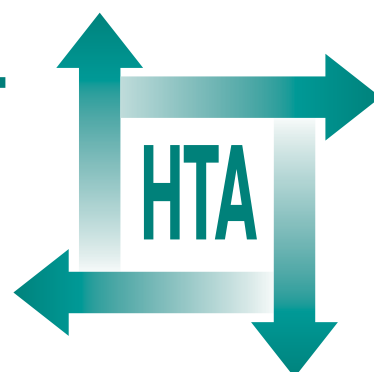


## **A multi-centre retrospective cohort study comparing the efficacy, safety and cost-effectiveness of hysterectomy and uterine artery embolisation for the treatment of symptomatic uterine fibroids. The HOPEFUL study**

A Hirst, S Dutton, O Wu, A Briggs,  
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A Nicholson and K McPherson

March 2008

**Health Technology Assessment**  
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The research reported in this issue of the journal was commissioned by the HTA Programme as project number 03/60/01. The contractual start date was in December 2003. The draft report began editorial review in October 2006 and was accepted for publication in July 2007. As the funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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## Abstract

### **A multi-centre retrospective cohort study comparing the efficacy, safety and cost-effectiveness of hysterectomy and uterine artery embolisation for the treatment of symptomatic uterine fibroids. The HOPEFUL study**

A Hirst,<sup>1</sup> S Dutton,<sup>1</sup> O Wu,<sup>2</sup> A Briggs,<sup>2</sup> C Edwards,<sup>3</sup> L Waldenmaier,<sup>1</sup> M Maresh,<sup>4</sup> A Nicholson<sup>5</sup> and K McPherson<sup>1\*</sup>

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**Objectives:** To examine and compare the medium-term results of hysterectomy and uterine artery embolisation (UAE) as a treatment for symptomatic uterine fibroids with regard to safety, efficacy, special issues in the UAE group, cost-effectiveness, and women's own perspectives on the treatments.

**Design:** Data were collected locally from patients' hospital records and also from patients themselves by postal questionnaire. Questionnaire data included free-text comments and this qualitative material was analysed using constant comparison. A two-stage probabilistic decision model was designed to estimate UK NHS costs and health outcomes in terms of quality-adjusted life-years (QALYs).

**Setting:** Eighteen NHS hospital trusts, 17 in England and one in Scotland.

**Participants:** Eligible women (972 UAE, 762 hysterectomies) who had received treatment specifically for symptomatic fibroids were identified.

**Interventions:** The UAE patients were treated by experienced interventional radiologists and all received their index UAE prior to the end of 2002, ensuring a minimum 2-year follow-up. The average length of follow-up was 8.6 years for the hysterectomy cohort and 4.6 years for the UAE cohort.

**Main outcome measures:** Primary outcome measures were complication rates to assess the comparative safety of the two interventions. Secondary outcome measures related to treatment efficacy including resolution of symptoms and patient-reported satisfaction with treatment. Further efficacy outcome

measures obtained in the UAE group included fibroid/uterine size shrinkage and further treatments required for unresolved fibroid symptoms. Data were also gathered on pregnancies post-UAE.

**Results:** Data were available for 1108 women (649 UAE and 459 hysterectomy). Fewer complications were experienced by women in the UAE cohort compared to the hysterectomy cohort: hysterectomy  $n = 120$  (26.1%), UAE  $n = 114$  (17.6%), adjusted odds ratio 0.48 [95% confidence interval (CI) 0.26 to 0.89]. When only the severe/major complications were considered, this odds ratio was reduced to 0.25 (95% CI 0.13 to 0.48). Expected general side-effects of UAE occurred in 32.7% of the UAE cohort, of which 8.9% also experienced complications. Obesity and medical co-morbidity predisposed women to complications, whereas prophylactic antibiotics appeared to protect against both complications and the expected side-effects of UAE. More women in the hysterectomy cohort reported relief from fibroid symptoms (89% versus 80% UAE,  $p < 0.0001$ ) and feeling better (81% versus 74% UAE,  $p < 0.0001$ ), but only 70% (compared with 86% UAE,  $p = 0.007$ ) would recommend their treatment to a friend. In the UAE cohort, 18.3% of the women went on to receive one or more further fibroid treatments including hysterectomy (11.2%). After adjusting for differential time of follow-up, the UAE women had up to a 23% (95% CI 19 to 27%) likelihood of requiring further treatment. The free-text data indicated that many women, in both cohorts, felt that their treatment had

