
16. Other specific issues

Rank scoring for appraising the clinical importance of benefit/harm

Source: (NHMRC 2000)

Title of review:

Title of study:

Author(s):

Year:

Comparators:

Clinically important effect:

Rank Score: /4

Ranking	Clinical importance of benefit/harm
1	A clinically important benefit for the full range of plausible estimates. The confidence limit closest to the measure of no effect (the 'null') rules out a clinically unimportant effect of the intervention.
2	The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.
3	The confidence interval does not include any clinically important effects.
4	The range of estimates defined by the confidence interval includes clinically important effects BUT the range of estimates defined by the confidence interval is also compatible with no effect, or a harmful effect.

Rank scoring for classifying the relevance of evidence

Source: (NHMRC 2000)

Title of review:

Title of study:

Author(s):

Year:

Comparators:

Rank Score: /5

Ranking	Relevance of the evidence
1	Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.
2	Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention.
3	Evidence of an effect on proven surrogate outcomes but for a different intervention.
4	Evidence of an effect on proven surrogate outcomes but for a different intervention and population.
5	Evidence confined to unproven surrogate outcomes.

Appendix F Profiles of included studies

Incidence and prevalence of symptomatic uterine fibroids

Study	Location	Study design	Study population	Measurement	Prevalence/incidence
Borgfeldt & Andolf (2000)	University Hospital, Lund, Sweden	Cross-sectional study	Random sample of asymptomatic women, aged 25–40 years, selected from the Swedish register in March 1996.	Transvaginal ultrasound and a vaginal transducer	Prevalence: 18/335 = 5.4% [3.0, 7.8%] 25–32 years = 3.3% [0.7–6.0%] 33–40 years = 7.8% [3.6–12.0%]
DeWaay et al (2002)	University of Iowa College of Medicine, Iowa	Prospective cohort study	64 initially asymptomatic, premenopausal women.–	Transvaginal ultrasound with saline infusion sonography	Point prevalence: 17/64 = 27% Cumulative Incidence: 7/64 = 13% per annum
Lippman et al (2003)	Desio, Italy	Population-based cross-sectional study using data from Seveso Women's Health Study (SWHS)	635 non–care-seeking women with an intact uterus	Gynaecologist performed transvaginal ultrasound	Prevalence: 96/635 = 15%
Maggino et al (1990)	Obstetric & Gynecologic Clinic, University of Padua, Italy	Cross-sectional study	885 asymptomatic women attending for screening	Gynaecologic examination	Prevalence: 102/885 = 11.5%
Marino et al (2004)	Italy	Population-based cross-sectional study using data from Seveso Women's Health Study (SWHS)	341 premenopausal women, aged 30–60 years, who had an intact uterus; were menstruating; and were not pregnant, lactating or using oral contraception or intra-uterine devices	Gynaecologist performed transvaginal ultrasound	Prevalence: 73/341 = 21.4%
Van der Leij & Lammes (1997)	Schieland Hospital, the Netherlands	Cross-sectional study	503 asymptomatic women who were undergoing sterilisation	Intra-uterine observations during sterilisation procedure	Prevalence: 17/503 = 3.4% [2.0–5.4%]

Effectiveness and safety of uterine artery embolisation (Level II/III-2)

Study	Location	Study design	Study participants	Inclusion/exclusion criteria	Procedure	Outcomes assessed	Length of follow-up
Beinfeld M Bosch J Gazelle S (2002)	Massa-chusetts General Hospital Massa-chusetts, United States	Retro-spective cohort study Level – III-2 QS – 17/27	UAE / HYS / p n: 57 / 300 Mean age (years): 43±5 / 47±7 / <0.001 Age range (years): NR / NR *Ethnic group* White: 39 (70%) / 228 (77%) / 0.01 Black: 16 (29%) / 42 (14%) Hispanic: 0 (0%) / 21 (7%) Asian: 1 (2%) / 5 (2%) *Number of fibroids* Mean ± SD: 2.8±1.4 / 2.0±1.1 / <0.001 *Type of dominant fibroid, n (%)* Intramural: 34 (72%) / 171 (62%) / 0.18 Subserosal: 9 (19%) / 52 (19%) Submucosal: 4 (9%) / 53 (19%) *Diameter of dominant fibroid (cm)* Mean ± SD: 8.0±3.0 / 6.3±3.2 / 0.001	*Includes* All patients treated for uterine fibroids with UAE or HYS between Oct 1998 and Mar 2001 No patient contact – medical records only	UAE HYS Total (80%), subtotal (7%), abdominal vaginal (8%), laparoscopic ally assisted vaginal (5%)	• Cost • Length of hospital stay • Complications (only those within the same hospital stay as the procedure)	NR
Broder M Goodwin S Chen G Tang L Costantino M et al (2002)	Single institution – not described	Retro-spective cohort study Level – III-2 QS – 16/27	UAE / MYO / p n: 51 / 30 Mean age (years): 44 / 38 / <0.001 Age range (years): 27–66 / 28–45 *Ethnic group* White: 23 (45%) / 14 (47%) / 0.53 [a] Black: 17 (33%) / 7 (23%) Hispanic: 3 (6%) / 2 (7%) Asian: 1 (2%) / 3 (10%) Other: 7 (14%) / 4 (13%) *Prior gynaecological treatment*	*Includes* All patients who underwent bilateral UAE or abdominal MYO between Feb 1996 and Aug 1997. Patients who consented via mailout in Dec 2000 to discuss symptoms, invasive procedures, satisfaction, other procedures before or after index operation.	UAE MYO Abdominal	Success or failure of the procedure assessed as: • Re-treatment • Symptom improvement – sum score of menorrhagia, dysmenorrhea, bulk symptoms, pelvic-abdominal pain Any woman who had an additional invasive procedure was excluded from other estimations of failure.	UAE mean 46 months (range: 41–59) MYO mean 49 months (range: 37–59) Length of

			Hormonal 13 (25%) 9 (30%) 0.66 MYO [b] 40 (78%) 1 (3%) <0.001 [a] for white vs non-white [b] Performed pre-operatively by clinical protocol in many embolisation patients				follow-up significantly different (p=0.03)
Healey S Buzaglo K Seti L Valenti D Tulandi T (2004)	University Teaching Hospital, Canada	Prospective cohort study Level – III-2 QS – 18/27	UAE HYS p n 68 16 Mean age (years) 45±4 44±4 Age distribution <45 years 28 (42%) 10 (63%) >45 years 40 (58%) 6 (38%) *Uterine volume* Mean ± SD (ml) 538±50 *Hormone level (FSH) as a marker of ovarian reserve* <10 IU/L 48 (71%) 12 (75%) *Prior gynaecological treatment* Endometrial ablation 1 (1%) 0 (0%) NS [a] MYO 5 (7%) 0 (0%) NS [a] *Type of dominant fibroid (n)* Intramural (submucosal component) 10 (15%) Completely intramural or subserosal 58 (85%) *Number of pregnancies* Nulligravida 17/68 (25%) 2/16 (13%) Nulliparous 11/51 (22%) 0/14 (0%) *Number of fibroids (n)* 1 11 (16%) NR NS [a] [a] There were no significant differences in demographics between the groups	*Includes* Healthy premenopausal women aged 39–50 years with symptoms, regular menstrual cycles and day-3 serum follicle stimulating hormone levels <40 IU/L between Aug 2000 and April 2003	UAE HYS Laparoscopic	• Uterine volume • Ovarian function / early menopause	3 months 6 months

McLucas B Adler L (2001)	Community Hospital United states	Retrospective cohort study Level – III-2 QS – 9/27	n	UAE 32	MYO 16		*Includes* All women who underwent elective MYO or UAE for the treatment of symptomatic fibroids in 1999	UAE MYO	• Hospital stay • Complications	NR
Pinto I Chimeno P Romo A Paul L Haya J De la Cal M Bajo J (2003)	University Hospital of Getafe, Spain	Randomised controlled trial Level – II QS – 24/27		UAE	HYS	p	*Includes* Women with bleeding uterine fibroids who were candidates for hysterectomy according to the American College of Obstetricians and Gynecologists criteria *Excludes* Patients: • who wished to preserve fertility • had fibroids >10 cm in diameter • had contraindications to surgery • had sensitivity to contrast material	UAE PVA particles of 400–600 µm HYS Abdominal (12 had one or both ovaries removed)	• Symptom improvement/resolution Bleeding reduction by 1/3, 2/3, the same or increased as assessed by the number of menstruation days and/or bleeding between menses and the number of tampons and/or sanitary napkins used after UAE • Dominant fibroid volume • Hospital stay (including readmission) • Frequency of readmissions • Emergency department visits • Resumption of normal daily activities	10 days 3 months 6 months
			n	38	19					
			Mean age (years)	46±4	45±5					
			Age range (years)	35–55	35–57					
			Number of fibroids	1.6±±0.5	1.6±0.5					
			Fibroid size (mm)	72±86	113±138					
			Fibroid type							
			Mural	16 (42%)	13 (68%)					
			Submucosal	15 (40%)	2 (11%)					
			Subserous	7 (18%)	4 (21%)					
			Prior gynaecological treatment							
			None	23 (61%)	9 (47%)					
			Hormonal	14 (37%)	10 (53%)					
			Myomectomy	1 (3%)	0 (0%)					
			Number of pregnancies	2.6±1.2	3.2±1.8					
			Menopausal status							
			Fertile	8 (21%)	4 (21%)					
			Premenopausal	27 (71%)	12 (63%)					
			Menopausal	3 (8%)	3 (16%)					

Pourrat X Fourquet F Guerif F Viratelle N Herbreteau D Marret H (2003)	Tours University Hospital, France	Retro-spective cohort study Level – III-2 QS – 16/27		UAE	HYS	p	*Includes* 39 women from 79 who underwent UAE, and 33 from 163 who had benefited from vaginal HYS between 1997 and 1999 No patient contact – medical records only	UAE HYS Vaginal	• Cost • Length of hospital stay • Inferred complications	6 months
			n	37	31					
			Mean age (years)	45	48	NS				
			Age range (years)	38–57	35–59					
			Number of fibroids (n)							
			Mean ± SD	1.6±0.9	1.7±1.3	NS				
			Range	1–4	1–5					
			Fibroid size (cm)							
			Mean ± SD	5.5±2.1	4.4±2.3	NS				
			Range	2–10	1–9					
			Number of pregnancies (n)							
			Mean ± SD	1.9±0.8	2.5±1.5	NS				
			Range	0–3	0–7					
Razavi M Hwang G Jahed A Modanloo S Chen B (2003)	Stanford University, California, United States	Retro-spective cohort study Level – III-2 QS – 18/27		UAE	MYO	p	*Excludes* 5 from UAE group because they underwent planned MYO within 3 months of UAE 4 from MYO group because their procedure was conducted for infertility rather than symptoms	UAE 350–500 µm PVA 500–700 µm Embosphere MYO Abdominal	• Successful control of symptoms of menorrhagia, pain, mass effect • Re-treatment • Further treatment within 30 days • Blood transfusion • Hospital stay • Days on narcotic medication • Resumption of normal activities	UAE mean 14.3 months MYO mean 14.6 months
			n	62	40					
			Mean age (years)	44	38	<0.05				
			Age range (years)	31–56	28–-48	NS				
Spies J Cooper J Worthington-Kirsch R Lipman J Mills B Benenati J (2004b)	11 locations, multicentre trial 5 centres UAE 4 centres HYS 2 centres UAE and HYS	Prospective cohort study Level – III-2 QS – 18/27		UAE	HYS	p	*Includes* 30–50-year-old women with symptomatic fibroids *Excludes* Patients who had • submucosal fibroids >50% of uterine volume • dominant pedunculated serosal fibroid	UAE 500–700 and 900–1,200 µm Embosphere HYS Trans-abdominal, laparoscopic or combined	• Hospital stay • In hospital adverse events • Symptom improvement/resolution – menorrhagia questionnaire (UAE only) – Pictorial blood loss assessment chart measurement (UAE only) – symptom questionnaire (pelvic pain and discomfort, urinary dysfunction) • Uterine size (UAE only)	UAE 3 months 6 months 12 months HYS 6 months 12 months to allow for complete recovery before being assessed
			n	102	50					
			Mean age (years)	43±4	42±50	0.26				
			Age range (years)	33–50	31–50					
			Ethnic group							
			Asian/Pacific island	1 (1%)	2 (4%)	<0.001				
			Black	61 (60%)	9 (18%)					
			Hispanic	7 (7%)	8 (16%)					
			White	31 (30%)	31 (62%)					
			Other	2 (2%)	0 (0%)					
			Number of pregnancies							
			0	19 (19%)	8 (16%)	0.62				

			1	24 (24%)	9 (18%)				
			≥2	59 (58%)	33 (66%)				
			Prior gynaecological treatment						
			None	53 (52%)	35 (70%)	0.04			
			GnRH therapy	9 (9%)	2 (4%)	0.34			
			Oral contraceptive	25 (25%)	5 (10%)	0.05			
			Other hormone therapy	5 (5%)	5 (10%)	0.30			
			Myomectomy	19 (19%)	4 (8%)	0.10			
			Curettage	16 (16%)	1 (2%)	0.01			
			Hysteroscopy	13 (13%)	2 (4%)	0.15			
			Other invasive	5 (5%)	3 (6%)	0.72			
			Leiomyoma (n)						
			1	27 (26%)	20 (40%)	0.02			
			2	33 (32%)	19 (38%)				
			>3	42 (41%)	10 (20%)				
			No response	0 (0%)	1 (2%)				
			Uterine volume						
			n	100	47				
			Mean ± SD (ml)	689±466	389±521	<0.001			
			Range	186–307	692–3,415				
			Dominant leiomyoma volume						
			n	93	42				
			Mean ± SD (ml)	147±159	91±3,550	0.33			
			Range	5–777	3–2,322				
			Type of dominant leiomyoma (n						
			Intramural	61 (60%)	32 (64%)	0.72			
			Subserosal	19 (19%)	8 (16%)	0.82			
			Submucosal	17 (17%)	13 (26%)	0.20			
			Transmural	11 (11%)	1 (2%)	0.11			
			Pedunculated	2 (2%)	4 (8%)	0.07			

Effectiveness and safety of uterine artery embolisation (Level IV)

Study	Location	Study design	Study participants Age in years Volume in ml	Inclusion/exclusion criteria	Procedure	Outcomes assessed	Length of follow-up
Ahmad A Qadan L Hassan N Najarian K (2003)	Kuwait	Case series pre-test/ post-test Level – IV QS – 3/3	n 32 Mean age 34 Age range 26–45 *Menopausal status* Premenopausal 30 (94%) Perimenopausal 2 (6%) *Dominant fibroid volume (US)* Median (range) 284 (140–500) *Gynaecological treatment/history* Myomectomy 4 (13%) Caesarean section 7 (22%) Ovarian resection 1 (3%) *Ethnicity* Middle Eastern NR	*Includes* Referred patients between Oct 1997 and Mar 2001 who had symptomatic uterine fibroids, were pre- or perimenopausal and who had no desire for future childbearing	UAE 300–500 µm PVA (Cook)	• Ovarian function using FSH measurement on day 2 of menstrual cycle • Symptom improvement/resolution – hot flashes and resumption of menstruation • Fibroid size (ultrasound)	3 months 6 months
Ahmad K Ray C Jnr Conyers R (2002)	NR USA	Case series pre-test/ post-test Level – IV QS – 2.5/3	n 19 Mean age 41 Age range 32–48	*Includes* Consecutive patients with symptomatic uterine fibroids between Jan 1999 and July 2000 *Excludes* Patients with any co-morbid conditions revealed during baseline transvaginal sonography scan	UAE 500–700 µm PVA (Cook)	• Overall symptom improvement (scale 1–5; 1 = mild cramping similar to hunger pains; 5 = worst pain ever experienced) • Follow-up surgery	3 months 6 months 12 months

Al Muzrakchi A Szmigielski W (2003)	Doha, Qatar	Case series pre-test/ post-test Level – IV QS – 1/3	n Mean age Age range	4 NR 35–44	*Includes* Women with severe fibroid related menorrhagia	Bilateral UAE using 500–750 µm PVA (Ivalon)	• Complications	3–9 months
Andersen P Lund N Justesen P Munk T Elle B Floridon C (2001)	Odense University Hospital, Denmark	Case series pre-test/ post-test Level – IV QS – 1.5/3	n Mean age Age range *Dominant fibroid volume (ml)* Mean (range)	62 43 29–54 162 (19–726)	*Includes* Referred patients between Jan 1999 and May 2000 with symptomatic uterine fibroids who were examined using ultra-sonography	UAE 355–500 µm PVA (Contour, Boston Scientific)	• Dominant fibroid volume • Complications and adverse events • Further treatment • Post-embolisation syndrome • Symptom improvement of bleeding, pain and bulk	N = 50 1 month 6 months 12 months N = 12 3 months 12 months
Bapuraj J Suri S Sidhu R Nadh O Vasistha K (2002)	NR India	Case series pre-test/ post-test Level – IV QS – 2.5/3	n Mean age Age range *Gynaecological treatment/history* Myomectomy Hormone therapy	11 32 22–50 4 (36%) 4 (36%)	*Includes* Patients with symptomatic fibroids between Mar 2000 and Mar 2001 *Excludes* Women with additional gynaecologic or medical problems such as malignancy, acute pelvic infection/inflammation, endometritis and connective tissue disorders, or those with contraindications to arteriography	UAE 350–500 µm PVA (Contour, Boston Scientific)	• Symptom improvement of bleeding, pain and bulk (5-point scale) • Uterine and fibroid volume (% reduction) • Hospital stay • Resumption of normal activities • Post-embolisation syndrome	0.5 months 2 months 6 months
Belenky A Cohen M Bachar G (2001)	NR Israel	Case series pre-test/ post-test Level – IV QS – 1.5/3	n Mean age Age range	9 47 44–63	*Includes* Patients with symptomatic fibroids from Feb 1999 onwards *Excludes* Women with other gynaecological problems and women with submucosal, subserosal and pedunculated fibroids	UAE 350–500 µm PVA (Boston Scientific)	• Fibroid volume (% reduction) • Hospital stay	2 months

Bradley E Reidy J Forman R Jarosz J Braude P (1998)	NR UK	Case series pre-test/ post-test Level – IV QS – 2/3	n 8 Median age 38 Age range 31–48 *Gynaecological treatment/history* Myomectomy 3 (38%) Hormone therapy 5 (63%) Previous pregnancies 7 (88%) Subfertility 5 (63%) *Ethnic group* Afro-Caribbean 7(88%) Caucasian 1 (12%)	*Includes* Patients who had a large fibroid uterus, had a desire to retain their uterus, <50 years of age *Excludes* History of coagulation disorder and asymptomatic fibroids	UAE 150–500 µm PVA (Contour, Boston Scientific)	• Uterine volume (MRI at 3 months) • Hospital stay • Post-embolisation syndrome • Symptom improvement/resolution – menorrhagia, pressure and pain symptoms before and after UAE	Mean (range) = 7.7 (2.9–9.2) months
Brunereau L Herbreteau D Gallas S Cottier J Lebrun J et al (2000)	NR France	Case series pre-test/ post-test Level – IV QS – 3/3	n 58 Mean age 45 Age range 33–65 *Dominant fibroid size (US)* Mean ± SD (cm) 5.7±2.9 Range 1.3–14.0 *Uterine size (US)* Mean ± SD (cm) 10.6±3.7 Range 3.9–24.0	*Includes* Patients who had symptomatic fibroids from 1997 onwards *Excludes* Contraindications included adnexal mass, uterine prolapse, stress incontinence and several pedunculated subserosal fibroids	UAE 150–250 µm PVA gelatin sponge	• Uterine and dominant fibroid volume (ultrasound measurement) • Hospital stay • Symptom improvement/resolution – menorrhagia, pressure and pain assessed on a 4-point scale • Further treatment • Post-embolisation syndrome • Readmission	3 months (n = 58) 6 months (n = 46) 12 months (n = 27) 24 months (n = 7)
Burn PR McCall JM Chinn RJ Healy JC (1999)	London, United Kingdom	Case series pre-test/ post-test Level – IV QS – 1/3	n 14 Mean age 39 Age range 31–51	*Includes* Women with confirmed symptomatic uterine fibroids *Excludes* Intending to conceive	Bilateral UAE using 350–500 µm PVA particles (Contour, Boston Scientific)	• Fibroid volume (reduction) • Symptom improvement/resolution • Pain • Duration of hospital stay • Adverse events (haematoma)	6 months

Burn PR McCall JM Chinn RJ Vashisht A Smith JR Healy JC (2000)	London, United Kingdom	Case series pre-test/ post-test Level – IV QS – 3/3	n Mean age Age range	18 39 NR	*Includes* Women with confirmed symptomatic fibroleiomyoma	Bilateral UAE using 350–500 µm PVA particles (Contour, Boston Scientific)	• Fibroid volume	6 months
Chiu CYU Wong WK Mak HLJ Chan CSS Kwok CHP et al (2001) (Chiu et al 2001)	Kowloon, Hong Kong	Case series pre-test/ post-test Level – IV QS – 1.5/3	n Mean age Age range	12 41.8 32–50	*Includes* Premenopausal Chinese women with symptomatic fibroids *Excludes* Uncontrolled bleeding diathesis, pregnancy, chronic pelvic inflammatory disease and asymptomatic fibroids	Bilateral UAE, using 300–500 µm PVA particles (Contour, Boston Scientific)	• Fibroid volume • Pain • Duration of hospital stay	6 months
Chrisman HB Saker MB Ryu RK Nemcek AA Gerbie MV et al (2000)	Chicago, USA	Case series pre-test/ post-test Level – IV QS – 1.5/3	n Mean age Age range	66 NR 30–55	*Includes* Premenopausal women with clinically confirmed uterine fibroids	Bilateral UAE using 355–700 µm PVA particles	• Ovarian function	Average 21 weeks (range 12–77)
Ciraru-Vigneron N Ravina JH Aymard A Merland JJ (1999)	Paris, France	Case series pre-test/ post-test Level – IV QS – 1.5/3	n Mean age Age range	184 42 21–54	*Includes* Not stated	Bilateral UAE using 150–500 µm PVA particles (Ivalon, Nycomed)	• Duration of procedure • Fibroid volume reduction, • Re-treatment • Symptom resolution/improvement – amenorrhea • Adverse events – haematoma, post-embolisation syndrome, infection	Mean duration 28 months (range 18–84)

Ciraru-Vigneron N Ravina JH Aymard A Merland JJ (1999)	Paris, France	Case series pre-test/ post-test Level – IV QS – 0.5/3	n 184 Mean age 42 Age range 21–54	*Includes* Not stated	Bilateral UAE using 150–500 µm PVA particles (Ivalon, Nycomed)	• Pregnancy	Not stated
Delaney ML Worthington-Kirsch RL Hutchins FL Berkowitz RP (1999)	Philadelphia, USA	Case series pre-test/ post-test Level – IV QS –2.5/3	n 126 Mean age NR Age range NR *Symptoms* Menorrhagia 46 Bulk symptoms 20 Menorrhagia + bulk 60	*Includes* Women with symptomatic fibroids	UAE using 500–700 µm PVA particles (Biodyne 500, Cook)	• Time to recovery • Uterine volume • Symptom resolution/improvement	3 months
Forman RG Reidy J Nott V Braude P (1999)	London, United Kingdom	Case series pre-test/ post-test Level – IV QS – 3/3	n 192 Mean age NR Age range NR	*Includes* Not stated	UAE	• Ability to conceive	Not stated
Goodwin SC McLucas B Chen G Perralla R Vedantham S et al (1999)	California, USA	Case series pre-test/ post-test Level – IV QS – 3/3	n 60 Mean age 43.5±6.1 Age range 27–66 *Ethnic group* African American 32% Caucasian 47% Other 20%	*Includes* Women with symptomatic fibroids	Bilateral UAE using 500–700 µm or 300–500 µm PVA particles (Contour, Boston Scientific or Trufil, Cordis or PVA, Cook)	• Uterine and fibroid volume reduction • Symptom resolution/improvement – amenorrhea • Adverse events – haematoma, infection, post-embolisation syndrome • Pain • Re-treatment/ rehospitalisation	Follow-up from 3 to 30 months (mean 16.3 ± 6.3 months)
Hald K Langebrekke A Klow N Noreng H Berge A Istre O (2004)	Ullevaal Hospital, University of Oslo, Oslo, Norway	Case series pre-test/ post-test Level – IV QS – 2/3	n 24 Mean age 42 Age range NR *Menopausal status* Premenopausal 24 (100%) *Ethnicity* Not clear, but it is likely that >95% of	*Includes* Clinic patients referred for symptomatic uterine fibroids *Excludes* Current pregnancy, breast feeding, current or recent pelvic inflammatory disease, abnormal pap smear, known endometriosis,	UAE 355–500 µm PVA (Contour, Boston Scientific)	• Uterus and fibroid volume (either MRI or ultrasound) • Symptom resolution/improvement (pictorial blood loss assessment chart measurement) • Post-operative pain via visual analogue scale	1 months 3 months 6 months

			sample were white *Dominant fibroid volume (US)* n 19 Mean±SD (ml) 263±196 *Dominant fibroid volume (MRI)* n 21 Mean±SD (ml) 293±245 *Uterine volume (MRI)* n 21 Mean±SD (ml) 833±469	breast cancer and history of DVTs, or thrombo-embolism or liver disease or hormone therapy in the 3 months prior to surgery		• Amount of analgesia usage during hospital stay • Hormone (FSH and 17 B oestradiol [E2]) assessment for determination of fertility (ie ovarian failure) combined with clinical markers (amenorrhea etc) • Re-treatment • Complications	
Huang LY Cheng YF Chang HW Chang SY Kung FT et al (2004)	Kaohsiung, Taiwan	Case series pre-test/ post-test Level – IV QS – 3/3	n 35 Mean age 40±5 Age range 29–51	*Includes* Patients with symptomatic myoma with menorrhagia refractory to medications or previous myomectomy, dysmenorrhea, desire to preserve the uterus or physical contraindications to surgery or anaesthesia *Excludes* Current pregnancy, active pelvic infection, severe contrast medium allergy, undiagnosed pelvic mass, severe renal insufficiency, acute vasculitis or desire for future pregnancy	Bilateral or unilateral UAE using gelatin sponge particles and lipiodol	• Pain • Menstrual bleeding • Sexual function • Complications • Uterine size	5/35 lost to follow-up Mean duration 8.1 months (range = 6–12 months)

Hutchins FL Worthington-Kirsch R Berkowitz RP (1999)	Philadelphia, USA	Case series pre-test/ post-test Level – IV QS –1.5/3	n Mean age Age range	305 NR NR	*Includes* Premenopausal women with symptomatic fibroids confirmed by ultrasound *Excludes* Pregnant women, those with active pelvic infection, severe contrast allergy, arteriovenous fistula or undiagnosed pelvic mass	Bilateral UAE using 500–700 µm PVA particles (Biodyne; Cook)	• Uterine size and volume • Time taken to resume normal activities, • Symptom resolution/improvement in menorrhagia and bulk-related symptoms • Patient satisfaction with procedure • Pain • Adverse events – haematoma • Re-treatment/ rehospitalisation • Pregnancy	At least 3 months up to 12 months
Joffre F Tubiana J-M Pelage J-P (2004)	Boulogne, France	Case series pre-test/ post-test Level – IV QS – 2.5/3	n Mean age *Menopausal status* Premenopausal	85 41.2±6.1 98%	*Includes* Premenopausal women with symptomatic fibroids, menorrhagia, metrorrhagia, menstrual pain, pelvic pressure, urinary pressure *Excludes* Patients with asymptomatic fibroids, pelvic inflammatory disease, who wanted to conceive, those with pedunculated subserosal fibroids or associated adenomyosis	Bilateral UAE using 500–700 µm or 700–900 µm tris-acryl gelatin (Embosphere, Biosphere Medical)	• Pain, • Symptom resolution/improvement in menorrhagia • Amenorrhea • Uterine and fibroid volume • Menopause • Re-treatment	Mean duration 15.7 months (range 6–24 months)

Katsumori T Nakajima K Mihara T Tokuhiro M (2002)	Shiga, Japan	Case series pre-test/ post-test Level – IV QS – 2/3	n Mean age Age range	60 435 32–52	*Includes* Women with symptomatic fibroids who were premenopausal and had clinical symptoms of menorrhagia, pain and bulk related symptoms	Gelatin sponge particles mixed with saline, contrast medium and antibiotics (2–4 gelatin sponge sheets: 500–1000 µm)	• Uterine volume reduction	Mean duration 10.6 months (range 1–38 months) 23 women followed up for more than 12 months 15 followed up for 4–12 months 12 followed up for 1–4 months
Khaund A Moss JG McMillan N Lumsden MA (2004)	Glasgow, United Kingdom	Case series pre-test/ post-test Level – IV QS – 2/3	n Mean age Age range	50 44 29–54	*Includes* Women with symptomatic fibroids	Bilateral UAE using 500–710 µm PVA particles	• Uterine volume changes • Menstrual blood loss	3, 6–9, 12–24, 24–36, 36–48 months
Klein A Schwartz ML (2001)	Oregon, USA	Case series pre-test/ post-test Level – IV QS – 2/3	n Mean age Age range	35 46 32–56	*Includes* Women with symptomatic uterine fibroids	Bilateral UAE using 350–500 µm PVA particles (Ivalon)	• Length of hospital stay • Uterine and fibroid volume reduction • Symptom resolution/improvement • Amenorrhea • Re-treatment/ rehospitalisation • Patient satisfaction	6 weeks and 6 months
Lang E Myers L (2004)	New Orleans, Louisiana	Case series pre-test/ post-test Level – IV QS - 2/3	n Mean age Age range	51 37 26–48	*Includes* Women treated between 1995 and 2002	Bilateral UAE using 500–710 µm PVA and 710–1,000 µm microspheres	• Symptom improvement • Uterine volume reduction	1,2, 3 and 12 months

Marrett H Alonso AM Cottier JP Tranquart F Herbreteau D Body G (2003) Possible follow-up of 2002 study by Tranquart et al	Tours, France	Case series pre-test/ post-test Level – IV QS – 2/3	n 85 Mean age NR Age range NR	*Includes* Women with symptomatic fibroids	Bilateral UAE using 150–250 µm PVA particles	• Uterine and fibroid volume • Recurrence of fibroids	Median follow-up 30 months (range 2–57 months)
McLucas B Goodwin SC Perrella R (1998)	California, USA	Case series pre-test/ post-test Level – IV QS – 2/3	n 25 Mean age 46 Age range 34–67	*Includes* Women with menorrhagia or postmenopausal bleeding associated with fibroids	Bilateral UAE using 500 µm PVA	• Uterine volume • Bleeding	6 months
McLucas B Adler L Perralla R (1999)	California, USA	Case series pre-test/ post-test Level – IV QS – 2.5/3	n 300 Mean age 43 Age range 29–63	*Includes* Women with menorrhagia or postmenopausal bleeding secondary to uterine myomata	Not stated	• Treatment failure, • Fibroid size • Further treatment / rehospitalisation • Time of procedure	6 months
McLucas B Goodwin S Adler L Rappaport A Reed R Perralla R (2001b) Follow-up study to McLucas (1999)	California, USA	Case series pre-test/ post-test Level – IV QS – 1.5/3	n 400 Mean age 41 Age range 26–67 139/400 identified wish to retain fertility	*Includes* Women with menorrhagia or postmenopausal bleeding secondary to uterine myomata	Not stated	• Pregnancy	6 months

McLucas B Adler L Perralla R (2001a)	California, USA	Case series pre-test/ post-test Level – IV QS – 1.5/3	n Mean age Age range Without leuprolide With leuprolide	167 43 29–63 155 12	*Includes* Women with menorrhagia or postmenopausal bleeding secondary to uterine myomata *Excludes* Those with active pelvic infection, diabetes mellitus or vasculitis	Bilateral UAE using 500 µm particles (first 107 patients) then 300 µm particles (last 60 patients)	• Technical success of UAE • Uterine volume and fibroid size reduction • Pain • Adverse events – infection, post-embolisation syndrome • Menopause • Reoperation • Symptom resolution/improvement • Radiation exposure	6 weeks and 6 months
Mehta H Sandhu C Matson M Belli A-M (2002)	London, United Kingdom	Retro-spective case series pre-test/ post-test Level – IV QS – 2/3	n Mean age Age range *Ethnic group* Afro-Caribbean Caucasian Asian	42 42 31–54 86% 9% 5%	*Includes* Women treated with UAE for uterine fibroids with presenting symptoms of menorrhagia, dysmenorrhoea or uterine bulk	Bilateral UAE using 300–500 µm PVA	• Readmission	Median follow-up 12 months (range 4–16 months)
Messina ML Bozzini N Halbe HW Pinotti JA (2002)	São Paulo, Brazil	Case series pre-test/ post-test Level – IV QS – 2.5/3	n Age range	26 33–49	*Includes* Women with symptoms of heavy menstrual bleeding, pelvic pain or pressure *Excludes* Patients with biochemical or clinical findings suggestive of menopause	Bilateral UAE using 500–710 µm PVA (Ivalon, Cook Inc and Trufill, Cordis)	• Uterine volume • FSH levels • Menstrual bleeding	Mean follow-up 16 months (range 12–22 months)
Pelage J-P LeDref O Soyer P Kardache M Dahan H et al (2000)	Paris, France	Case series pre-test/ post-test Level – IV QS – 3/3	n Mean age Age range	80 44.7 30–54	*Includes* Women with symptomatic uterine fibroids – haemorrhage as a referring symptom *Excludes* Desired future pregnancy	Bilateral UAE 150–300 µm PVA (Ivalon, Nycomed)	• Fibroid volume • Amenorrhea • Reoperation • Pain • Symptom resolution/improvement • Adverse events – post-embolisation syndrome	Ultrasound at 2 and 6 months, questionnaires at 12 and 24 months

Pelage J-P Le Dref O Beregi J-P Nonent M Robert Y et al (2003)	Paris, France	Case series pre-test/ post-test Level – IV QS – 3/3	n 20 Mean age 43 Age range 36–53	*Includes* Women with symptomatic uterine fibroids presenting with menorrhagia and/or pelvic pain *Excludes* Desired future pregnancy	Bilateral UAE using 300–1,200 µm tris-acryl gelatin (Embosphere, Biosphere Medical)	• Pain • Complications	Mean = 30.2 months (range 24–48 months)
Park K Kim J Shin J Kwon J Koo J et al (2003)	Yonsei Medical Center Seoul Korea	Case series pre-test/ post-test Level – IV QS – 2.5/3	n 23 Mean age 41±2 Age range NR *Dominant fibroid volume* N 23 Mean±SD (ml) 212±21	*Includes* 23 patients who were treated via UAE between Jan 1999 and Oct 2000	UAE 500–700 µm PVA (Cook)	• Uterine and dominant fibroid volume (ultrasound) • Symptom resolution/ improvement (pictorial blood loss assessment chart measurement) • Adverse events – complication of fever, severe pain or bleeding related to UAE	3 months 6 months 12 months
Prollius A De Vries C Loggenberg E Nel M du Plessis A et al (2004b)	Bloemfontein, South Africa	Case series pre-test/ post-test Level – IV QS – 2.5/3	n 64 Median age 40 Age range 19–62 *Ethnic group* African 89% Caucasian 6% Mixed 5%	*Includes* Women with symptomatic uterine fibroids	Bilateral UAE using 150–550 µm PVA particles	• Uterine volume • Symptom resolution/ improvement • Re-treatment/ rehospitalisation • Adverse events – post-embolisation syndrome, haematoma, infection • Time spent in hospital	12 months
Pron G Bennett J Common A Sniderman K Asch M et al (2003a) Pron G Mocarski E Vilos G Bennett J	Eight Ontario hospitals, Canada	Case series pre-test/ post-test Level – IV QS – 2/3	n 555 Mean age 43±6 Age range 18–59 *Ethnic group* % white women 65% *Number of pregnancies* % nulliparous 50% *Previous surgery for fibroids* Myomectomy 70 (14%)	*Includes* Patients with ultrasound-diagnosed fibroids that were symptomatic *Excludes* Women with acute pelvic inflammatory disease, renal insufficiency, undiagnosed pelvic mass, or who were pregnant	UAE 355–500 µm PVA (Contour, Boston Scientific)	• Uterine and dominant fibroid volume (ultrasound) • Symptom resolution/ improvement (symptom questionnaire on dysmenorrhea, menorrhagia, mass and pressure effects and urinary urgency/frequency) • Pregnancies • Intra-procedural pain • Length of hospital stay	3 months Note: this study reported data collection at 0.5, 3 and 6 months with annual follow-up for 5 years. They also reported a median follow-

Common A et al (2003b) Pron G Mocarski E Bennett J Vilos G Common A Zaidi M et al (2003c) Pron G Mocarski E. Cohen M Colgan T Bennett J et al (2003d) Pron G Mocarski E Bennett J Vilos G Common A Vanderburgh L (2003e) Abstract Pron G Mocarski E Bennett J Vilos G Common A Vanderburgh L (2005)			Endometrial ablation 3% *Number of fibroids (n)* 1 150 (30%) 2–4 220 (44%) ≥5 133 (26%) *Dominant fibroid volume* Mean±SD 308±380 *Uterine volume* Mean±SD 704±586 *Menopausal status* Premenopausal 431 (80%) Perimenopausal 92 (17%) Postmenopausal 14 (3%) *Type of dominant fibroid* Intramural 285 (60%) Intramural (subserosal or submucosal) 63 (13%) Subserosal 92 (19%) Submucosal 33 (7%)			• Analgesic use • Hospital readmission • Time to recovery • Adverse events including haematoma, reaction to contrast agent • Time taken to perform procedure	up of 8.2 months. However, their results focused mainly on the 3-month follow-up.
Ravina J Vigneron N Aymard A	Paris, France	Case series pre-test/	n 12 Mean age 36 Age range 22–41	*Includes* Pregnant women who had been treated previously by UAE	Bilateral UAE using 150–300 µm and	• Miscarriage	NA