been a complete success. In the UAE cohort there were several areas where expectations were apparently high and outcome had not fulfilled their expectations. Disappointment was expressed mainly about continuation or return of symptoms or failure to become pregnant. Many continued to have remaining questions about their treatment. The economic analysis indicated that UAE is less expensive than hysterectomy even after further treatments for unresolved or recurrent symptoms are taken into account, with little difference in QALYs between the two treatments. Younger women are exposed to the risk of recurrent fibroids and subsequent additional procedures over a longer period and consequently UAE may no longer be cost-effective. **Conclusions:** The study results suggest that both UAE and hysterectomy are safe. No unexpected problems were detected following UAE after a long follow-up period (average 5 years). Complications are less common for UAE than hysterectomy. The cost-effectiveness analysis favours embolisation even after

taking account of complications, expected side-effects associated with the procedure and subsequent re-treatments for women with a preference for uterus preservation. It is important to improve the management of expectations following UAE, particularly regarding fertility. The data suggested that fertility and miscarriage rate are consistent with those of age-matched women with fibroids. UAE is an effective treatment for some women with fibroids and our trial supports the National Institute for Health and Clinical Excellence guidance that it should be made available as one of the options for treatment, with a possible reduction in the need for hysterectomy as the first-line treatment. Further research is needed into which women will be treated most successfully by UAE, the best method of achieving effective embolisation, advice for women who desire future fertility, the role of prophylactic antibiotics in UAE, and the effects of HRT use after UAE on recurrence of fibroid symptoms.



# Contents

<b>List of abbreviations</b> .....	vii	Predictors of outcome .....	77
<b>Executive summary</b> .....	ix	Post-UAE fertility .....	79
<b>1 Background and rationale</b> .....	1	Key findings – UAE cohort only .....	80
Uterine fibroids .....	1	<b>8 Health economics</b> .....	81
Treatments for symptomatic fibroids .....	1	Introduction .....	81
Status of UAE – evidence review .....	3	Literature review .....	81
<b>2 Methods</b> .....	17	Methods .....	82
Study design and objectives: introductory	17	Results .....	90
remarks .....	17	Discussion .....	92
Participant recruitment .....	18	Conclusions .....	95
Treatments .....	19	<b>9 Analysis of additional free-text</b>	
Study procedures .....	20	<b>comments</b> .....	97
Flow of patient numbers .....	29	Introduction .....	97
Confounding variables .....	29	Free-text comments about the experience	
Outcome measures .....	32	of hysterectomy .....	97
UAE-specific topics .....	39	Discussion of hysterectomy findings .....	102
<b>3 Analysis</b> .....	41	Free-text comments about the experience	
Statistical analysis .....	41	of UAE .....	103
Free-text analysis .....	44	Discussion of UAE findings .....	108
Health economics methods .....	45	Conclusions .....	109
<b>4 Results: recruitment, baseline</b>		Key findings – free-text .....	110
<b>characteristics, confounders and</b>		<b>10 Discussion</b> .....	111
<b>missing values</b> .....	47	Introduction .....	111
Recruitment .....	47	Methodological/design issues .....	111
Baseline characteristics .....	47	Results .....	112
Confounders .....	50	<b>11 Conclusions</b> .....	117
Missing values and primary outcome		Introduction .....	117
analysis .....	52	Implications for healthcare .....	117
Key findings – baseline characteristics .....	52	Implications for further research .....	119
<b>5 Results: primary outcome measures</b> .....	53	HOPEFUL study conclusions .....	120
Comparative safety (UAE versus Hyst) .....	53	<b>Acknowledgements</b> .....	121
UAE-only: general side-effects .....	57	<b>References</b> .....	123
Key findings – primary outcomes (safety) ..	58	<b>Appendix 1</b> UAE collaborators: for each	
<b>6 Results: secondary outcome measures</b> .....	61	centre the lead clinician (principal	
Comparative efficacy (UAE versus Hyst) ...	61	investigator) and researcher/research	
UAE-only efficacy .....	70	nurse are acknowledged .....	127
Key findings – secondary outcomes		<b>Appendix 2</b> Hysterectomy collaborators:	
(efficacy) .....	75	for each centre the lead clinician (principal	
<b>7 Results: UAE-specific topics</b> .....	77	investigator) and researcher/research nurse	
Factors influencing choice of treatment		are acknowledged .....	129
(Q21) .....	77		

<b>Appendix 3</b> Trial steering committee members .....	131	<b>Appendix 12</b> Patient questionnaire .....	189
<b>Appendix 4</b> Initial patient contact letter ..	133	<b>Appendix 13</b> Patient questionnaire 4-week reminder letter .....	201
<b>Appendix 5</b> Patient information sheet .....	135	<b>Appendix 14</b> Primary outcome analyses – details of logistic regression and coefficients .....	203
<b>Appendix 6</b> HOPEFUL consent form .....	139	<b>Appendix 15</b> Health economics .....	207
<b>Appendix 7</b> Cause of death recorded on death certificates .....	141	<b>Appendix 16</b> Q24a and f – expectations not fulfilled and why and problems caused by the treatment .....	211
<b>Appendix 8</b> Second letter to non-consenters (first chase) .....	143	<b>Health Technology Assessment reports published to date</b> .....	229
<b>Appendix 9</b> Non-consenters reasons tick box sheet .....	145	<b>Health Technology Assessment Programme</b> .....	245
<b>Appendix 10</b> UAE clinical data form and instruction sheet .....	147		
<b>Appendix 11</b> Hysterectomy clinical data form and instruction sheet .....	173		





## List of abbreviations

ACOG	American College of Obstetricians and Gynecologists	MREC	Multi-Centre Research Ethics Committee
BMI	body mass index	MRI	magnetic resonance imaging
BP	blood pressure	NICE	National Institute for Health and Clinical Excellence
BSIR	British Society of Interventional Radiology	NRS	numerical rating scale
CAS	carotid artery stenting	NSAID	non-steroidal anti-inflammatory drug
CI	confidence interval	NSTS	NHS Strategic Tracing Service
D&C	dilatation and curettage	OR	odds ratio
DCRI	Duke Clinical Research Institute	PES	post-embolisation syndrome
DUB	dysfunctional uterine bleeding	PI	principal investigator
DVT	deep vein thrombosis	POF	premature ovarian failure
FEMISA	Fibroid Embolisation: Information, Support and Advice	PVA	poly(vinyl alcohol)
GnRH	gonadotrophin-releasing hormone	QALY	quality-adjusted life-year
GSE	general side-effect (of UAE)	QoL	quality of life
HMB	heavy menstrual bleeding	RCOG	Royal College of Obstetricians and Gynaecologists
HOPEFUL	Hysterectomy Or Percutaneous Embolisation For Uterine Leiomyomata	RCR	Royal College of Radiologists
HRQoL	health-related quality of life	RCT	randomised controlled trial
HRT	hormone replacement therapy	RR	relative risk
Hyst	hysterectomy cohort	SAE	serious adverse event
IBS	irritable bowel syndrome	SD	standard deviation
ITT	intention-to-treat	SF-36	Short Form with 36 Items
LREC	Local Research Ethics Committee	SIR	Society of Interventional Radiology
		TCRE	transcervical resection of the endometrium

*continued*

### List of abbreviations *continued*

UAE	uterine artery embolisation	US	ultrasound
UFS-QOL	Uterine Fibroid Symptom and Quality of Life Questionnaire	VALUE	Vaginal, Abdominal or Laparoscopic Uterine Excision

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices in which case the abbreviation is defined in the figure legend or at the end of the table.