Le Dref O Merland J (2000b)		post-test Level – IV QS – 2/3			300–600 µm Ivalon microparticles		
Razavi MK Wolanske KA Hwang GL Sze DY Kee ST Dake MD (2002)	California, USA	Case series pre-test/ post-test Level – IV QS – 3/3	n 76 Mean age 46 Age range 29–56 4/76 (5.3%) women had ovarian-uterine artery fibroid connections and underwent bilateral (n = 1) or unilateral (n = 3) ovarian artery embolisation	*Includes* Women with symptomatic uterine fibroids	Bilateral UAE using 355–500 µm PVA particles (Trufill, Cordis) or 500–700 µm tris-acryl gelatin (Embosphere, Biosphere Medical)	• Clinical success, • Symptom resolution/ improvement • Reoperation • Amenorrhea, anastomoses	3 months
Roth AR Spies JB Walsh SM Wood BJ Gomez-Jorge J Levy EB (2000)	Washington, USA	Case series pre-test/ post-test Level – IV QS – 1.5/3	n 81 Mean age NR Age range NR	*Includes* Women with symptomatic fibroids and complete patient-controlled analgesia records	UAE using 500–710 µm PVA particles (Contour, Boston Scientific; Ivalon, Cook; Trufill, Cordis)	• Uterine and fibroid volume • Pain • Analgesia • Symptom resolution/ improvement (bleeding and pressure symptoms) • Patient satisfaction	Follow-up 3 and 12 months
Sena-Martins M Roteli-Martins CM De Souza GA Kisilevzky N Lazar F (2003)	São Paulo, Brazil	Case series pre-test/ post-test Level – IV QS – 2/3	n 32 Mean age 40 Age range 27–51	*Includes* Women with symptomatic fibroids who wished to retain their uterus	UAE using 355–700 µm PVA particles	• Uterine volume • Post-embolisation syndrome	I, 6 and 12 weeks
Shan H Huang M-S Guan S-H Jiang Z-B Zhu K-S Li Z-R (2004)	Guangzhou, China	Case series pre-test/ post-test Level – IV QS – 3/3	n 100 Mean age 38 Age range 21–48	*Includes* Premenopausal women with symptomatic uterine leiomyoma	Bilateral UAE, using pingyangmycin-lipiodol emulsion (PLE)	• Symptom resolution/ improvement in menorrhagia and bulk related symptoms • Pain • Reoperation • Uterine volume	Range 3–21 months
Siskin GP Stainken BF Dowling K	Albany, USA	Case series pre-test/	n 49 Mean age 44.5 Age range 28–54	*Includes* Women with symptomatic fibroids	UAE using 350–500 µm PVA	• Length of hospital stay • Immediate post-UAE symptoms	24 hours, 3 and 6 months

Meo P Ahn J Dolen EG (2000)		post-test Level – IV QS – 1.5/3			(Contour) (n = 44) and Gelfoam pledgets (Pharmacia) (n = 5)	• Uterine volume reduction	
Smith WJ Upton E Shuster EJ Klein AJ Schwartz ML (2004) Follow-up study from Klein et al (2001)	Oregon, USA	Case series pre-test/ post-test Level – IV QS – 1.5/3	n 81 Mean age 45.6 Age range 32–56 *Ethnic group* African American 9.6% Caucasian 80.8% Hispanic 8.2% Asian 1.4%	*Includes* Women with symptomatic fibroids	Bilateral UAE using 350–500 µm PVA particles (Ivalon) for the first 53 patients then tris-acryl gelatin (Embosphere, Biosphere Medical)	• Health related quality of life (HRQOL) • Symptom resolution/ improvement • Pain • Uterine volume • Rehospitalisation	Mean interval from procedure to follow-up was 32.1 ± 13.5 months (range 6.0–57.5 months)
Spies JB Warren EH Mathias SD Walsh SM Roth AR Pentecost MJ (1999)	Washington, USA	Case series pre-test/ post-test Level – IV QS – 2/3	n 50 Mean age 43 Age range 30–52 *Ethnic group* African American 46.9% Caucasian 38.8% Hispanic 6.1% Asian 4.1% Other 4.1%	*Includes* Women with symptomatic fibroids	Bilateral UAE using 500–710 µm PVA particles (Contour, Boston Scientific, Ivalon, Cook, or Trufill, Cordis)	• Health related quality of life (HRQOL)	3,6, 9 and 12 months
Spies JB Benenati JF Worthington-Kirsch RL Pelage J-P (2001)	Washington, USA	Case series pre-test/ post-test Level – IV QS – 2/3	n 30 Mean age 42.5 Age range 30–50 *Ethnic group* African American 43% Caucasian 40% Hispanic 13% Other 3%	*Includes* Premenopausal women with uterine leiomyomata and one or more of the following symptoms: heavy menstrual bleeding, pelvic pain or pressure, urinary frequency *Excludes* Patients who: were currently pregnant, desired future fertility, had a history of gynaecological	Bilateral UAE using either 500–700 µm or 700–900 µm tris-acryl gelatin microspheres	• Uterine volume • Haematoma • Allergic reaction • Menorrhagia	3 and 6 months

				malignancy, endometrial hyperplasia, adenomyosis, pelvic inflammatory disease or known contrast/gelatin allergy			
Spies JB Ascher SA Roth AR Kim J Levy EB Gomez-Jorge J (2001)	Washington, USA	Case series pre-test/ post-test Level – IV QS – 2/3	n 200 Mean age 43 Age range 30–52 *Ethnic group* African American 50% Caucasian 45% Hispanic 1.5% Asian 2.5% Other 1%	*Includes* Women with uterine leiomyomata and one or more of the following symptoms: heavy menstrual bleeding, pelvic pain or pressure, urinary frequency *Excludes* Patients currently pregnant, those with infertility attributed to leiomyomata, women with a primary goal of becoming pregnant	Bilateral UAE using 500–710 µm PVA particles (Contour, Boston Scientific)	• Uterine and fibroid volume • Symptom resolution/ improvement (menstrual blood loss, bulk symptoms) • Length of hospital stay • Patient assessed quality of life • Return to normal activities • Pain • Adverse events – haematoma, embolism (pulmonary) • Rehospitalisation/ re-treatment	Mean follow-up 21 months (minimum 12 months)
Spies JB Spector A Roth AR Baker CM Mauro L Murphy-Skrynarz K (2002b) Follow-up study to Spies et al (2001a)	Washington, USA	Case series pre-test/ post-test Level – IV QS – 3/3	n 400 Mean age 43 Age range 27–57 *Ethnic group* African American 53% Caucasian 43% Hispanic 1.8% Other 1.5%	*Includes* All women with uterine leiomyomata and one or more of the following symptoms: heavy menstrual bleeding, pelvic pain or pressure, urinary frequency *Excludes* Patients currently pregnant, those with infertility attributed to leiomyomata, women with a primary goal of becoming pregnant	Bilateral UAE using 500–710 µm PVA particles (first 300 patients: Contour, Boston Scientific, last 100 patients: Embosphere, Biosphere Medical)	• Factors predicting successful UAE outcome, • Uterine and fibroid volume • Fibroid location, • Symptom resolution/ improvement (menstrual bleeding)	30 days and 3 months
Spies JB Allison S Flick P McCullough M Sterbis K Cramp M et al (2004a)	Washington, United States	Case series pre-test/ post-test Level – IV QS – 2.5/3	n 100 Mean age 43±0.5 Age 95% CI [42,44] *Dominant fibroid volume (US)* n 96 Mean ± SD 150±16 95% CI [118,181] *Uterine volume (US)*	*Includes* Women with symptomatic uterine fibroids aged between 30 and 55 years and treated within a single institution between March 2002 to February 2003 *Excludes* Women who were pregnant or breastfeeding or with a primary aim	PVA particles of 355–710 µm and tri-acryl microspheres of 500–700 µm	• Complications • Fibroid specific quality of life • Analgesia use • Peak pain experienced in hospital • Return to normal activities	1 week, 1 and 3 months

Bruno J Sterbis K Flick P McCullough M Cramp M et al. (2004)			n 96 Mean ± SD 628±34 95% CI [560,695] *Ethnicity* African American 61% Caucasian 34% Other 5%	of pregnancy after treatment; patients with uterine infection or pelvic inflammatory disease			
Toh C-H Wu C-H Tsay P-K Yeow K-M Pan K-T Tseng J-H Hung C-F (2003)	Tao Yuan, Taiwan	Case series pre-test/ post-test Level – IV QS – 2/3	n 46 Mean age 38 Age range 22–54	*Includes* All women with uterine leiomyomata and menorrhagia, dysmenorrhea or bulk symptoms *Excludes* Patients currently pregnant, history of pelvic radiation; acute vasculitis; pelvic inflammatory disease; ovarian, uterine, endometrial or cervical cancer; and subserosal leiomyoma	UAE using 400–600 µm PVA particles (Ultra-Drivalon, CathNet-Science)	• Symptom improvement • Uterine volume	Mean duration follow-up 10.9 months (range 6–22 months)
Tranquart F Brunereau L Cottier J-P Marret H Gallas S Lebrun J-L Body G Herbreteau D Pourcelot L (2002) Follow-up study of Brunereau et al 2000	Tours, France	Case series pre-test/ post-test Level – IV QS – 3/3	n 58 Mean age 45 Age range 33–65	*Includes* Women with symptomatic fibroids	Bilateral UAE using 150–250 µm PVA particles	• Uterine and fibroid volume • Symptom resolution/ improvement	Follow-up 3 (n = 58), 6 (n = 46), 12 (n = 36) and 24 (n = 19) months
Tropeano G Stasi C Litwicka K Romano D Draisci G Mancuso S	Universita Cattolica del Sacro Cuore, Rome, Italy	Case series pre-test/ post-test Level – IV QS – 2.5/3	n 20 Mean age 35 Age range 33–39 *Uterine volume (US)* Mean ± SD 371±213	*Includes* Women less than 40 years, regularly menstruating, normal FSH levels, no history of infertility or ovarian surgery and no desire	Bilateral UAE using 150–250 µm PVA particles	• Early menopause	3,6 and 12 months

(2004)			Range 71–901	for further pregnancy			
Tulandi T Sammour A Valenti D Child TJ Seti J Tan S (2002)	Montreal, Canada	Case series pre-test/ post-test Level – IV QS – 3/3	n 48 Mean age 44±2 Age range NR	*Includes*	Bilateral UAE using 350–500 µm PVA particles (Boston Scientific)	• Ovarian function	1 month, 3 months
Vashisht A Studd JWW Carey AH McCall J Burn PR Healey JC Smith JR (2000)	Chelsea and Westminster hospital, London	Case series pre-test/ post-test Level – IV QS – 2.5/3	n 21 Mean age 40 Age range 29–52	*Includes* 21 women who underwent bilateral UAE for fibroids between June 1997 and January 1999	NR	• Mortality (n = 1; also reported as a case report) • Sex life	6 months (range 3–12 months)
Walker W Green A Sutton C (1999)	Surrey, United Kingdom	Case series pre-test/ post-test Level – IV QS – 1.5/3	n 200 Mean age NR Age range NR	*Includes* Not stated	Bilateral UAE using 355–500 µm PVA particles	• Symptom resolution/ improvement • Uterine volume • Rehospitalisation/ re-treatment • Pain • Adverse events – haemorrhage	Follow-up 3,6,12,18 and 24 months
Walker W Pelage J (2002)	The Royal Surrey County hospital, United Kingdom	Case series pre-test/ post-test Level –IV QS – 2/3	n 400 Mean age 43.2 Age range NR *Ethnic group* Caucasian 324 (81%) Afro-Caribbean 47 (12%) Indian 3 (1%) Chinese 6 (1%) Other 20 (5%) *Menopausal status* 5 women (1%) were postmenopausal *Uterine volume (US)* n 284	*Includes* 400 women who had technically successful UAE between Dec 1996 and Feb 2001 (had to be done twice in 17 women). Symptoms had to include: heavy menstrual bleeding or pressure symptoms such as bloating, urinary frequency, back pain or sciatica because of fibroids *Exclude* Women being treated for infertility	UAE n = 66 150–250 µm 355–500 µm PVA (Contour, Boston Scientific) n = 334 355–500 µm PVA (Contour, Boston Scientific) Platinum coil	• Uterus and fibroid volume using either MRI or US (same modality used within the individual) • Pain • Resumption of normal activities and work • Symptom resolution/improvement • Pregnancy outcome in women actively trying to get pregnant • Follow-up surgery, recurrence of symptoms • Infection	Mean±SD (range) = 17±10 (1.5–24); but noted that 383 patients completed follow-up questionnaire at either 6 weeks, >1 or 2 years Ultrasound evaluation available for

			Mean±SD 787±648 Range 103–5,627 *Uterine volume (MRI)* n 110 Mean±SD 949±533 Range 250–3,123 *Dominant fibroid volume (US)* n 95 Mean±SD 248±354 Range 1-2120 *Dominant fibroid volume (MRI)* n 60 Mean±SD 403±517 Range 8–3,566			• Post-procedural amenorrhea / early menopause • Post-procedural fertility measured by hormone (FSH, luteinising hormone and 17 B oestradiol [E2]) (ie ovarian failure) combined with clinical markers (amenorrhea etc)	353/378 women at an average of 10 months (range–1.5 to 42 months)
Watson GMT Walker WJ (2002)	Surrey, United Kingdom	Case series pre-test/ post-test Level – IV QS – 3/3	n 114 Mean age 42 Age range NR *Number of fibroids* 165	*Includes* Not stated	Bilateral UAE using 355–500 µm PVA particles (Boston Scientific)	• Symptom resolution/ improvement • Fibroid volume dominant	Follow-up 6 weeks, 3,6,12, 18 and 24 months
Zupi E Pocek M Dauri M Marconi D Sbracia M Piccione E Simonetti G (2003)	Rome, Italy	Case series pre-test/ post-test Level – IV QS – 3/3	n 26 Mean age 39.5 ± 3.3 Age range 32–54	*Includes* Women with uterine bleeding, with a single myoma and fertile age *Excludes* Uterine fibromatosis or adenomyosis, subserosus localisation, other gynaecological diseases	UAE using 355–500 µm PVA particles (Tagest)	• Fibroid volume • Menorrhagia • Pain • Abdominal bulk	Follow-up at 1, 3, 6 and 12 months

Appendix G Excluded studies

Alonso, A.M., Marret, H. et al (2003). 'Prospective clinical and sonographic assessment of uterine artery embolization as the treatment of symptomatic uterine leiomyomata', *Gynecologie Obstetrique Fertilite,* 31 (2), 117–122.

Bai, S.W., Jang, J.B. et al (2002). 'Uterine arterial embolization for the treatment of uterine leiomyomas', *Yonsei Medical Journal,* 43 (3), 346–350.

Banovac, F., Ascher, S.M. et al (2002). 'Magnetic resonance imaging outcome after uterine artery embolization for leiomyomata with use of tris-acryl gelatin microspheres', *Journal of Vascular and Interventional Radiology,* 13 (7), 681–687.

Berkowitz, R.P., Hutchins Jr., F.L. & Worthington-Kirsch, R.L. (1999). 'Vaginal expulsion of submucosal fibroids after uterine artery embolization. A report of three cases.' *Journal of Reproductive Medicine for the Obstetrician and Gynecologist,* 44 (4), 373–376.

Chen, C., Lu, J. et al (2002). 'Clinical analysis of 42 cases uterine myoma by uterine arterial embolization', *Zhonghua fu chan ke za zhi,* 37 (1), 8–11.

Cornelis, F., Ferrand, J. et al (1999). 'Morphological features of embolised myomata', *Minimally Invasive Therapy and Allied Technologies,* 8 (6), 437–439.

deSouza, N.M. & Williams, A.D. (2002). 'Uterine arterial embolization for leiomyomas: Perfusion and volume changes at MR imaging and relation to clinical outcome', *Radiology,* 222 (2), 367–374.

Fencl, P., Svarovsky, J. et al (2001). 'One-year experience with treatment of uterine myomas by embolization of the uterine arteries', *Ceska Radiologie,* 55 (3), 208–213.

Fleischer, A.C., Donnelly, E.F. et al (2000). 'Three-dimensional color doppler sonography before and after fibroid embolization', *Journal of Ultrasound in Medicine,* 19 (10), 701–705.

Goldberg, J., Pereira, L. et al (2004b). 'Pregnancy outcomes after treatment for fibromyomata: Uterine artery embolization versus laparoscopic myomectomy', *American Journal of Obstetrics and Gynecology,* 191 (1), 18–21.

Golfieri, R., Muzzi, C. et al (2000). 'The percutaneous treatment of uterine fibromas by means of transcatheter arterial embolization', *Radiologia Medica,* 100 (1–2), 48–55.

Goodwin, S.C., Vedantham, S. et al (1997). 'Preliminary experience with uterine artery embolization for uterine fibroids', *Journal of Vascular and Interventional Radiology,* 8 (4), 517–526.

Goodwin, S.C. & Walker, W. J. (1998). 'Uterine artery embolization for the treatment of uterine fibroids', *Current Opinion in Obstetrics and Gynecology,* 10 (4), 315–320.

Jha, R.C., Ascher, S.M. et al (2000). 'Symptomatic fibroleiomyomata: MR imaging of the uterus before and after uterine arterial embolization', *Radiology,* 217 (1), 228–235.

Jones, K., Walker, W. & Sutton, C. (2000). 'Sequestration and extrusion of intramural fibroids following arterial embolization: a case series', *Gynaecological Endoscopy,* 9, 309–313.

Kroencke, T.J., Gauruder-Burmester, A. et al (2004). 'Technical success rate, peri-interventional complications and radiation exposure of the transarterial embolization for leiomyomas of the uterus', *Rofo-Fortschritte Auf Dem Gebiet Der Rontgenstrahlen Und Der Bildgebenden Verfahren,* 176 (4), 580–589.

Kroencke, T.J., Gauruder-Burmester, A. et al (2005). 'Transarterial embolization for uterine fibroids: Clinical success rate and results of magnetic resonance imaging', *Rofo-Fortschritte Auf Dem Gebiet Der Rontgenstrahlen Und Der Bildgebenden Verfahren,* 177 (1), 89–98.

Li, L., Chen, Y. et al (2004). 'Effect of superselective uterine artery embolization on the quality of life of patients with symptomatic uterine myoma', *Chinese Journal of Clinical Rehabilitation,* 8 (23), 4676–4677.

Li, W., Brophy, D.P. et al (2000). 'Semiquantitative assessment of uterine perfusion using first pass dynamic contrast-enhanced MR imaging for patients treated with uterine fibroid embolization', *Journal of Magnetic Resonance Imaging,* 12 (6), 1004–1008.

Lohle, P.N.M., Lampmann, L.E.H. et al (2001). 'Embolisation as a treatment for symptomatic uterine myomata', *Nederlands Tijdschrift voor Geneeskunde,* 145 (16), 791–794.

Maltau, J.M., Kumar, S. et al (2003). 'Embolization of uterine myoma', *Tidsskrift for den Norske Laegeforening,* 123 (5), 614–616.

Manyonda, I.T., Sinthamoney, E. et al (2003). 'Uterine artery embolisation for symptomatic fibroids: clinical results in 400 women with imaging follow up', *Bjog-an International Journal of Obstetrics and Gynaecology,* 110 (12), 1139–1139.

Maskova, J., Drbohlav, P. et al (2001). 'Endovascular treatment of uterine leiomyomata: Our first experience', *Ceska Radiologie,* 55 (6), 364–369.

McLucas, B. & Adler, L. (2000). 'Uterine artery embolization as therapy for myomata', *Infertility and Reproductive Medicine Clinics of North America,* 11 (1), 77–94.

McLucas, B., Reed, R.A. et al (2002). 'Outcomes following unilateral uterine artery embolisation', *British Journal of Radiology,* 75 (890), 122–126.

Murgo, S., Simon, P. & Golzarian, J. (2002). 'Embolization of uterine fibroids', *Revue Medicale de Bruxelles,* 23 (5), 435–442.

Nicholson, T. (2004). 'Outcome in patients undergoing unilateral uterine artery embolization for symptomatic fibroids', *Clinical Radiology,* 59 (2), 186–191.