## Executive summary

### Background

The standard treatment for symptomatic uterine fibroids is hysterectomy. During the mid-1990s a minimally invasive uterus-conserving treatment was described known as uterine artery embolisation (UAE). Evidence from a few small randomised controlled trials comparing the two treatments suggested that UAE is a safe, effective treatment up to 12 months. Long-term safety and efficacy remain unknown. HOPEFUL is a pragmatic observational study that has investigated and compared the two treatments in the medium term.

### Objectives

The medium-term results of hysterectomy and UAE as a treatment for symptomatic uterine fibroids were examined and compared with regard to

- safety
- efficacy
- special issues in UAE group
- cost-effectiveness
- women's own perspectives on the treatments.

### Design

HOPEFUL is a multi-centre retrospective cohort study. Inherent biases were minimised by rigorous design, protocol and analyses. Data were collected locally from patients' hospital records and also from patients themselves by postal questionnaire. Questionnaire data included free-text comments and this qualitative material was analysed using constant comparison. A two-stage probabilistic decision model was designed to estimate UK NHS costs and health outcomes in terms of quality-adjusted life-years (QALYs).

### Setting

The setting was 18 NHS hospital trusts, 17 in England and one in Scotland. The UAE cohort included patients treated in both NHS and private hospitals, reflecting UK practice at the time of

treatment. The entire hysterectomy cohort was NHS patients.

### Participants

Patients were eligible for inclusion if they had received one of the treatments under comparison specifically for symptomatic fibroids. We identified 1734 eligible women (972 UAE, 762 hysterectomies). The hysterectomy cohort underwent their index treatment in the 12 months beginning October 1994 as part of a national audit of hysterectomies (VALUE study). The UAE patients were treated by interventional radiologists who had pioneered its use since 1996 and all received their index UAE prior to the end of 2002, ensuring a minimum follow-up of at least 2 years. The average length of follow-up was 8.6 years [standard deviation (SD) 3.4] for the hysterectomy cohort and 4.6 years (SD 2.0) for the UAE cohort.

### Interventions

The majority of the HOPEFUL patients had total abdominal hysterectomies (86.7%). All UAE centres used poly(vinyl alcohol) (PVA) embolic particles and in addition some used gelfoam or coils.

### Main outcome measures

Primary outcome measures were complication rates to assess the comparative safety of the two interventions. Complications were defined as unintended consequences of treatment categorised according to the severity of their impact on health and the interventions required to rectify their impact. Categories were agreed *a priori* by the project team into severe, major or minor complications. The general side-effects of treatment in the UAE cohort including post-embolisation syndrome and vaginal discharge were considered a normal consequence of the embolisation process.

Secondary outcome measures related to treatment efficacy including resolution of symptoms and

patient-reported satisfaction with treatment. Both quantitative and qualitative analyses were undertaken. Further efficacy outcome measures obtained in the UAE group included fibroid/uterine size shrinkage and further treatments required for unresolved fibroid symptoms. Data were also gathered on pregnancies post-UAE.

## Results

Data were available for 1108 women (649 UAE and 459 hysterectomy). As expected, the cohorts presented a different baseline profile for many confounders including educational level (UAE higher), ethnicity (UAE more ethnically diverse) and parity (more UAE women nulliparous).

After adjusting for confounders, clustering by centre and missing values, fewer complications were experienced by women in the UAE cohort compared to the hysterectomy cohort – raw data, hysterectomy  $n = 120$  (26.1%), UAE  $n = 114$  (17.6%), adjusted odds ratio 0.48 [95% confidence interval (CI) 0.26 to 0.89]. When only the severe/major complications were considered, this odds ratio was reduced to 0.25 (95% CI 0.13 to 0.48). Expected general side-effects of UAE occurred in 32.7% of the UAE cohort, of which 8.9% also experienced complications. Obesity and medical co-morbidity predisposed women to complications whereas prophylactic antibiotics appeared to protect against both complications and the expected side-effects of UAE.

More women in the hysterectomy cohort reported relief from fibroid symptoms (89% versus 80% UAE,  $p < 0.0001$ ) and feeling better (81% versus 74% UAE,  $p < 0.0001$ ), but only 70% (compared with 86% UAE,  $p = 0.007$ ) would recommend their treatment to a friend.

In the UAE cohort, 18.3% of the women went on to receive one or more further fibroid treatments including hysterectomy (11.2%). After adjusting for differential time of follow-up, the UAE women had up to a 23% (95% CI 19 to 27%) likelihood of requiring further treatment.

Twenty-seven women (average age 38 years, SD 3.3) reported 37 pregnancies post-UAE. There were 15 miscarriages, two ectopic pregnancies, one termination and 19 live births observed in this study. Some 79% of the live births were delivered by Caesarean section, six for complications of pregnancy or delivery.

The free-text data indicated that many women, in both cohorts, felt that their treatment had been a complete success. In the UAE cohort there were several areas where expectations were apparently high and outcome had not fulfilled their expectations. Disappointment was expressed mainly about continuation or return of symptoms or failure to become pregnant. Many continued to have remaining questions about their treatment.

The economic analysis indicated that UAE is less expensive than hysterectomy even after further treatments for unresolved or recurrent symptoms are taken into account, with little difference in QALYs between the two treatments. Younger women are exposed to the risk of recurrent fibroids and subsequent additional procedures over a longer period and consequently UAE may no longer be cost-effective, although this would depend on the quality of life placed by an individual woman on uterine preservation.

## Conclusions

This study provides comparable medium-term follow-up for the two treatments.

### Safety

Our results suggest that both UAE and hysterectomy are safe. No unexpected problems were detected following UAE after a long follow-up period (average 5 years). Complications are less common for UAE than hysterectomy, particularly severe/major complications.

One-third of women experienced general expected side-effects post-UAE. The likelihood of requiring further fibroid treatment after UAE was 23%. However, for women wishing to retain their uterus these risks may be worth taking.

### Cost-effectiveness

The cost-effectiveness analysis favours embolisation even after taking account of complications, expected side-effects associated with the procedure and subsequent re-treatments for women with a preference for uterus preservation. For younger women the cost to the NHS may become slightly more than for hysterectomy due to the longer period prior to the menopause and thus the increased potential requirement of further fibroid treatment.

### Communication/information

Our results provide reliable evidence of short- and medium-term outcomes, and of treatment failure,

needed to inform decision-making. The way in which women described their experiences showed that, for them, the intervention was not an event, but a process, and this needs to be reflected in the communication strategy in this area. Radiologists practising UAE should see patients in outpatients both before and after treatment.

It is important to improve the management of expectations following UAE, particularly regarding fertility. Our data suggested that fertility and miscarriage rates are consistent with those of age-matched women with fibroids.

### Impact on NHS

UAE is an effective treatment for some women with fibroids and our trial supports the National Institute for Health and Clinical Excellence guidance that it should be made available as one of the options for treatment, with a possible reduction in the need for hysterectomy as the first-line treatment.

### Recommendations for research

In addition to confirming the medium-term safety of UAE, this study has generated hypotheses of great importance for women with symptomatic fibroids.

- *Who will benefit from UAE?*

Conclusions regarding which subgroups of women will be treated most successfully by UAE (size, position and number of fibroids) were not possible from this study. Further research on these areas will have important implications for advising patients, and for health economics.