Nicholson, T.A., Pelage, J.P. & Ettles, D.F. (2001). 'Fibroid calcification after uterine artery embolization: Ultrasonographic appearance and pathology', *Journal of Vascular and Interventional Radiology,* 12 (4), 443–446.

Nikolic, B., Spies, J.B. et al (2000). 'Patient radiation dose associated with uterine artery embolization', *Radiology,* 214 (1), 121–125.

Pelage, J.-P., Guaou, N.G. et al (2004). 'Uterine fibroid tumors: Long-term MR imaging outcome after embolization', *Radiology,* 230 (3), 803–809.

Pinto, I., Chimeno, P. et al (2002). 'Embolization of uterine arteries to treat symptomatic myomas', *Radiologia,* 44 (5), 201–206.

Prollius, A., de Vries, C. et al (2004a). 'Uterine artery embolisation for symptomatic fibroids: the effect of the large uterus on outcome', *Bjog-an International Journal of Obstetrics and Gynaecology,* 111 (3), 239–242.

Ravina, J.H., Aymard, A. et al (1998). 'Selective arterial embolization for hemorrhagic uterine leiomyomas', *Presse Medicale,* 27 (7), 299–303.

Ravina, J.H., Aymard, A. et al (2000). 'Arterial embolization of uterine myomata: Results in 286 cases', *Journal de Gynecologie Obstetrique et Biologie de la Reproduction,* 29 (3), 272–275.

Ravina, J.-H., Aymard, A. et al (2003). 'Uterine fibroids embolization: Results about 454 cases', *Gynecologie Obstetrique Fertilite,* 31 (7–8), 597–605.

Ravina, J.H., Bouret, J.M. et al (1995a). 'Advantage of pre-operative embolization of fibroids: About a multicentric set of 31 cases', *Contraception Fertilite Sexualite,* 23 (1), 45–49.

Ravina, J.H., Bouret, J.M. et al (1997). 'Recourse to particular arterial embolization in the treatment of some uterine leiomyoma', *Bulletin de l'Academie Nationale de Medecine,* 181 (2), 233–243; discussion 244.

Ravina, J.H., Herbreteau, D. et al (1995b). 'Arterial embolisation to treat uterine myomata', *Lancet,* 346 (8976), 671–672.

Ravina, J.H., Merland, J.J. et al (1994). 'Preoperative embolization of uterine fibroma. Preliminary results (10 cases)', *Presse Medicale (Paris, France: 1983),* 23, 1540–1533.

Richter, G.M., Radeleff, B. et al (2004). '[Uterine fibroid embolization with spheric micro-particles using flow guiding: safety, technical success and clinical results]', *Rofo-Fortschritte Auf Dem Gebiet Der Rontgenstrahlen Und Der Bildgebenden Verfahren,* 176 (11), 1648–1657.

Ryu, R.K., Omary, R.A. et al (2003). 'Comparison of pain after uterine artery embolization using tris-acryl gelatin microspheres versus polyvinyl alcohol particles', *Cardiovascular and Interventional Radiology,* 26 (4), 375–378.

Salerno, S. & Belli, A.M. (2001). 'Percutaneous treatment of uterine fibroleiomyomas: analysis of complications and quality of life after embolization', *Radiologia Medica,* 101 (5), 360–364.

Simonetti, G., Romanini, C. et al (2001). 'Embolization of the uterine artery in the treatment of uterine myoma', *Radiologia Medica,* 101 (3), 157–164.

Siskin, G.P., Tublin, M.E. et al (2001). 'Uterine artery embolization for the treatment of adenomyosis: Clinical response and evaluation with MR imaging', *American Journal of Roentgenology,* 177 (2), 297–302.

Spies, J.B., Roth, A.R. et al (2001c). 'Ovarian function after uterine artery embolization for leiomyomata: assessment with use of serum follicle stimulating hormone assay.' *Journal of vascular and interventional radiology,* 12 (4), 437–442.

Spies, J.B., Roth, A.R. et al (2002a). 'Leiomyomata treated with uterine artery embolization: Factors associated with successful symptom and imaging outcome', *Radiology,* 222 (1), 45–52.

Stancato-Pasik, A., Katz, R. et al (1999). 'Uterine artery embolisation of myomas: Preliminary results of gelatin sponge pledgets as the embolic agent', *Minimally Invasive Therapy and Allied Technologies,* 8 (6), 393–396.

Szabo, E., Nagy, E. et al (2001). 'Uterine artery embolization for the conservative management of leiomyoma', *Orvosi Hetilap,* 142 (13), 675–680.

Walker, W.J., Carpenter, T.T. & Kent, A.S.H. (2004). 'Persistent vaginal discharge after uterine artery embolization for fibroid tumors: Cause of the condition, magnetic resonance imaging appearance, and surgical treatment', *American Journal of Obstetrics and Gynecology,* 190 (5), 1230–1233.

Wang, J., Zhang, G.Y. et al (2002). 'Dextran uterine artery embolization to treat fibroids', *Chinese Medical Journal,* 115 (8), 1132–1136.

Weintraub, J.L., Romano, W.J. et al (2002). 'Uterine artery embolization - Sonographic imaging findings', *Journal of Ultrasound in Medicine,* 21 (6), 633–637.

Zhou, S.-K., Li, S.-B. & Zhang, H.-W. (2003a). 'Interventional therapy in the treatment of hysteromyoma', *Bulletin of Hunan Medical University,* 28 (1), 79–82.

Zhou, S.-K., Li, S.-B. & Zhang, Z.-S. (2003b). 'Influential factors to therapeutic efficacy of uterine artery embolization in the treatment of uterine fibroids', *Bulletin of Hunan Medical University,* 28 (4), 409–411.

Appendix H Case reports for safety

Study	Patient	Adverse events
Aungst et al (2004)	39-year-old woman with primary antiphospholipid syndrome presenting with severe menorrhagia.	Eight weeks post-UAE patient readmitted with vaginal bleeding, cramping and fever, diagnosed as septic shock. IV antibiotics and aggressive fluid resuscitation were commenced. Patient received 6 units packed RBC, vitamin K and 5 units of fresh frozen plasma before undergoing a total abdominal hysterectomy and bilateral salpingo-oophorectomy. Examination of the uterus revealed 10 cm infarcted necrotic fibroid and blood cultures grew anaerobic gram negative bacteria. Full heparin anticoagulation and antibiotics were continued and patient was discharged day 8 post-operatively.
Bedaiwy & Paraiso (2004)	50-year-old woman with uterine fibroids.	Presented to clinic 15 months post-UAE with symptoms of pelvic pressure and urinary incontinence. Examination revealed stage II uterovaginal prolapse. Patient underwent a total vaginal hysterectomy, uterosacral vaginal vault suspension, anterior colporrhaphy with Kelly plication, posterior colporrhaphy and cystoscopy.
de Blok et al (2003)	42-year-old woman presenting with secondary infertility and symptoms of dysmenorrhea. Examination revealed uterine fibroids.	Five days post-UAE patient readmitted with gastrointestinal symptoms and abdominal pain. Colloids were delivered IV; however, the patient's condition deteriorated. An emergency laparoscopy was performed and revealed an abdomen full of pus and a necrotic uterus. Resuscitation failed and the patient died from septic shock resulting in disseminated intravascular coagulation and multiple organ failure.
Burnham et al (2000)	33-year-old woman presenting with menorrhagia associated with uterine fibroids.	Patient readmitted 6 weeks post-UAE with persistent menorrhagia and severe iliac fossa pain. Imaging revealed a large fibroid obstructing drainage from the fundus and a fibroid resection was performed. Patient experienced pain 2 weeks post-resection and a hysteroscopy was performed, with a large necrotic fibroid removed during this procedure. Patient continued to experience mild pain, therefore a laparoscopy and hysteroscopy were performed. Patient was then discharged without further incident.
Dietz et al (2004)	46-year-old woman with a history of morbid obesity, hypertension and asthma presented with uterine fibroids.	Two weeks post-UAE the patient presented with buttock pain. On examination 2 large ecchymotic patches were noted, however the skin was intact. Four weeks post-UAE the skin had broken revealing underlying necrosis. Patient was readmitted and administered IV antibiotics and operative debridement was performed. Lesions healed over 14 weeks and patient required Panadol for pain relief.
El-Shalakany et al (2003)	41-year-old woman presenting with heavy menstrual loss and pelvic pressure associated with uterine fibroids.	Patient readmitted 8 days post-UAE with profuse watery vaginal discharge and urinary incontinence. Examination revealed widespread necrosis of the cervix and vaginal vault, extending to the bladder. An indwelling urinary catheter was inserted. Ten weeks post-UAE surgical repair of the fistula and an abdominal hysterectomy were performed. The bladder defect was closed followed by a partial colpocliesis. A urethral catheter remained in place until recovery.
Felemban et al (2001)	43-year-old woman presenting with menorrhagia associated with uterine fibroids.	Patient required hospitalisation for abdominal pain and fever post-UAE. Pain was resolved with analgesics and NSAIDs. In addition, a urinary tract infection was treated with antibiotics. Pain resolved in 10 days. Spontaneous expulsion of fibroid tissue via the vagina occurred 21 days post-UAE, and again at 27 and 35 days post-UAE.
Fogt et al (2003)	42-year-old woman presenting with menorrhagia and pelvic pain associated with uterine fibroids.	Two months post-UAE patient presented with intractable pelvic pain. Imaging revealed necrosis and fibroid degeneration. A total abdominal hysterectomy and a bilateral salpingo-oophorectomy were performed. The uterus was found to be filled with large amounts of pus and microspheres. Microspheres were also found within the bilateral fallopian tube cavities.
Godfrey & Zbella	47-year-old woman presenting with menorrhagia and anaemia	Two months post-UAE the patient presented with pelvic pain and copious amounts of malodorous vaginal discharge. Infection with *T. vaginalis* was

(2001)	associated with uterine fibroids. Patient had cocaine detected in system prior to UAE.	observed and treated. Three months post-UAE patient presented with fever, pain and discharge. IV antibiotics were administered and a laparotomy was performed, which revealed a necrotic uterus and extensive adhesions of the uterus to the small bowel, omentum and hydrosalpinx. A total abdominal hysterectomy and left salpingo-oopherectomy were performed. The patient was discharged 4 days post-operatively.
Goldberg et al (2004a)	45-year-old woman presenting with pelvic pain, dysmenorrhea and menorrhagia associated with uterine fibroids.	Five weeks post-UAE the patient underwent a hysteroscopic resection of a necrotic fibroid due to pain, vaginal discharge and fever. Diagnosis was acute purulent endometritis, granulation of tissue and a fragmented submucosal fibroid. Symptoms resolved. Thirteen months post-UAE the patient re-presented with pelvic pain and bleeding. At laparotomy, a soft mass was noted with a necrotic centre and a parasitic blood supply from the anterior rectum. A total hysterectomy and a unilateral oopherectomy were performed. Pathology found the mass to be a leiomyosarcoma with low-grade endometrial stromal sarcoma. A subsequent laparotomy removed the left ovary, appendix and debulked peritoneal implants. After becoming symptomatic with recurrent disease the patient underwent chemotherapy and died 44 months post-UAE.
Hascalik et al (2004)	42-year-old woman presenting with menorrhagia and anaemia associated with uterine fibroids.	Six weeks post-UAE the patient reported amenorrhea, hot flushes and insomnia and a diagnosis of ovarian failure was made (elevated FSH levels). HRT was prescribed and symptoms resolved. FSH levels were reduced and menstruation recommenced 2 months later.
Hehenkamp et al (2004)	54-year-old woman presenting with dysmenorrhea and anaemia associated with uterine fibroids.	Ten weeks post-UAE the patient reported abdominal pain, fever and a foul smelling vaginal discharge. Examination revealed a mass prolapsed through a dilated cervix. The necrotic fibroid was removed under general anaesthesia 3 days later and IV antibiotics were administered. Symptoms resolved.
De Iaco et al (2001)	38-year-old woman presenting with menorrhagia and pelvic discomfort associated with uterine fibroids.	Six months post-UAE the patient experienced metrorrhagia and sonography revealed a fibroid displacing the endometrial lining. Resection of the fibroid was performed.
De Iaco et al (2002)	54-year-old woman presenting with a history of pelvic pain and intermenstrual bleeding associated with uterine fibroids.	Fourteen months post-UAE the patient presented with metrorrhagia. A hysteroscopy revealed a defect in the uterine wall, opening into the uterine cavity via a fistula of endometrium and myometrium.
Joyce et al (2001)	51-year-old woman presenting with anaemia and increasing abdominal girth. Examination revealed calcified fibroids.	One month post-UAE patient reported a continuous vaginal discharge. Patient then underwent a total abdominal hysterectomy and a bilateral salpingo-oopherectomy. Histologic examination revealed a leiomyosarcoma.
Kerlan et al (2003)	48-year-old woman presenting with menorrhagia associated with uterine fibroids.	One month post-UAE patient was readmitted with vaginal haemorrhage and patient was hypotensive. Fluid resuscitation was commenced and 2 units of packed RBC were infused. Haemorrhage recurred within 48 hours and an emergency total abdominal hysterectomy was performed.
Kuhn & Mitchell (1999)	43-year-old woman presenting with pressure symptoms and menorrhagia associated with fibromyomatous uterus.	Three days post-UAE patient experienced lower abdominal pain requiring oral narcotic analgesia and NSAIDs. Pain resolved. Variable vaginal blood loss persisted for 9 weeks post-UAE.
Lai et al (2000)	41-year-old woman presenting with menorrhagia and pelvic pain	Loss of sexual function post-UAE (6-month follow-up)
Laverge et al (2003)	45-year-old woman presenting with menorrhagia and dysmenorrhea associated with uterine fibroids.	Ten weeks post-UAE patient presented with pelvic pain and an offensive vaginal discharge. Examination revealed a necrotic mass protruding from vagina, which was removed. A second mass was passed the following day. Antibiotics were prescribed. Symptoms resolved 3 weeks after expulsion of necrotic mass.
Lowenstein et al (2004)	49-year-old woman presenting with dysmenorrhea and lower abdominal pain associated with uterine fibroids.	Four days post-UAE patient presented to emergency room with severe pain in the genital region with dysuria and purulent vaginal discharge. On examination a painful necrotic ulcer on the vaginal wall and urinary retention were observed. A urinary catheter was inserted and urine was

		drained. Pain was controlled with morphine and prophylactic antibiotics were administered for 10 days. Symptoms resolved and patient was discharged after 11 days hospitalisation.
Nikolic et al (2004)	50-year-old woman presenting with severe sciatic pain and a history of right sided hydrosalpinx. Examination revealed uterine fibroids.	Four weeks post-UAE patient presented to emergency with severe abdominal cramping. Examination revealed a fluid-containing right adnexal mass. Patient's condition worsened and a laparotomy was performed revealing a right pyosalpinx, a left fallopian tube fluid collection and an enlarged myomatous uterus. A hysterectomy and a bilateral oophorectomy were performed.
Payne et al (2002)	39-year-old woman presenting with menorrhagia associated with uterine fibroids.	Seven days post-UAE patient was readmitted with symptoms suggestive of a pelvic infection. Treatment consisted of hydration and antibiotics. Patient's condition deteriorated and an exploratory laparoscopy was performed followed by a hysterectomy, a bilateral salpingo-oophorectomy, extensive adhesiolysis and bowel serotomy repair. Histological examination revealed intravascular embolic microspheres throughout the myometrium.
Payne & Haney (2003)	39-year-old woman presenting with menorrhagia due to uterine fibroids	Seven days post-UAE patient readmitted with symptoms of post-embolisation syndrome. Leukocytosis developed overnight, treated with IV antibiotics. Scan revealed a necrotic fibroid. Epigastric pain developed. Day 14 post-UAE the patient underwent laparotomy, abdominal hysterectomy, bilateral salpingo-oophorectomy, extensive adhesiolysis, bowel serotomy repair and a blood transfusion. Discharged 7 days post-operatively.
	39-year-old woman presenting to emergency with menorrhagia and anaemia due to uterine fibroids. Originally, declined blood transfusion due to religious beliefs.	Epigastric pain developed day 2 post-UAE and treated with proton pump inhibitor. Patient became febrile on day 3 post-UAE and developed leukocytosis on day 4 post-UAE. Diagnosed with post-UAE sepsis secondary to uterine infection. Received 4 units of packed RBC and treated with IV antibiotics. Patient underwent laparotomy, supracervical hysterectomy and adhesiolysis. The patient received a further transfusion of 2 units of packed RBC and was discharged on day 7 post-UAE.
Rastogi et al (2004)	26-year-old woman presenting with severe dysfunctional uterine bleeding and anaemia associated with uterine fibroids.	Four days post-UAE the patient experienced anorexia, vomiting, and abdominal pain. A slight creatinine rise was observed. Seven days post-UAE the patient was readmitted for renal failure. Two units of RBC were administered and hydration with normal saline. Patient was discharged 4 days after admission and monitored, with creatinine levels gradually falling.
Sabatini et al (2003)	39-year-old woman presenting with pelvic pain and secondary infertility. Examination revealed uterine fibroids.	Four weeks post-UAE the patient presented to emergency with a week-long history of pain, fever and an offensive vaginal discharge previously treated with antibiotics prescribed by GP. IV antibiotics were administered and a laparotomy was performed, with a large necrotic fibroid being removed.
Shashoua et al (2002)	44-year-old woman presenting with menometrorrhagia due to uterine fibroids.	One month post-UAE the patient experienced moderate vaginal bleeding, a malodorous vaginal discharge and abdominal pain, which was treated with ibuprofen. Two months post-UAE patient developed chronic pain with a probable diagnosis of necrosing fibroids. Three months post-UAE patient was readmitted with severe abdominal pain and an exploratory laparoscopy was performed, revealing a large volume of pus in the abdominal cavity. A necrotic uterus was revealed and a hysterectomy was performed. Patient received 3 units of packed RBC and 2 units of fresh-frozen plasma and was administered IV antibiotics. The incision site was left open to drain and the patient was admitted to ICU for 2 days. Incision site was closed 6 days post-operatively and patient was discharged the next day.
Smith et al (1999)	39-year-old woman presenting with severe menorrhagia and pelvic pain due to uterine fibroids.	Two weeks post-UAE patient complained of pelvic pain and vaginal bleeding. At 5 months post-UAE these symptoms had not resolved and a hysterectomy was performed.
Stringer et al (2001)	53-year-old postmenopausal woman presenting with pelvic pain. Examination revealed	Right-sided pelvic pain developed 2 weeks post-UAE and symptoms persisted despite administration of pain relief. Laparoscopy was performed 6 months post-UAE.

	uterine fibroids.	
Stringer et al (2000)	45-year-old woman presenting with menorrhagia and dysmenorrhea due to uterine fibroids.	Five days post-UAE patient developed severe post-embolisation syndrome and was readmitted. Nine days post-UAE developed symptoms of menopause (elevated FSH). Symptoms persisted and ovarian failure was diagnosed.
Sultana et al (2002)	43-year-old woman presenting with menorrhagia and pelvic pressure associated with uterine fibroids.	Patient presented 17 days post-UAE with fever, urinary frequency and copious vaginal discharge. Antibiotics were prescribed for 7 days. Six weeks post-UAE a discharge through the urethra was observed in addition to fever. Antibiotics were again prescribed. At 3 months post-UAE the patient reported loss of urine via the vagina. Examination revealed a large defect in the bladder. A laparotomy for repair of the bladder was performed in addition to a hysterectomy and resection of necrotic bladder tissue.
Takeda et al (2004)	41-year-old woman presenting with abdominal distension and anaemia associated with uterine fibroids.	One day post-UAE patient developed enlargement of lower abdomen and generalised oedema of the face, body and extremities, possibly associated with elevated levels of vascular endothelial growth factor.
Tan & Rafla (2004)	27-year-old woman presenting with dysmenorrhea and menorrhagia associated with uterine fibroids.	Three days post-UAE patient was readmitted with pelvic pain, vaginal discharge, nausea and fever. Treatment consisted of analgesics and antibiotics. Scans revealed a bulky anteverted uterus with calcified fibroids. Menorrhagia and dysmenorrhea recurred 3 ½ years later. These symptoms eased after the vaginal passage of further calcified pieces of fibroid.
Tropeano et al (2003)	44-year-old woman presenting with menorrhagia and anaemia associated with uterine fibroids.	Serial FSH and oestradiol measurements were taken and a hysteroscopy with endometrial biopsy were performed at 6 months post-UAE. The patient remained amenorrheic at 12-month follow-up with no other menopausal symptoms.
Vashisht et al (1999)	51-year-old woman presenting with heavy menstrual flow associated with uterine fibroids.	Seven days post-UAE patient was readmitted with abdominal pain, diarrhoea, vomiting, low blood pressure and fever. Resuscitation, IV antibiotics and analgesia were administered. Patient became hypotensive with low haemoglobin levels. A laparotomy was performed, revealing a necrotic fibroid. A total hysterectomy and bilateral salpingo-oopherectomy were performed. The patient received 10 units of blood, 4 units fresh frozen plasma, 6 units of cryoprecipitate and 2 infusions of platelets, but remained oliguric and acidotic. Blood cultures grew *E. coli.* After 15 days in ICU the patient died.
Wolanske et al (2003)	39-year-old woman presenting with menometrorrhagia and bulky pelvic symptoms associated with uterine fibroids.	During UAE procedure, retrograde flow of embolic mixture up the ovarian artery was observed and the embolisation of the left uterine artery was terminated and no complications were reported. The patient's symptoms didn't resolve and a hysterectomy was performed.
Worthington-Kirsch et al (1999)	49-year-old woman presenting with menorrhagia and urinary frequency due to uterine fibroids	Patient developed bilateral buttock pain, treated with NSAIDs and resolved by day 24 post-UAE
	48-year-old woman presenting with menorrhagia, abdominal distension and urinary frequency due to uterine fibroids	Patient developed bilateral buttock pain, treated with ibuprofen and resolved by day 14 post-UAE
	44-year-old woman presenting with menorrhagia and dysmenorrhea due to uterine fibroids	Patient developed bilateral buttock pain, treated with ibuprofen and resolved by day 18 post-UAE
Yeagley et al (2002)	38-year-old woman presenting with worsening abdominal pain associated with uterine fibroids.	Patient developed right lower extremity pain immediately post-UAE and treated with analgesics. One day post-UAE patient developed vulvovaginal burning but discharged day 3 post-UAE. Vulvar pain and urinary retention increased day 5 post-UAE and patient was readmitted. A urinary catheter drained urine; infection not detected. IV analgesics and antibiotics were administered. Patient discharged day 9 post-UAE and

symptoms continued to improve.

NSAIDs = non-steroidal anti-inflammatory drugs; RBC = red blood cells; IV = intravenous; FSH = follicle stimulating hormone; ICU = intensive care unit; HRT = hormone replacement therapy

Appendix I Case series for effectiveness

Menstrual blood loss (level IV evidence)

Study	Quality score [a]	Population	Menorrhagia or blood loss
Huang et al (2004)	3/3	35 premenopausal consecutive women with symptomatic fibroids	Self-reported menstrual bleeding symptoms 9/35 (26%) much better 20/35 (57%) slightly better 6/35 (17%) unchanged 0/35 (0%) worse
Pelage et al (2000)	3/3	80 consecutive women with symptomatic uterine fibroids	74/80 (92%) normal menstruation by the first cycle post-UAE 72/80 (90%) complete cessation of menorrhagia 3/80 (4.0%) marked improvement 5/80 (6.0%) no improvement, underwent myomectomy or hysterectomy
Shan et al (2004)	3/3	100 premenopausal consecutive women	Abnormal bleeding 99/100 (99%) improvement in symptoms 27/100 (27%) complete cessation of menorrhagia 48/100 (48%) great improvement 20/100 (20%) moderate improvement 4/100 (4%) slight improvement
Zupi et al (2003)	3/3	26 consecutive women with symptomatic uterine fibroids	Menorrhagia n = 21 Resolved: 12/21 (57%); Mild reduction: 6/21 (29%); Same: 3/21 (14%)
Bapuraj et al (2002)	2.5/3	11 women with symptomatic uterine fibroids	Menorrhagia (2-month follow-up) n (%) Resolved: 4 (36); Improved [b]: 6 (55); Same: 1 (9); Worse: 0 (0) 11
Delaney et al (1999)	2.5/3	126 women with symptomatic fibroids	Menorrhagia (3-month follow-up) n (%) Resolved Improved [b] Same Worse Patients with menorrhagia n = 46 10 (22) 35 (76) 0 (0) 1 (2) Patients with menorrhagia and bulk symptoms n = 60 13 (22) 43 (71) 4 (7) 0 (0)
Messina et al (2002)	2.5/3	26 women with symptomatic uterine fibroids	21/24 (88%) of patients presenting with this symptom reported an improvement in menorrhagia and anaemia
Park et al [c] (2003)	2.5/3	23 women with clinically confirmed uterine fibroids	Mean bleeding score; % reduction Baseline 380 6-month 47 88
Prollius et al (2004b)	2.5/3	64 consecutive women with symptomatic uterine fibroids	12-month follow-up Menorrhagia Pre (n) Post (n) % improvement [95% CI] 60 6 90 [80,95]
Bradley et al (1998)	2/3	8 women with symptomatic uterine fibroids	3-month follow-up 4/5 (80%) menorrhagia resolution 1/5 (20%) no improvement

Hald et al [c] (2004)	2/3	24 premenopausal women with symptomatic fibroids	PBAC / % reduction Baseline: 374±258 (n = 23) 1 month: 110±83 (n = 20); 64±27 3 month: 116±97 (n = 21); 63±29 6 month: 98±64 (n = 18); 67±29
Katsumori et al (2002)	2/3	60 women with symptomatic uterine fibroids	20/60 followed up at 12 months 20/20 (100%) reported markedly or moderately improved menorrhagia symptoms
Khaund et al (2004)	2/3	50 women with symptomatic uterine fibroids	Menstrual blood loss (ml) Months (n) / Median (range) / Median reduction [95% CI] Pre (50): 162 (9–1339) 3 (34): 60 (0–767); 85 [67,218]; *p*<0.001 6–9 (34): 70 (0–1283); 59 [41,158]; *p*<0.001 12–24 (25): 37 (0–265); 123 [67,236]; *p*<0.001 24–36 (17): 18 (0–205); 136 [93,305]; *p*<0.001 36–48 (6): 41 (0–66); 186 [93,683]; *p*<0.05
Lang and Myers (2004)	2/3	51 women	% who report improved menorrhagia 1 month (n = 51): 74 2 months (n = 51): 86 3 months (n = 51): 90 12 months (n = 51): 92
Pron et al (2003b)	2/3	555 consecutive women with confirmed uterine fibroids	Menorrhagia (%, [95% CI]) Improved / Same / Worse 3 months (n = 429): 83 [80,87]; 10; 7
Sena-Martins et al (2003)	2/3	32 women with symptomatic uterine fibroids	Menstrual regularity n (%) Equal / Regular / Irregular 3 months: 7 (23); 22 (71); 2 (6) Change in menstrual volume n (%) Equal / Lower 3 months: 3 (10); 28 (90) Change in menstrual duration n (%) Equal / Shorter 3 months: 6 (19); 25 (81)
Spies et al (2001b)	2/3	30 women with symptomatic uterine fibroids	Menstrual bleeding / Heavy Baseline: 26/30 (87%) 3 months: 13/30 (43%) 6 months: 9/30 (31%) PBAC score (n = 21) Baseline: 481±433 3-month: 204±250; Change from baseline: 277±252; p=0.001 6-month: 159; Change from 3 to 6 month: 44±291; p=0.49
Spies et al (2001a)	2/3	200 women with confirmed uterine fibroids	Menstrual bleeding (%, [95% CI]) Improved / Same / Worse 3 months (n = 181): 87 [82,92]; 10 [6,15]; 3 [1,6] 6 months (n = 158): 89 [83,93]; 6 [3,11]; 5 [3,10] 12 months (n = 167): 90 [86,95]; 8 [5,13]; 2 [1, 5]
Walker & Pelage (2002)	2/3	400 consecutive women with symptomatic fibroids	255/400 (54%) followed up 214/255 (84%) reported an improvement in menorrhagia at mean 16.7 months follow-up

Andersen et al (2001)	1.5/3	62 women with symptomatic uterine fibroids	6-month follow-up of only 30/62 (48%) women 29/62 (47%) reported a reduction in bleeding
Chrisman et al (2000)	1.5/3	66 premenopausal women	Menorrhagia at baseline n (%) Improved Same Worse 35 32 (91) 3 (9) 0 (0)
Ciraru-Vigneron et al (1999)	1.5/3	184 women	19/184 (10%) minimal menorrhagia
Hutchins et al (1999)	1.5/3	305 premenopausal women	Menorrhagia (n = 179) n (%) Resolved Improved [b] Same Worse 3 months (n = 179) 55/179 (31) 113/179 (63) 9/179 (5) 2/179 (1) 6 months (n = 116) 37/116 (32) 71/116 (61) 7/116 (6) 1/116 (1) 12 months (n = 58) 24/58 (41) 32/58 (55) 0/58 (0) 2/58 (4) Clinical success (% improvement [95% CI]) (defined as moderate or better improvement in menorrhagia) 3 months 87 [81,91] 6 months 87 [80,92] 12 months 86 [75,93]
Roth et al (2000)	1.5/3	81 women	Change in bleeding symptoms (n = 73) Mean +3.3 ±2.0, range –3 to +5 (–5 = markedly worse, +5 = markedly improved, 0 = unchanged, +1 slightly improved, +3 moderately improved)
Walker et al (1999)	1.5/3	200 women	Menorrhagia improved in 79% of patients (n = 111) at 3-month follow-up

[a] Quality score is a reflection of a priori hypotheses, appropriate patient selection and adequate follow-up; PBAC = pictorial blood loss assessment chart score; [b] Improved includes great, moderate and slight improvement; [c] Studies by Hald et al (2004) and Park et al (2003) compared UAE with laparoscopy which is not a comparator in this report; therefore, only the results from the UAE arm are described

Occurrence of pressure or bulk symptoms (level IV evidence)

Study	Quality score [a]	Population	Pressure or bulk symptoms
Shan et al (2004)	3/3	100 premenopausal consecutive women	64 women reported with bulk related symptoms pre-UAE 8/64 (13%) complete cessation 21/64 (33%) great improvement 15/64 (25%) moderate improvement 20/64 (32%) no change
Zupi et al (2003)	3/3	26 consecutive women with symptomatic uterine fibroids	Abdominal weight n = 18 Resolved Mild reduction Same 10/18 (56%) 7/18 (39%) 1/18 (6%)
Bapuraj et al (2002)	2.5/3	11 women with symptomatic uterine fibroids	Bulk symptoms (2-month follow-up) n (%) Resolved Improved [a] Same Worse 6 3 (50) 3 (50) 0 (0) 0 (0)
Delaney et al (1999)	2.5/3	126 women with symptomatic uterine fibroids	Bulk symptoms (3-month follow-up) n (%) Resolved Improved [b] Same Worse Patients with menorrhagia n = 20 5 (25) 14 (70) 1 (5) 0 (0) Patients with menorrhagia and bulk n = 60 21 (35) 31 (52) 7 (11) 1 (2)

Prollius et al (2004b)	2.5/3	64 consecutive women with symptomatic uterine fibroids	Bulk symptoms (12-month follow-up) Pre (n) / Post (n) / % improvement [95% CI] Mass 35 / 9 / 74 [58, 86] Discomfort 43 / 5 / 88 [76, 95] Dyspareunia 21 / 2 / 91 [71, 97]
Bradley et al (1998)	2/3	8 women with symptomatic uterine fibroids	8/8 (100%) reported an improvement in pressure symptoms of fibroids such as sciatica and urinary frequency
Katsumori et al (2002)	2/3	60 women with symptomatic uterine fibroids	19/60 followed up at 12 months 19/19 (100%) reported markedly or moderately improved bulk symptoms
Lang and Myers (2004)	2/3	51 women	% who report improved bulk symptoms 1 month (n = 51) 55 2 months (n = 51) 66 3 months (n = 51) 75 12 months (n = 51) 85
Pron et al (2003b)	2/3	555 consecutive women with confirmed uterine fibroids	Bulk symptoms (% [95% CI]) Improved / Same / Worse 3 months (n = 464) 84 [80,87] / 16 / 4
Spies et al (2001a)	2/3	200 women with confirmed uterine fibroids	Bulk symptoms (% [95% CI]) Improved / Same / Worse 3 months (n = 181) 93 [88,96] / 4 [2,9] / 3 [1,8] 6 months (n = 158) 92 [87,96] / 5 [3,11] / 3 [1,7] 12 months (n = 167) 92 [88,96] / 2 [1,6] / 6 [3,10]
Walker & Pelage (2002)	2/3	400 consecutive women with symptomatic fibroids	255/400 (54%) followed up 209/255 (82%) reported an improvement in abdominal swelling or bloating at mean 16.7 months follow-up
Andersen et al (2001)	1.5/3	62 women with symptomatic uterine fibroids	6-month follow-up of only 30/62 (48%) women 18/62 (29%) reported a reduction in bulk symptoms
Chrisman et al (2000)	1.5/3	66 premenopausal women	Bulk symptoms at baseline n (%) / Improved / Same / Worse 31 / 27 (87) / 2 (6) / 1 (3)
Hutchins et al (1999)	1.5/3	305 premenopausal women	Bulk symptoms (n = 121) n (%) / Resolved / Improved [a] / Same / Worse 3 months (n = 121) 43/121 (36) / 65/121 (54) / 10/121 (8) / 3/121 (3) 6 months (n = 86) 44/86 (51) / 29/86 (34) / 10/86 (12) / 3/86 (4) 12 months (n = 42) 23/42 (55) / 15/42 (36) / 4/42 (10) / 0/42 (0) Clinical success (% improvement [95% CI]) (defined as moderate or better improvement in menorrhagia) 3 months 85 [78,90] 6 months 83 [74,89] 12 months 86 [72,93]
Roth et al (2000)	1.5/3	81 women	Change in pressure symptoms (n = 65) Mean +3.4 ±1.8, range –3 to +5 (–5 = markedly worse, +5 = markedly improved, 0 = unchanged, +1 slightly improved, +3 moderately improved)

Walker et al (1999)	1.5/3	200 women	Pressure symptoms improved and resolved in 69% and 23% of patients, respectively (n = 111) at 3-month follow-up Improvements in sciatica (77%) and urinary (83%) symptoms

[a] Quality score is a reflection of a priori hypotheses, appropriate patient selection and adequate follow-up; [b] Improved includes great, moderate and slight improvement

Pelvic pain (level IV evidence)

Study	Quality score [a]	Population	Pelvic/menstrual pain
Huang et al (2004)	3/3	35 premenopausal consecutive women with symptomatic fibroids	Self-reported pain symptoms 9/35 (26%) much better 18/35 (51%) slightly better 8/35 (23%) unchanged 0/35 (0%) worse
Zupi et al (2003)	3/3	26 consecutive women with symptomatic uterine fibroids	Pain Resolved / Mild reduction / Same n = 9: 7/9 (78%) / 1/9 (11%) / 1/9 (11%)
Bapuraj et al (2002)	2.5/3	11 women with symptomatic uterine fibroids	Pelvic pain (2-month follow-up) n (%): Resolved / Improved [a] / Same / Worse n = 7: 2 (28) / 5 (72) / 0 (0) / 0 (0)
Messina et al (2002)	2.5/3	26 women with symptomatic uterine fibroids	16/19 (84.2%) of patients with this presenting symptom reported an improvement
Prollius et al (2004b)	2.5/3	64 consecutive women with symptomatic uterine fibroids	12-month follow-up Dysmenorrhea (median) Pain scale (0 = no pain, 10 = severe pain) Pre / Post / median difference [95% CI] 5/10 / 1/10 / -4 [-5, -4]
Bradley et al (1998)	2/3	8 women with symptomatic uterine fibroids	4/7 (57%) reported an improvement in menstrual pain
Lang and Myers (2004)	2/3	51 women	% who report improved pain 1 month (n = 51): 52 2 months (n = 51): 75 3 months (n = 51): 88 12 months (n = 51): 88
Pron et al (2003b)	2/3	555 consecutive women with confirmed uterine fibroids	Dysmenorrhea (% improvement [95% CI]) Improved / Same / Worse 3 months (n = 322): 77 [72,82] / 13 / 9
Walker & Pelage (2002)	2/3	400 consecutive women with symptomatic fibroids	255/400 (53.5%) followed up 201/255 (79%) reported an improvement in menstrual pain at mean 16.7 months follow-up
Andersen et al (2001)	1.5/3	62 women with symptomatic uterine fibroids	6-month follow-up of only 30/62 (48%) women 21/62 (33.9%) reported a reduction in pelvic pain

[a] Quality score is a reflection of a priori hypotheses, appropriate patient selection and adequate follow-up

Pregnancy outcome (level IV evidence)

Study	Quality score [a]	Population	Pregnancy outcome
Forman et al (1999)	3/3	192 consecutive women	17/192 (9%) women trying to conceive 2/17 (12%) became pregnant 1/2 (50%) normal delivery at term 1/2 (50%) currently pregnant
Bradley et al (1998)	2/3	8 women with symptomatic uterine fibroids	1/8 (13%) pregnancies Not stated how many women intended to conceive prior to UAE
Khaund et al (2004)	2/3	50 women with symptomatic uterine fibroids	2/50 (4%) conceived post-UAE Not stated how many women intended to conceive prior to UAE
Pron et al (2003d) Abstract	2/3	555 consecutive women with symptomatic uterine fibroids	172/555 (31%) desired future pregnancy Follow-up ranged from 12 months in 483/555 (87%) and 24 months in 444/555 (80%) 20 pregnancies within 2-year follow-up resulted in 14 live births, 3 miscarriages, 1 planned abortion and 2 pregnancies in progress
Walker & Pelage (2002)	2/3	400 consecutive women with symptomatic fibroids	10/24 (42%) of women became pregnant out of 24 women actively trying to become pregnant after UAE 12 women contributed to 13 pregnancies in total: 8 term pregnancies 1 caesarean at 27 weeks 2 miscarriages 1 ectopic pregnancy 1 induced abortion
Hutchins et al (1999)	1.5/3	305 premenopausal women	2/305 (1%) pregnant, (1) delivered healthy singleton and (1) twins following IVF Not stated how many women intended to conceive prior to UAE
McLucas et al (2001b) Follow-up study to McLucas (1999)	1.5/3	400 women, 139 of whom wished to maintain fertility	14/400 (4%) reported 17 pregnancies: 10/17 (70%) reported normal term deliveries 5/17 (29%) reported spontaneous abortion 2/17 (12%) currently pregnant Although 139 women wanted to maintain fertility it was not stated how many women intended to conceive. It was not reported how many women attempted conception and were unsuccessful.
Ciraru-Vigneron et al (1999)	0.5/3	184 women	7/184 (4%) women conceived with a total of 8 pregnancies Mean time to pregnancy = 13 months (range 4–27 months) 4/7 (57%) women gave birth to 5 infants, of which 2 were term deliveries, 2 were pre-term Of the pre-term deliveries, 1 was twins with toxaemia (35 weeks), the other mother had severe AIDS (28 weeks) 1/7 (14%) miscarriage twice (mother >40 years of age) 2/7 (29%) currently pregnant Not stated how many women intended to conceive prior to UAE

[a] Quality score is a reflection of a priori hypotheses, appropriate patient selection and adequate follow-up

Further treatment (level IV evidence)

Study	Quality score [a]	Population	Further treatment
Ahmad et al (2003)	3/3	19 consecutive women with symptomatic uterine fibroids	1/19 (5%) required hysterectomy 4 months post-UAE due to lack of symptom resolution
Goodwin et al (1999)	3/3	60 consecutive women with symptomatic fibroids	7/60 (12%) required hysterectomy 2/60 (3%) required repeat embolisation
Pelage et al (2000)	3/3	80 consecutive women with symptomatic uterine fibroids	4/80 (5%) required myomectomy due to lack of symptom resolution 1/80 (1%) required hysterectomy due to lack of symptom resolution
Pron et al (2003a)	3/3	555 consecutive women with confirmed uterine fibroids	15/555 (3%) had successful UAE on second attempt
Razavi et al (2002)	3/3	76 consecutive women with symptomatic uterine fibroids	3/76 (4%) required myomectomy due to lack of symptom resolution 7/76 (1%) required hysterectomy due to menorrhea
Tranquart et al (2002) Follow-up study of Brunerea u et al (2000)	3/3	58 consecutive women with symptomatic fibroids	1/58 (2%) required hysterectomy at 6-month follow-up 1/58 (2%) repeat embolisation at 6-month follow-up
Walker & Watson (2002)	3/3	114 consecutive women	2/114 (2%) required hysteroscopy to remove fibroids
Joffre et al (2004)	2.5/3	85 women with symptomatic uterine fibroids	8/85 (9%) women required delayed hysterectomy due to failure of treatment 3/8 (38%) at 6 months 2/8 (25%) at 12 months 3/8 (38%) at 18 months 3/8 (38%) had undiagnosed adenomyosis 2/85 (2%) required hysteroscopic resection
Klein & Schwartz (2001)	2/3	35 women with symptomatic uterine fibroids	1/35 (3%) required multiple myomectomies performed 8 months post-UAE due to lack of symptom resolution 1/35 (3%) required second UAE procedure
Hald et al [b] (2004)	2/3	24 premenopausal women with symptomatic fibroids	2/24 (8%) women had further treatment 1/2 required transcervical resection of the myometrium 1/2 required D&C
Khaund et al (2004)	2/3	50 women with symptomatic uterine fibroids	6/50 (12%) required elective hysterectomy due to lack of symptom resolution 2/50 (4%) required myomectomy due to lack of relief of pelvic pressure symptoms
McLucas et al (1998)	2/3	25 women with symptomatic uterine fibroid	3/25 (12%) required hysterectomy

Sena-Martins et al (2003)	2/3	32 women with symptomatic uterine fibroids	1/32 (3%) required myomectomy due to myoma degeneration
Spies et al (2001a)	2/3	200 women with confirmed uterine fibroids	21/200 (11%) [7,15] required gynaecological intervention and/or readmission in the long term (weeks post-operative): 2/200 (1%) repeated embolisation (100 and 116 weeks) 5/200 (3%) D&C (12–96 weeks) 4/200 (2%) hysteroscopic resection (7–12 weeks) 1/200 (1%) abdominal myomectomy (32 weeks) 9/200 (5%) [3,9] hysterectomy (12–88 weeks)
Walker & Pelage (2002)	2/3	400 consecutive women with symptomatic fibroids	23/400 (6%) women had clinical failure of UAE or symptom recurrence 3/400 (1%) required repeat UAE procedure 4/400 (1%) required follow-up myomectomies 2/400 (1%) required hysteroscopies which resulted in one transcervical endometrial ablation
Andersen et al (2001)	1.5/3	62 women with symptomatic uterine fibroids	1/62 (2%) required hysterectomy due to lack of symptom resolution 1/62 (2%) required laparoscopic removal of fibroid 2/62 (3%) treated for fibroid in *status nascendi*
Hutchins et al (1999)	1.5/3	305 premenopausal women	11/305 (4%) required further treatment 6/305 (2%) underwent hysterectomy, 1/305 (0.4%) following severe post-embolisation syndrome 5/305 (2%) underwent myomectomy
Smith et al (2004)	1.5/3	81 women	1/81 (1%) required embolisation of contralateral artery within 9 months 12/81 (15%) underwent hysterectomy 4/81 (5%) underwent myomectomy 1/81 (1%) required repeat UAE procedure Mean time to subsequent treatment was 19 months (range 7–30 months)
Siskin et al (2000)	1.5/3	49 women with symptomatic uterine fibroids	1/49 (2%) required myomectomy for relief of menorrhagia
Walker et al (1999)	1.5/3	200 women	3/200 (1.5%) had successful UAE on second attempt

[a] Quality score is a reflection of a priori hypotheses, appropriate patient selection and adequate follow-up; HYS = hysterectomy, D&C = dilation and curettage; [b] Study by Hald et al (2004) compared UAE with laparoscopy which is not a comparator in this report; therefore, only the results from the UAE arm are described

Uterine size (level IV evidence)

Study	Quality score [a]	Population	Uterine size		
Brunereau et al (2000)	3/3	58 consecutive women with symptomatic fibroids		Uterine size (range)	% reduction (range)
			Baseline (n = 58)	11±4 (4–24) cm	
			3 months (n = 58)		13 (0–50)
			6 months (n = 46)		23 (0–55)
			12 months (n = 27)		26 (0–60)
			24 months (n = 7)		38 (0–60)

Goodwin et al (1999)	3/3	60 consecutive women with symptomatic fibroids		Uterine volume (ml) (range)		% reduction (range)
			Baseline	844 (120–9,273)		
			Mean 10.2 months			42.8 ± 31.7 (–129–87) [b]
Huang et al (2004)	3/3	35 consecutive women with symptomatic fibroids	US	Uterine volume (ml)		% reduction
			Baseline (n = 35)	282±137		
			8.1 months (n = 30)	153±74		40±25
Shan et al (2004)	3/3	100 premenopausal consecutive women	US			% reduction (range)
			3 months (n = 99)			42 (0–76)
			6 months (n = 67)			48 (0–78)
			CT			
			3 months (n = 99)			46 (23–76)
			9 months (n = 63)			75 (48–86)
Tranquart et al (2002)	3/3	58 consecutive women with symptomatic fibroids	US	Uterine volume (ml) (range)		% reduction
			Baseline	305 (65–1,403)		
Follow-up study of Brunereau et al (2000)			3 months (n = 58)			17 (p=0.0001)
			6 months (n = 46)			26 (p=0.0001)
			12 months (n = 36)			37 (p=0.0001)
			24 months (n = 19)			45 (p=0.001)
Bapuraj et al (2002)	2.5/3	11 women with symptomatic uterine fibroids	US	Uterine volume (ml)		% reduction
			Baseline (n = 11)	NA		
			2 months (n = 11)	NA		28
			6 months (n = 6)	NA		45
Delaney et al (1999)	2.5/3	120 women with symptomatic fibroids		Uterine volume (ml)		% reduction (range)
				Mean (range)		
			Menorrhagia only (n = 46)			
			Baseline	653 (105–2,506)		
			3 months	321 (69–1,007)		41 (0–80)
			Bulk symptoms (n = 20)			
			Baseline	2,204 (235-–19,640 [e])		
			3 months	1,005 (179–4,524)		45 (13–77)
			Menorrhagia + bulk (n = 60)			
			Baseline	1,002 (159–4,058)		
			3 months	505 (109–1,007)		48 (0–81)
Joffre et al (2004)	2.5/3	85 women with symptomatic uterine fibroids	US or MRI (n = 47)	Uterine volume (ml)		
			Baseline	809±922 (median 513, range 73–4,297)		
			% reduction			
			6 months	37±47 (median 36, range –122 [b] –94)		
McLucas et al (1999)	2.5/3	300 women	6/300 (2%)	women considered treatment failure due to an increase in total uterine volume (no data given)		
Messina et al (2002)	2.5/3	26 women with symptomatic uterine fibroids	US	Uterine volume (ml)		
				Median	Mean±SD (range)	
			Baseline	440	386±189 (132–722)	
			3 months	222	255±114 (88–449)	
			12 months	185	202±99 (50–402)	
				% reduction		
			3 months	28	29±20 (65–11)	p<0.001
			12 months	45	41±25 (91–2)	p<0.001

Park et al [c] (2003)	2.5/3	23 women with clinically confirmed uterine fibroids	US Baseline 3 months 6 months	Uterine volume (ml) 212±21 149 154	reduction p=0.01 [d] p=0.07
Spies et al (2004a) Bruno et al (2004)	2.5/3	100 women with symptomatic uterine fibroids who do not desire future pregnancy	Tri-acryl microspheres PVA particles	35±17% reduction in uterine volume 20±17% reduction in uterine volume	
Prollius et al (2004b)	2.5/3	64 consecutive women with symptomatic uterine fibroids	 Baseline 12 months (n = 51) Median difference	Uterine volume (ml) Median (range) 412 (70–3,005) 283 (33–1,596) 188 [147, 236]	% reduction Median (range) 38 (13–84)
Bradley et al (1998)	2/3	8 women with symptomatic uterine fibroids	MRI Baseline (n = 7) 3 months (n = 7)	Uterine volume (ml) 1179±584 583±397	% reduction 49
Hald et al [c] (2004)	2/3	24 premenopausal women with symptomatic fibroids	MRI Baseline (n = 21) 6 months (n = 21)	Uterine volume (ml) 833±469 NA	% reduction 40±20
Katsumori et al (2002)	2/3	60 women with symptomatic uterine fibroids	MRI Baseline (n = 60) 1–4 months (n = 12) 12 months (n = 23)	Uterine volume (ml) NR	% reduction (range) 40 (14–66) 56 (21–87)
Khaund et al (2004)	2/3	50 women with symptomatic uterine fibroids	6 months (n = 46) Median reduction = 40%, 95% CI [33,50], p<0.001		
Klein & Schwartz (2001)	2/3	35 women with symptomatic uterine fibroids	US Baseline 19 weeks (n = 24) Paired t-test	Uterine volume (ml) (range) 787 (98–2,366)	% reduction (range) 36 (11–80) p=0.0001
Marrett et al (2003)	2/3	85 women with symptomatic uterine fibroids	US Baseline (n = 52) 2 months (n = 41) 6 months (n = 35) 12 months (n = 31) 24 months (n = 26) 36 months (n = 20) 48 months (n = 5)	Uterine volume (ml) 373 277 250 173 189 145 254	
Lang and Myers (2004)	2/3	51 women	MRI Baseline 1 months (n = 51) 2 months (n = 51) 3 months (n = 51) 12 months (n = 51)	Uterine volume (ml) NR	% reduction 24 27 32 38
McLucas et al (1998)	2/3	25 women with symptomatic uterine fibroid	US Baseline (n = 25) 6 months (n = 24)	Uterine volume (ml) (range) 871 (230–2,997)	% reduction 46

Pron et al (2003c)	2/3	555 consecutive women with confirmed uterine fibroids	US	Uterine volume (ml)	% reduction	
			Baseline (n = 555)	704±586 (555)		
			3 months (n = 464)	428±322 (331)	27 [23,32]	
Sena-Martins et al (2003)	2/3	32 women with symptomatic uterine fibroids	US	Uterine volume (ml) (range)	% reduction	% increase
			Baseline (n = 32)	455 (84–1325)		
			3 months	(75–1,055)	42 (n = 27)	6 (n = 4)
Spies et al (2001a)	2/3	200 women with confirmed uterine fibroids	MRI	Uterine volume (ml)	Reduction (ml)	
			Baseline (n = 200)	714±482		
			3 months (n = 174)	NR	27±29	
			12 months (n = 116)	NR	38±31	
			A significant time effect was noted for the percentage of reduction in uterine volume $F_1 = 26.26$, $p<0.001$			
Spies JB (2001b)	2/3	30 women with symptomatic uterine fibroids	US	Uterine volume (ml)	% reduction	
			Baseline (n = 30)	664±443		
			3 months (n = 30)	NR	18	
			6 months (n = 29)	NR	28	
Toh et al (2003)	2/3	46 women with symptomatic uterine fibroids	MRI	Uterine volume (ml)	% reduction	
			Baseline (n = 46)	578±411		
			6 months			
			Submucosal (n = 16)		58±20	
			Intramural (n = 15)		51±9	
			Adenomyosis (n = 12)		42±9	
Walker & Pelage (2002)	2/3	400 consecutive women with symptomatic fibroids	US	Uterine volume (ml) (range)	% reduction (range)	
			Baseline (n = 284)	787±648 (103–5,627)		
			9.7 months (n = 265)	326±246 (17–1,323)	55±18 (0–96)	
			MRI			
			Baseline (n = 110)	949±533 (250–3,123)		
			6.4 months (n = 99)	432±269 (63–1,265)	53±17 (0–90)	
Hutchins et al (1999)	1.5/3	305 premenopausal women	US	Uterine volume (ml)	% reduction (range)	
			Baseline (n = 305)	993		
			3 months (n = 92)		48 (1–90) [44, 52]	
			2 patients had an increased uterine volume but were removed from analysis – no data given			
McLucas et al (2001)	1.5/3	167 women 155 without leuprolide, 12 with leuprolide	No leuprolide			
			US	Uterine volume (ml) (range)	% reduction	
			Baseline (n = 155)	1389 (117–8,804)		
			6 weeks (n = 125)	864 (102–4,640)	36	
			6 months (n = 98)	619 (75–3,474)	49	
			12 months (n = 46)	608 (103–3,716)	52	
Roth et al (2000)	1.5/3	81 women	MRI	Uterine volume (ml) (range)	% reduction (range)	
			Baseline (n = 79)	692±419 (84–1,961)		
			3 months (n = 71)	481±342 (73–1,875)	30±21 (–12–91) [b]	
Smith et al (2004)	1.5/3	81 women	US	Uterine volume (ml) (range)	% reduction	
			Baseline	678 (98–2,366)		
			4.3 months	504	26 [20, 33]	
			11.2 months	455	41	

Walker et al (1999)	1.5/3	200 women	US	Uterine volume (ml) (range)	% reduction
			Baseline	698 (4–5,627)	
			3 months (n = 88)		48
			6 months (n = 58)		59
			12 months (n = 69)		69
Katsumori et al (2001)	1/3	36 symptomatic women	MRI	Uterine volume (ml)	% reduction (range)
			Baseline	NR	
			4 months (n = 26)		44 (16–66)
			12 months (n = 12)		58 (21–77)

[a] Quality score is a reflection of a priori hypotheses, appropriate patient selection and adequate follow-up; [b] negative values indicate some patients experienced an increase in uterine volume; US = ultrasound; CT = computed tomography; NA = not available; MRI = magnetic resonance imaging; [c] Study by Hald et al (2004) and Park et al (2003) compared UAE with laparoscopy which is not a comparator in this report; therefore, only the results from the UAE arm are described; [d] 2 sided t-test from baseline values; [e] author's reported value; NR = not reported

Glossary

ACOG	American College of Obstetrics and Gynaecology
AGES	Australian Gynaecological Endoscopic Society
AHTA	Adelaide Health Technology Assessment
AHMAC	Australian Health Ministers' Advisory Council
AIHW	Australian Institute of Health and Welfare
AR-DRG	Australian Refined Diagnosis Related Group
95% CI	95% confidence interval
D&C	dilation and curettage
FSH	follicle stimulating hormone
GnRH	gonadotrophin releasing hormone (antagonists)
HRT	hormone replacement therapy
HYS	hysterectomy
MBS	Medicare Benefits Schedule
MRI	magnetic resonance imaging
MSAC	The Medical Services Advisory Committee
MYO	myomectomy
NA	not applicable
NR	not reported
NS	not significant
NHMRC	National Health and Medical Research Council
NNTB	number needed to treat to benefit
NNTH	number needed to treat to harm
NSAID	non-steroidal anti-inflammatory drug
PBAC	Pictorial blood loss assessment chart
RANZCR	Royal Australian and New Zealand College of Radiologists
RB	relative benefit (score)

RBC	red blood cells
RR	relative risk or rate ratio
UAE	uterine artery embolisation
US	ultrasound

References

ACOG (2004). 'Uterine artery embolization', *ACOG Committee Opinion No. 293,* 103 (2), 403–404.

Ahmad, A., Qadan, L. et al (2002). 'Uterine artery embolization treatment of uterine fibroids: Effect on ovarian function in younger women', *Journal of Vascular and Interventional Radiology,* 13 (10), 1017–1020.

Ahmad, I., Ray Jr., C.E. & Conyers, C. (2003). 'Transvaginal sonographic appearance of thrombosed uterine arteries after uterine artery embolization: The "white snake" sign', *Journal of Clinical Ultrasound,* 31 (8), 401–406.

AIHW (2005). *AIHW National Hospital Morbidity Database* [internet], Australian Institute of Health and Welfare. Available from: www.aihw.gov.au/cognos/cgi-bin/ppdscgi.exe [accessed 15/7/04].

Al Muzrakchi, A. & Szmigielski, W. (2003). 'Uterine artery embolization for the treatment of symptomatic uterine fibroids. Early experience in Hamad Medical Corporation and a review of the literature', *Qatar Medical Journal,* 12 (1), 35–39.

Alonso, A.M., Marret, H. et al (2003). 'Prospective clinical and sonographic assessment of uterine artery embolization as the treatment of symptomatic uterine leiomyomata', *Gynecologie Obstetrique Fertilite,* 31 (2), 117–122.

Andersen, P.E., Lund, N. et al (2001). 'Uterine artery embolization of symptomatic uterine fibroids. Initial success and short-term results.' *Acta Radiologica,* 42 (2), 234–238.

Aungst, M., Wilson, M. et al (2004). 'Necrotic Leiomyoma and Gram-Negative Sepsis Eight Weeks After Uterine Artery Embolization', *Obstetrics & Gynecology,* 104 (5), 1161–1164.

Australian Bureau of Statistics (2002). *A Snapshot of Australia* [internet], Australian Bureau of Statistics. Available from: www.abs.gov.au/ [accessed 14/3/05].

Bai, S.W., Jang, J.B. et al (2002). 'Uterine arterial embolization for the treatment of uterine leiomyomas', *Yonsei Medical Journal,* 43 (3), 346–350.

Baker, C.M., Winkel, C.A. et al (2002). 'Estimated costs for uterine artery embolization and abdominal myomectomy for uterine leiomyomata: A comparative study at a single institution', *Journal of Vascular and Interventional Radiology,* 13 (12), 1207–1210.

Bandolier (1999). *Diagnostic testing emerging from the gloom?* [internet], Bandolier. Available from: http://www.jr2.ox.ac.uk/bandolier/band70/b70-5.html [accessed 30/3/05]

Banovac, F., Ascher, S.M. et al (2002). 'Magnetic resonance imaging outcome after uterine artery embolization for leiomyomata with use of tris-acryl gelatin microspheres', *Journal of Vascular and Interventional Radiology,* 13 (7), 681–687.

Bapuraj, J.R., Suri, S. et al (2002). 'Uterine artery embolisation for the treatment of symptomatic uterine fibroids: short-term results of work in progress', *Australian & New Zealand Journal of Obstetrics & Gynaecology,* 42 (5), 508–512.

Bedaiwy, M.A. & Paraiso, M.F.R. (2004). 'Pelvic organ prolapse after uterine artery embolization for uterine myoma', *International Urogynecology Journal,* 15 (3), 214–215.

Beinfeld, M.T., Bosch, J.L. & Gazelle, G.S. (2002). 'Hospital costs of uterine artery embolization and hysterectomy for uterine fibroid tumors', *Academic Radiology,* 9 (11), 1300–1304.

Belenky, A., Cohen, M. & Bachar, G.N. (2001). 'Uterine arterial embolization for the management of leiomyomas', *Israel Medical Association Journal,* 3 (10), 719–721.

Berkowitz, R.P., Hutchins Jr., F.L. & Worthington-Kirsch, R.L. (1999). 'Vaginal expulsion of submucosal fibroids after uterine artery embolization. A report of three cases', *Journal of Reproductive Medicine for the Obstetrician and Gynecologist,* 44 (4), 373–376.

Borgfeldt, C. & Andolf, E. (2000). 'Transvaginal ultrasonographic findings in the uterus and the endometrium: Low prevalence of leiomyoma in a random sample of women age 25-40 years', *Acta Obstetricia et Gynecologica Scandinavica,* 79 (3), 202–207.

Bradley, E.A., Reidy, J.F. et al (1998). 'Transcatheter uterine artery embolisation to treat large uterine fibroids', *British Journal of Obstetrics and Gynaecology,* 105 (2), 235–240.

Braunwald, E., Hauser, S.L. et al (eds) (2001). *Harrison's principles of internal medicine,* McGraw-Hill, New York.

Broder, M.S., Goodwin, S. et al (2002). 'Comparison of long-term outcomes of myomectomy and uterine artery embolization', *Obstetrics & Gynecology,* 100 (5), 864–868.

Broder, M.S., Harris, K. et al (1999). *Uterine artery embolization: a systematic review of the literature and proposal for research,* RAND Corporation, USA.

Brunereau, L., Herbreteau, D. et al (2000). 'Uterine artery embolization in the primary treatment of uterine leiomyomas: Technical features and prospective follow-up with clinical and sonographic examinations in 58 patients', *American Journal of Roentgenology,* 175 (5), 1267–1272.

Bruno, J., Sterbis, K. et al (2004). 'Recovery after uterine artery embolization for leiomyomas: A detailed analysis of its duration and severity', *Journal of Vascular and Interventional Radiology,* 15 (8), 801–807.

Burn, P., McCall, J. et al (1999). 'Embolization of uterine fibroids', *British Journal of Radiology,* 72 (FEB.), 159–161.

Burn, P.R., McCall, J.M. et al (2000). 'Uterine fibroleiomyoma: MR imaging appearances before and after embolization of uterine arteries', *Radiology,* 214 (3), 729–734.

Burnham, A., Crystal, A. & Torrie, E.P.H. (2000). 'An unusual clinical and histological consequence of uterine arterial embolization of a fibroid', *Gynaecological Endoscopy,* 9, 201–203.

Carpenter, T.T. & Walker, W.J. (2005). 'Pregnancy following uterine artery embolisation for symptomatic fibroids: a series of 26 completed pregnancies', *Bjog-an International Journal of Obstetrics and Gynaecology,* 112 (3), 321–325.

Chen, C., Lu, J. et al (2002). 'Clinical analysis of 42 cases uterine myoma by uterine arterial embolization', *Zhonghua fu chan ke za zhi,* 37 (1), 8–11.

Chiu, C.Y., Wong, W.K. et al (2001). 'Uterine artery embolisation for treatment of fibroids: experience in Chinese women.' *Singapore Medical Journal,* 42 (4), 148–154.

Chrisman, H.B., Saker, M.B. et al (2000). 'The impact of uterine fibroid embolization on resumption of menses and ovarian function', *Journal of Vascular and Interventional Radiology,* 11 (6), 699–703.

Ciraru-Vigneron, N., Ravina, J.H. et al (1999). 'Pregnancy after embolisation of uterine myomata', *Minimally Invasive Therapy and Allied Technologies,* 8 (6), 407–410.

Cornelis, F., Ferrand, J. et al (1999). 'Morphological features of embolised myomata', *Minimally Invasive Therapy and Allied Technologies,* 8 (6), 437–439.

De Blok, S., De Vries, C. et al (2003). 'Fatal sepsis after uterine artery embolization with microspheres', *Journal of Vascular and Interventional Radiology,* 14 (6), 779–783.

De Iaco, P., Golfieri, R. et al (2001). 'Uterine fistula induced by hysteroscopic resection of an embolized migrated fibroid: A rare complication after embolization of uterine fibroids', *Fertility and Sterility,* 75 (4), 818–820.

De Iaco, P.A., Muzzupapa, G. et al (2002). 'A uterine wall defect after uterine artery embolization for symptomatic myomas', *Fertility and Sterility,* 77 (1), 176–178.

Delaney, M.L., Worthington-Kirsch, R.L. et al (1999). 'Uterine artery embolisation for the management of myomata in patients without complaints of menorrhagia', *Minimally Invasive Therapy and Allied Technologies,* 8 (6), 455–458.

deSouza, N.M. & Williams, A.D. (2002). 'Uterine arterial embolization for leiomyomas: Perfusion and volume changes at MR imaging and relation to clinical outcome', *Radiology,* 222 (2), 367–374.

DeWaay, D.J., Syrop, C.H. et al (2002). 'Natural history of uterine polyps and leiomyomata', *Obstetrics & Gynecology,* 100 (1), 3–7.

Dietz, D.M., Stahlfeld, K.R. et al (2004). 'Buttock necrosis after uterine artery embolization', *Obstetrics & Gynecology,* 104 (5 Pt 2), 1159–1161.

Downs, S.H. & Black, N. (1998). 'The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions', *Journal of Epidemiology and Community Health,* 52 (6), 377–384.

Egger, M., Juni, P. et al (2003). 'How important are comprehensive literature searches and the assessment of trial quality in systematic reviews? Empirical study.' *Health Technology Assessment,* 7 (1), 76.

El-Shalakany, A.H., El-Din, M.H.N. et al (2003). 'Massive vault necrosis with bladder fistula after uterine artery embolisation', *Bjog-an International Journal of Obstetrics and Gynaecology,* 110 (2), 215–216.

Felemban, A., Stein, L. & Tulandi, T. (2001). 'Uterine restoration after repeated expulsion of myomas after uterine artery embolization', *Journal of the American Association of Gynecologic Laparoscopists,* 8 (3), 442–444.

Fencl, P., Svarovsky, J. et al (2001). 'One-year experience with treatment of uterine myomas by embolization of the uterine arteries', *Ceska Radiologie,* 55 (3), 208–213.

Fleischer, A.C., Donnelly, E.F. et al (2000). 'Three-dimensional color doppler sonography before and after fibroid embolization', *Journal of Ultrasound in Medicine,* 19 (10), 701–705.

Fogt, F., Hinds, N. & Zimmerman, R. L. (2003). 'Histologic features of uterine leiomyomata treated with microsphere embolization', *Obstetrics & Gynecology,* 102 (3), 600–602.

Forman, R.G., Reidy, J. et al (1999). 'Fibroids and fertility', *Minimally Invasive Therapy and Allied Technologies,* 8 (6), 415–419.

Godfrey, C.D. & Zbella, E.A. (2001). 'Uterine necrosis after uterine artery embolization for leiomyoma', *Obstetrics & Gynecology,* 98 (5 SUPPL. 1), 950–952.

Goldberg, J., Burd, I. et al (2004a). 'Leiomyosarcoma in a premenopausal patient after uterine artery embolization', *American Journal of Obstetrics and Gynecology,* 191 (5), 1733–1735.

Goldberg, J., Pereira, L. et al (2004b). 'Pregnancy outcomes after treatment for fibromyomata: Uterine artery embolization versus laparoscopic myomectomy', *American Journal of Obstetrics and Gynecology,* 191 (1), 18–21.

Golfieri, R., Muzzi, C. et al (2000). 'The percutaneous treatment of uterine fibromas by means of transcatheter arterial embolization', *Radiologia Medica,* 100 (1–2), 48–55.

Goodwin, S.C., McLucas, B. et al (1999). 'Uterine artery embolization for the treatment of uterine leiomyomata midterm results', *Journal of Vascular and Interventional Radiology,* 10 (9), 1159–1165.

Goodwin, S.C., Vedantham, S. et al (1997). 'Preliminary experience with uterine artery embolization for uterine fibroids', *Journal of Vascular and Interventional Radiology,* 8 (4), 517–526.

Goodwin, S.C. & Walker, W.J. (1998). 'Uterine artery embolization for the treatment of uterine fibroids', *Current Opinion in Obstetrics and Gynecology,* 10 (4), 315–320.

Hald, K., Langebrekke, A. et al (2004). 'Laparoscopic occlusion of uterine vessels for the treatment of symptomatic fibroids: Initial experience and comparison to uterine artery embolization', *American Journal of Obstetrics and Gynecology,* 190 (1), 37–43.

Hascalik, S., Celik, O. et al (2004). 'Transient ovarian failure: a rare complication of uterine fibroid embolization', *Acta Obstetricia Et Gynecologica Scandinavica,* 83 (7), 682–685.

Healey, S., Buzaglo, K. et al (2004). 'Ovarian function after uterine artery embolization and hysterectomy', *Journal of the American Association of Gynecologic Laparoscopists,* 11 (3), 348–352.

Hehenkamp, W.J., Volkers, N.A. et al (2004). 'Myoma expulsion after uterine artery embolization: Complication or cure?' *American Journal of Obstetrics and Gynecology,* 191 (5), 1713–1715.

Hovsepian, D.M., Siskin, G.P. et al (2004). 'Quality improvement guidelines for uterine artery embolization for symptomatic leiomyomata', *Journal of Vascular and Interventional Radiology,* 15, 535–542.

Huang, L.Y., Cheng, Y.F. et al (2004). 'Quantified short-term outcome of uterine artery embolization with gelatin sponge particles and lipiodol for symptomatic myoma', *Fertility and Sterility,* 81 (5), 1375–1382.

Hutchins Jr., F.L., Worthington-Kirsch, R. & Berkowitz, R.P. (1999). 'Selective uterine artery embolization as primary treatment for symptomatic leiomyomata uteri', *Journal of the American Association of Gynecologic Laparoscopists,* 6 (3), 279–284.

Indman, P. (2000). *Advanced Gynaecology Solutions: Fibroids* [internet]. Available from: http://www.gynalternatives.com/fibroids [accessed 27/10/04].

Jha, R.C., Ascher, S.M. et al (2000). 'Symptomatic fibroleiomyomata: MR imaging of the uterus before and after uterine arterial embolization', *Radiology,* 217 (1), 228–235.

Joffre, F., Tubiana, J.M. & Pelage, J.P. (2004). 'FEMIC (Fibromes Embolises aux MICrospheres calibrees): Uterine Fibroid Embolization using Tris-acryl Microspheres. A French Multicenter Study', *CardioVascular and Interventional Radiology,* 27 (6), 600–606.

Jones, K., Walker, W. & Sutton, C. (2000). 'Sequestration and extrusion of intramural fibroids following arterial emolization: a case series', *Gynaecological Endoscopy,* 9, 309–313.

Joyce, A., Hessami, S. & Heller, D. (2001). 'Leiomyosarcoma after uterine artery embolization: A case report', *Journal of Reproductive Medicine for the Obstetrician and Gynecologist,* 46 (3), 278–280.

Juni, P., Altman, D.G. & Egger, M. (2001). 'Systematic reviews in health care: assessing the quality of controlled clinical trials', *British Medical Journal,* 323 (7303), 42–46.

Katsumori, T., Nakajima, K. & Tokuhiro, M. (2001). 'Gadolinium-enhanced MR imaging in the evaluation of uterine fibroids treated with uterine artery embolization', *American Journal of Roentgenology,* 177 (2), 303–307.

Katsumori, T., Nakajima, K. et al (2002). 'Uterine artery embolization using gelatin sponge particles alone for symptomatic uterine fibroids: Midterm results', *American Journal of Roentgenology,* 178 (1), 135–139.

Kerlan, R.K., Coffey, J.O. et al (2003). 'Massive vaginal hemorrhage after uterine fibroid embolization', *Journal of Vascular and Interventional Radiology,* 14 (11), 1465–1467.

Khan, K.S., Ter Riet, G. et al (2001). *Undertaking systematic reviews of research on effectiveness. CRD's guidance for those carrying out or commissioning reviews,* NHS Centre for Reviews and Dissemination, University of York, York.

Khaund, A., Moss, J.G. et al (2004). 'Evaluation of the effect of uterine artery embolisation on menstrual blood loss and uterine volume', *Bjog-an International Journal of Obstetrics and Gynaecology,* 111 (7), 700–705.

Klein, A., Schwartz, M.L. et al (2001). 'Uterine artery embolization for the treatment of uterine fibroids: An outpatient procedure', *American Journal of Obstetrics and Gynecology,* 184 (7), 1556–1563.

Kroencke, T.J., Gauruder-Burmester, A. et al (2004). 'Technical success rate, peri-interventional complications and radiation exposure of the transarterial embolization for leiomyomas of the uterus', *Rofo-Fortschritte Auf Dem Gebiet Der Rontgenstrahlen Und Der Bildgebenden Verfahren,* 176 (4), 580–589.

Kroencke, T.J., Gauruder-Burmester, A. et al (2005). 'Transarterial embolization for uterine fibroids: Clinical success rate and results of magnetic resonance imaging', *Rofo-Fortschritte Auf Dem Gebiet Der Rontgenstrahlen Und Der Bildgebenden Verfahren,* 177 (1), 89–98.

Kuhn, R. & Mitchell, P. (1999). 'Embolic occlusion of the blood supply to uterine myomas: Report of 2 cases', *Australian and New Zealand Journal of Obstetrics and Gynaecology,* 39 (1), 120–122.

Lai, A.C., Goodwin, S.C. et al (2000). 'Sexual dysfunction after uterine artery embolization', *Journal of Vascular and Interventional Radiology,* 11 (6), 755–758.

Lang, E.K. & Myers, L. (2004). 'Outcome of superselective uterine artery embolization of fibroids', *Journal of Women's Imaging,* 6 (1), 23–30.

Laverge, F., D'Angelo, A. et al (2003). 'Spontaneous expulsion of three large fibroids after uterine artery embolization', *Fertility and Sterility,* 80 (2), 450–452.

Li, L., Chen, Y. et al (2004). 'Effect of superselective uterine artery embolization on the quality of life of patients with symptomatic uterine myoma', *Chinese Journal of Clinical Rehabilitation,* 8 (23), 4676–4677.

Li, W., Brophy, D.P. et al (2000). 'Semiquantitative assessment of uterine perfusion using first pass dynamic contrast-enhanced MR imaging for patients treated with uterine fibroid embolization', *Journal of Magnetic Resonance Imaging,* 12 (6), 1004–1008.

Lijmer, J.G., Mol, B.W. et al (1999). 'Empirical evidence of design-related bias in studies of diagnostic tests.' *Journal of the American Medical Association,* 282 (11), 1061–1066.

Lippman, S.A., Warner, M. et al (2003). 'Uterine fibroids and gynecologic pain symptoms in a population-based study', *Fertility and Sterility,* 80 (6), 1488–1494.

Lohle, P.N.M., Lampmann, L.E.H. et al (2001). 'Embolisation as a treatment for symptomatic uterine myomata', *Nederlands Tijdschrift voor Geneeskunde,* 145 (16), 791–794.

Lowenstein, L., Solt, I. et al (2004). 'Focal cervical and vaginal necrosis following uterine artery embolisation [7]', *European Journal of Obstetrics Gynecology and Reproductive Biology,* 116 (2), 250–251.

Maggino, T., De Rita, R. et al (1990). 'Prevalence and risk factors of uterine fibromas in asymptomatic women', *Journal of Gynaecological Endocrinology,* 6 (1–4), 15–20.

Maltau, J.M., Kumar, S. et al (2003). 'Embolization of uterine myoma', *Tidsskrift for den Norske Laegeforening,* 123 (5), 614–616.

Manyonda, I.T., Sinthamoney, E. et al (2003). 'Uterine artery embolisation for symptomatic fibroids: clinical results in 400 women with imaging follow up', *Bjog-an International Journal of Obstetrics and Gynaecology,* 110 (12), 1139–1139.

Marino, J.L., Eskenazi, B. et al (2004). 'Uterine leiomyoma and menstrual cycle characteristics in a population-based cohort study', *Human Reproduction,* 19 (10), 2350–2355.

Marret, H., Alonso, A.M. et al (2003). 'Leiomyoma recurrence after uterine artery embolization', *Journal of Vascular and Interventional Radiology,* 14 (11), 1395–1399.

Maskova, J., Drbohlav, P. et al (2001). 'Endovascular treatment of uterine leiomyomata: Our first experience', *Ceska Radiologie,* 55 (6), 364–369.

McLucas, B. & Adler, L. (2000). 'Uterine artery embolization as therapy for myomata', *Infertility and Reproductive Medicine Clinics of North America,* 11 (1), 77–94.

McLucas, B. & Adler, L. (2001). 'Uterine fibroid embolization compared with myomectomy', *International Journal of Gynecology and Obstetrics,* 74 (3), 297–299.

McLucas, B., Adler, L. & Perrella, R. (1999). 'Predictive factors for success in uterine fibroid embolisation', *Minimally Invasive Therapy and Allied Technologies,* 8 (6), 429–432.

McLucas, B., Adler, L. & Perrella, R. (2001a). 'Uterine fibroid embolization: Nonsurgical treatment for symptomatic fibroids', *Journal of the American College of Surgeons,* 192 (1), 95–105.

McLucas, B., Goodwin, S.C. & Perrella, R. (1998). 'Embolisation of myomata for pelvic haemorrhage: An alternative to hysterectomy', *Minimally Invasive Therapy and Allied Technologies,* 7 (3), 261–265.

McLucas, B., Goodwin, S. et al (2001b). 'Pregnancy following uterine fibroid embolization', *International Journal of Gynecology and Obstetrics,* 74 (1), 1–7.

McLucas, B., Reed, R.A. et al (2002). 'Outcomes following unilateral uterine artery embolisation', *British Journal of Radiology,* 75 (890), 122–126.

Mehta, H., Sandhu, C. et al (2002). 'Review of readmissions due to complications from uterine fibroid embolization', *Clinical Radiology,* 57 (12), 1122–1124.

Messina, M.L., Bozzini, N. et al (2002). 'Uterine artery embolization for the treatment of uterine leiomyomata', *International Journal of Gynecology and Obstetrics,* 79 (1), 11–16.

Moher, D., Pham, B. et al (1998). 'Does quality of reports of randomised trials affect estimates of intervention efficacy reported in meta-analyses?' *Lancet,* 352 (9128), 609–613.

Murgo, S., Simon, P. & Golzarian, J. (2002). 'Embolization of uterine fibroids', *Revue medicale de Bruxelles,* 23 (5), 435–442.

NHMRC (1999). *A guide to the development, implementation and evaluation of clinical practice guidelines,* National Health and Medical Research Council, Commonwealth of Australia, Canberra, ACT.

NHMRC (2000). *How to use the evidence: assessment and application of scientific evidence,* National Health and Medical Research Council, Canberra.

NHMRC (2001). *How to compare the costs and benefits: evaluation of the economic evidence,* National Health and Medical Research Council, Canberra.

NHMRC (2005). *NHMRC additional levels of evidence and grades for recommendations for developers of guidelines* [internet], NHMRC. Available from: www.health.gov.au/nhmrc/ [accessed 2/6/05].

Nicholson, T. (2004). 'Outcome in patients undergoing unilateral uterine artery embolization for symptomatic fibroids', *Clinical Radiology,* 59 (2), 186–191.

Nicholson, T.A., Pelage, J.P. & Ettles, D.F. (2001). 'Fibroid calcification after uterine artery embolization: Ultrasonographic appearance and pathology', *Journal of Vascular and Interventional Radiology,* 12 (4), 443–446.

Nikolic, B., Nguyen, K. et al (2004). 'Pyosalpinx developing from a preexisting hydrosalpinx after uterine artery embolization', *Journal of Vascular and Interventional Radiology,* 15 (3), 297–301.

Nikolic, B., Spies, J.B. et al (2000). 'Patient radiation dose associated with uterine artery embolization', *Radiology,* 214 (1), 121–125.

Park, K.-H., Kim, J.-Y. et al (2003). 'Treatment outcomes of uterine artery embolization and laparoscopic uterine artery ligation for uterine myoma', *Yonsei Medical Journal,* 44 (4), 694–702.

Payne, J.F. & Haney, A.F. (2003). 'Serious complications of uterine artery embolization for conservative treatment of fibroids', *Fertility and Sterility,* 79 (1), 128–131.

Payne, J.F., Robboy, S.J. & Haney, A.F. (2002). 'Embolic microspheres within ovarian arterial vasculature after uterine artery embolization', *Obstetrics & Gynecology,* 100 (5), 883–886.

Pelage, J.-P., Guaou, N.G. et al (2004). 'Uterine fibroid tumors: Long-term MR imaging outcome after embolization', *Radiology,* 230 (3), 803–809.

Pelage, J.-P., Le Dref, O. et al (2000). 'Fibroid-related menorrhagia: Treatment with superselective embolization of the uterine arteries and midterm follow-up', *Radiology,* 215 (2), 428–431.

Pelage, J.-P., Le Dref, O. et al (2003). 'Limited uterine artery embolization with tris-acryl gelatin microspheres for uterine fibroids', *Journal of Vascular and Interventional Radiology,* 14 (1), 15–20.

Phillips, B., Ball, C. et al (2001). *Oxford Centre for Evidence-Based Medicine Levels of Evidence (May 2001)* [internet], Centre for Evidence-Based Medicine. Available from: http://www.cebm.net/levels_of_evidence.asp [accessed 28/1/04].

Pinto, I., Chimeno, P. et al (2002). 'Embolization of uterine arteries to treat symptomatic myomas', *Radiologia,* 44 (5), 201–206.

Pinto, I., Chimeno, P. et al (2003). 'Uterine fibroids: Uterine artery embolization versus abdominal hysterectomy for treatment - A prospective, randomized, and controlled clinical trial', *Radiology,* 226 (2), 425–431.

Pourrat, X.J.L., Fourquet, F. et al (2003). 'Medico-economic approach to the management of uterine myomas: a 6-month cost-effectiveness study of pelvic embolization versus vaginal hysterectomy', *European Journal of Obstetrics Gynecology and Reproductive Biology,* 111 (1), 59–64.

Prollius, A., de Vries, C. et al (2004a). 'Uterine artery embolisation for symptomatic fibroids: the effect of the large uterus on outcome', *Bjog-an International Journal of Obstetrics and Gynaecology,* 111 (3), 239–242.

Prollius, A., de Vries, C. et al (2004b). 'Uterine artery embolization for symptomatic fibroids', *International Journal of Gynecology and Obstetrics,* 84 (3), 236–240.

Pron, G., Bennett, J. et al (2003a). 'Technical results and effects of operator experience on uterine artery embolization for fibroids: The Ontario Uterine Fibroid Embolization Trial', *Journal of Vascular and Interventional Radiology,* 14 (5), 545–554.

Pron, G., Bennett, J. et al (2003b). 'The Ontario Uterine Fibroid Embolization Trial. Part 2. Uterine fibroid reduction and symptom relief after uterine artery embolization for fibroids', *Fertility and Sterility,* 79 (1), 120–127.

Pron, G., Mocarski, E. et al (2003c). 'Tolerance, hospital stay, and recovery after uterine artery embolization for fibroids: The Ontario Uterine Fibroid Embolization Trial', *Journal of Vascular and Interventional Radiology,* 14 (10), 1243–1250.

Pron, G., Mocarski, E. et al (2003d). 'Hysterectomy for complications after uterine artery embolization for leiomyoma: Results of a Canadian multicenter clinical trial', *Journal of the American Association of Gynecologic Laparoscopists,* 10 (1), 99–106.

Pron, G., Mocarski, E. et al (2003e). 'Pregnancy after fibroid uterine artery embolization - results from the Ontario Uterine Fibroid Embolization Trial', *Fertility and Sterility,* 80, S88–S89.

Pron, G., Mocarski, E. et al (2005). 'Pregnancy after uterine artery embolization for leiomyomata: the Ontario multicenter trial', *Obstetrics & Gynecology,* 105 (1), 67–76.

Pugh, M. (2000). *Stedman's medical dictionary*. 27th edition, Lippincott Williams & Wilkins, Philadelphia.

RANZCR (2004). *MSAC Application 1081. Uterine Artery Embolisation,* Royal Australian and New Zealand College of Radiologists, Sydney, New South Wales.

Rastogi, S., Wu, Y.-H. et al (2004). 'Acute renal failure after uterine artery embolization', *CardioVascular and Interventional Radiology,* 27 (5), 549–550.

Ravina, J.H., Aymard, A. et al (1998). 'Selective arterial embolization for hemorrhagic uterine leiomyomas', *Presse Medicale,* 27 (7), 299–303.

Ravina, J.H., Aymard, A. et al (2000a). 'Arterial embolization of uterine myomata: Results in 286 cases', *Journal de Gynecologie Obstetrique et Biologie de la Reproduction,* 29 (3), 272–275.

Ravina, J.-H., Aymard, A. et al (2003). 'Uterine fibroids embolization: Results about 454 cases', *Gynecologie Obstetrique Fertilite,* 31 (7–8), 597–605.

Ravina, J.H., Bouret, J.M. et al (1995a). 'Advantage of pre-operative embolization of fibroids: About a multicentric set of 31 cases', *Contraception Fertilite Sexualite,* 23 (1), 45–49.

Ravina, J.H., Bouret, J.M. et al (1997). 'Recourse to particular arterial embolization in the treatment of some uterine leiomyoma', *Bulletin de l'Academie Nationale de Medecine,* 181 (2), 233–243; discussion 244.

Ravina, J.H., Herbreteau, D. et al (1995b). 'Arterial embolisation to treat uterine myomata', *Lancet,* 346 (8976), 671–672.

Ravina, J.H., Merland, J.J. et al (1994). 'Preoperative embolization of uterine fibroma. Preliminary results (10 cases)', *Presse medicale (Paris, France: 1983),* 23, 1540–1533.

Ravina, J.H., Vigneron, N.C. et al (2000b). 'Pregnancy after embolization of uterine myoma: Report of 12 cases', *Fertility and Sterility,* 73 (6), 1241–1243.

Razavi, M.K., Hwang, G. et al (2003). 'Abdominal myomectomy versus uterine fibroid embolization in the treatment of symptomatic uterine leiomyomas', *American Journal of Roentgenology,* 180 (6), 1571–1575.

Razavi, M.K., Wolanske, K.A. et al (2002). 'Angiographic classification of ovarian artery-to-uterine artery anastomoses: Initial observations in uterine fibroid embolization', *Radiology,* 224 (3), 707–712.

Richter, G.M., Radeleff, B. et al (2004). '[Uterine fibroid embolization with spheric micro-particles using flow guiding: safety, technical success and clinical results]', *Rofo-Fortschritte Auf Dem Gebiet Der Rontgenstrahlen Und Der Bildgebenden Verfahren,* 176 (11), 1648–1657.

Roth, A.R., Spies, J.B. et al (2000). 'Pain after uterine artery embolization for leiomyomata: Can its severity be predicted and does severity predict outcome?' *Journal of Vascular and Interventional Radiology,* 11 (8), 1047–1052.

Ryu, R.K., Omary, R.A. et al (2003). 'Comparison of pain after uterine artery embolization using tris-acryl gelatin microspheres versus polyvinyl alcohol particles', *CardioVascular and Interventional Radiology,* 26 (4), 375–378.

Sabatini, L., Atiomo, W. & Magos, A. (2003). 'Successful myomectomy following infected ischaemic necrosis of uterine fibroids after uterine artery embolisation', *Bjog-an International Journal of Obstetrics and Gynaecology,* 110 (7), 704–706.

Salerno, S. & Belli, A.M. (2001). 'Percutaneous treatment of uterine fibroleiomyomas: analysis of complications and quality of life after embolization', *Radiologia Medica,* 101 (5), 360–364.

Schulz, K.F., Chalmers, I. et al (1995). 'Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials', *Journal of the American Medical Association,* 273 (5), 408–412.

Sena-Martins, M., Roteli-Martins, C.M. et al (2003). 'Uterine artery embolization for the treatment of symptomatic myomas in Brazilian women', *Sao Paulo Medical Journal,* 121 (5), 185–190.

Shan, H., Huang, M.-S. et al (2004). 'Superselective uterine arterial embolization with pingyangmycin-lipiodol emulsion for management of symptomatic uterine leiomyoma', *Chinese Medical Journal,* 117 (1), 75–78.

Shashoua, A.R., Stringer, N.H. et al (2002). 'Ischemic uterine rupture and hysterectomy 3 months after uterine artery embolization', *Journal of the American Association of Gynecologic Laparoscopists,* 9 (2), 217–220.

Simonetti, G., Romanini, C. et al (2001). 'Embolization of the uterine artery in the treatment of uterine myoma', *Radiologia Medica,* 101 (3), 157–164.

Siskin, G.P., Stainken, B.F. et al (2000). 'Outpatient uterine artery embolization for symptomatic uterine fibroids: Experience in 49 patients', *Journal of Vascular and Interventional Radiology,* 11 (3), 305–311.

Siskin, G.P., Tublin, M.E. et al (2001). 'Uterine artery embolization for the treatment of adenomyosis: Clinical response and evaluation with MR imaging', *American Journal of Roentgenology,* 177 (2), 297–302.

Smith, S. J. (2000). 'Uterine fibroid embolization', *American Family Physician,* 61, 3601–3607, 3611–3602.

Smith, S.J., Sewall, L.E. & Handelsman, A. (1999). 'A clinical failure of uterine fibroid embolization due to adenomyosis', *Journal of Vascular and Interventional Radiology,* 10 (9), 1171–1174.

Smith, W.J., Upton, E. et al (2004). 'Patient satisfaction and disease specific quality of life after uterine artery embolization', *American Journal of Obstetrics and Gynecology,* 190 (6), 1697–1703.

Spies, J.B., Allison, S. et al (2004a). '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,* 15 (8), 793–800.

Spies, J.B., Ascher, S.A. et al (2001a). 'Uterine artery embolization for leiomyomata', *Obstetrics & Gynecology,* 98 (1), 29–34.

Spies, J.B., Benenati, J.F. et al (2001b). 'Initial experience with use of tris-acryl gelatin microspheres for uterine artery embolization for leiomyomata', *Journal of Vascular and Interventional Radiology,* 12 (9), 1059–1063.

Spies, J.B., Cooper, J.M. et al (2004b). 'Outcome of uterine embolization and hysterectomy for leiomyomas: Results of a multicenter study', *American Journal of Obstetrics and Gynecology,* 191 (1), 22–31.

Spies, J., Niedzwiecki, G. et al (2003). 'Training standards for physicians performing uterine artery embolization for leiomyomata. Consensus statement developed by the Task Force on Uterine Artery Embolization and the Standards Division of the Society of Interventional Radiology–August 2000', *Journal of Vascular and Interventional Radiology,* 14 (9 Pt 2), S369–S371.

Spies, J.B., Roth, A.R. et al (2001c). 'Ovarian function after uterine artery embolization for leiomyomata: assessment with use of serum follicle stimulating hormone assay.' *Journal of Vascular and Interventional Radiology,* 12 (4), 437–442.

Spies, J.B., Roth, A.R. et al (2002a). 'Leiomyomata treated with uterine artery embolization: Factors associated with successful symptom and imaging outcome', *Radiology,* 222 (1), 45–52.

Spies, J.B., Spector, A. et al (2002b). 'Complications after uterine artery embolization for leiomyomas', *Obstetrics & Gynecology,* 100 (5), 873–880.

Spies, J.B., Warren, E.H. et al (1999). 'Uterine fibroid embolization: Measurement of health-related quality of life before and after therapy', *Journal of Vascular and Interventional Radiology,* 10 (10), 1293–1303.

Stancato-Pasik, A., Katz, R. et al (1999). 'Uterine artery embolisation of myomas: Preliminary results of gelatin sponge pledgets as the embolic agent', *Minimally Invasive Therapy and Allied Technologies,* 8 (6), 393–396.

Stata Corporation (2004). *Intercooled Stata 8.2 for Windows,* Stata Corporation, College City, Texas.

Stringer, N.H., DeWhite, A. et al (2001). 'Laparoscopic myomectomy after failure of uterine artery embolization', *Journal of the American Association of Gynecologic Laparoscopists,* 8 (4), 583–586.

Stringer, N.H., Grant, T. et al (2000). 'Ovarian failure after uterine artery embolization for treatment of myomas', *Journal of the American Association of Gynecologic Laparoscopists,* 7 (3), 395–400.

Sultana, C.J., Goldberg, J. et al (2002). 'Vesicouterine fistula after uterine artery embolization: A case report', *American Journal of Obstetrics and Gynecology,* 187 (6), 1726–1727.

Szabo, E., Nagy, E. et al (2001). 'Uterine artery embolization for the conservative management of leiomyoma', *Orvosi Hetilap,* 142 (13), 675–680.

Takeda, T., Osuga, K. et al (2004). 'A case of generalised oedema secondary to uterine artery embolisation for leiomyomata', *Bjog-an International Journal of Obstetrics and Gynaecology,* 111 (2), 179–180.

Tan, T.L. & Rafla, N. (2004). 'Retained calcified fibroid fragments after uterine artery embolization for fibroids', *Fertility and Sterility,* 81 (4), 1145–1147.

Technology Evaluation Center (2002). *Uterine artery embolization for treatment of symptomatic uterine fibroids,* Blue Cross and Blue Shield Association, Chicago, Illinois.

Toh, C.-H., Wu, C.-H. et al (2003). 'Uterine artery embolization for symptomatic uterine leiomyoma and adenomyosis', *Journal of the Formosan Medical Association,* 102 (10), 701–706.

Topfer, L., Hailey, D. (2002). *Issues in Emerging Health Technologies: Uterine artery embolization for the treatment of fibroids,* Canadian Coordinating Office for Health Technology Assessment, Ottawa.

Tranquart, F., Brunereau, L. et al (2002). 'Prospective sonographic assessment of uterine artery embolization for the treatment of fibroids', *Ultrasound in Obstetrics and Gynecology,* 19 (1), 81–87.

Tropeano, G., Di Stasi, C. et al (2004). 'Uterine artery embolization for fibroids does not have adverse effects on ovarian reserve in regularly cycling women younger than 40 years', *Fertility and Sterility,* 81 (4), 1055–1061.

Tropeano, G., Litwicka, K. et al (2003). 'Permanent amenorrhea associated with endometrial atrophy after uterine artery embolization for symptomatic uterine fibroids', *Fertility and Sterility,* 79 (1), 132–135.

Tulandi, T., Sammour, A. et al (2002). 'Ovarian reserve after uterine artery embolization for leiomyomata', *Fertility and Sterility,* 78 (1), 197–198.

Van der Leij, G. & Lammes, F.B. (1997). 'Prevalence of hysteroscopic abnormalities and anomalies observed in a population without gynaecological complaints', *Gynaecological Endoscopy,* 6 (6), 347–351.

Vashisht, A., Studd, J. et al (1999). 'Fatal septicaemia after fibroid embolisation', *Lancet,* 354 (9175), 307–308.

Vashisht, A., Studd, J.W.W. et al (2000). 'Fibroid embolisation: A technique not without significant complications', *British Journal of Obstetrics and Gynaecology,* 107 (9), 1166–1170.

Walker, W., Green, A. & Sutton, C. (1999). 'Bilateral uterine artery embolisation for myomata: Results, complications and failures', *Minimally Invasive Therapy and Allied Technologies,* 8 (6), 449–454.

Walker, W.J., Carpenter, T.T. & Kent, A.S.H. (2004). 'Persistent vaginal discharge after uterine artery embolization for fibroid tumors: Cause of the condition, magnetic resonance imaging appearance, and surgical treatment', *American Journal of Obstetrics and Gynecology,* 190 (5), 1230–1233.

Walker, W.J. & Pelage, J.P. (2002). 'Uterine artery embolisation for symptomatic fibroids: clinical results in 400 women with imaging follow up', *Bjog-an International Journal of Obstetrics and Gynaecology,* 109 (11), 1262–1272.

Wang, J., Zhang, G.Y. et al (2002). 'Dextran uterine artery embolization to treat fibroids', *Chinese Medical Journal,* 115 (8), 1132–1136.

Watson, G.M.T. & Walker, W.J. (2002). 'Uterine artery embolisation for the treatment of symptomatic fibroids in 114 women: reduction in size of the fibroids and women's views of the success of the treatment', *Bjog-an International Journal of Obstetrics and Gynaecology,* 109 (2), 129–135.

Weintraub, J.L., Romano, W.J. et al (2002). 'Uterine artery embolization - Sonographic imaging findings', *Journal of Ultrasound in Medicine,* 21 (6), 633–637.

Whiting, P., Rutjes, A.W.S. et al (2003). The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. *BMC Medical Research Methodology*, 3, 25.

Wolanske, K.A., Gordon, R.L. et al (2003). 'Reversal of flow in the ovarian artery during uterine artery embolization', *Journal of Vascular and Interventional Radiology,* 14 (6), 785–787.

Worthington-Kirsch, R.L., Smith, S.J. & Berkowitz, R.P. (1999). 'Transient buttock pain after uterine artery embolisation for the management of fibroids', *Minimally Invasive Therapy and Allied Technologies,* 8 (6), 425–427.

Yeagley, T.J., Goldberg, J. et al (2002). 'Labial necrosis after uterine artery embolization for leiomyomata', *Obstetrics & Gynecology,* 100 (5), 881–882.

Young, J., Hyde, C. et al (1999). 'Lung volume reduction surgery (LVRS) for chronic obstructive pulmonary disease (COPD) with underlying severe emphysema.' *Thorax,* 54 (9), 779–789.

Zhou, S.-K., Li, S.-B. & Zhang, H.-W. (2003a). 'Interventional therapy in the treatment of hysteromyoma', *Bulletin of Hunan Medical University,* 28 (1), 79–82.

Zhou, S.-K., Li, S.-B. & Zhang, Z.-S. (2003b). 'Influential factors to therapeutic efficacy of uterine artery embolization in the treatment of uterine fibroids', *Bulletin of Hunan Medical University,* 28 (4), 409–411.

Zupi, E., Pocek, M. et al (2003). 'Selective uterine artery embolization in the management of uterine myomas', *Fertility and Sterility,* 79 (1), 107–111.