- *What UAE techniques are the most successful?*

The best method of achieving effective embolisation is also still not clear, with a number of different agents being used at varying cost. All the centres in HOPEFUL used PVA particles. Since then, a range of different embolic materials and techniques have become available. Randomised studies would determine the optimal materials and techniques for UAE.

- *What advice can be given to women who desire future fertility?*

Our observations suggest that live births after UAE are possible, but the actual probabilities and factors that determine who conceives, miscarries or achieves a live birth remain poorly understood. Randomisation between myomectomy and embolisation may determine the more cost-effective and successful option particularly in the infertile patient and those who are undergoing *in vitro* fertilisation therapy.

- *What role does prophylactic antibiotics have in UAE?*

The role of antibiotics in the prevention of complications and side-effects has strong support from this study, but the results should be viewed with caution. Antibiotic use was highly confounded with collaborating centre. The uncertainty that remains warrants randomised trials.

- *What are the effects of HRT use after UAE on recurrence of fibroid symptoms?*

Our free-text analysis suggested that a common question amongst women after UAE is whether using HRT will lead to recurrent fibroid symptoms. Currently patients are advised against the use of HRT, as its effects after embolisation are unknown. Further research is warranted to help clarify this question.



# Chapter I

## Background and rationale

### Uterine fibroids

Uterine fibroids (leiomyomata or myomas) are benign tumours of smooth muscle cells and fibrous connective tissue that develop within the walls of the uterus. They are the most common gynaecological problem experienced by women in the UK, being of clinical significance in 20–40% of women of childbearing age.<sup>1,2</sup> The true prevalence of uterine fibroids is unknown because the majority of these tumours are asymptomatic. One American study carried out gross serial sectioning at 2-mm intervals as an adjunct to routine pathology in 100 consecutive total hysterectomy uteri, finding fibroids present in 77% of the women.<sup>3</sup> In this study, fibroids were found in the uteri of 50/68 (74%) premenopausal women and 27/32 (84%) postmenopausal women. The average number of fibroids and the average size were higher in premenopausal women than in postmenopausal women (7.6 versus 4.2 and 18.8 mm versus 11.5 mm). Another study in the USA screening for fibroids with ultrasound (US) estimated a cumulative incidence of greater than 80% for black women and 70% for white women at 50 years of age.<sup>4</sup>

Uterine fibroids may occur singly but most often are multiple and vary in size from an unnoticeable few millimetres to over 20 cm in diameter, significantly enlarging the abdominal cavity. They are named according to their location. Intramural fibroids lie wholly within the uterine walls, submucosal fibroids project into the uterine cavity and subserosal fibroids project from the outer surface of the uterus. They may also be pedunculated, where they are attached to the uterine wall by a stalk-like structure.

The aetiology and pathogenesis of fibroids are not fully understood, but their occurrence during the female reproductive lifespan indicates an association with the hormones oestrogen and progesterone. The prevalence of clinically significant fibroids peaks in the peri-menopausal years, declining after the menopause.<sup>5</sup> Known risk factors for fibroids include early menarche, nulliparity, later reproductive years, obesity, Afro-Caribbean ethnic origin and tamoxifen. Conversely, menopause, increasing parity and

smoking reduce the risk.<sup>5</sup> There is thought to be a genetic element to the development of fibroids suggested by biochemical and epidemiological evidence.<sup>6,7</sup> Fibroids appear to be 2–3-fold more common in first-degree relatives of women with fibroids, compared with the general population.<sup>8,9</sup>

Most fibroids cause no symptoms and are an incidental finding during a clinical or US examination. Such fibroids require no treatment other than routine monitoring. However, uterine fibroids are responsible for significant morbidity in the female population. The most common clinical symptoms are associated with menstruation and include prolonged and/or heavy menstrual bleeding (HMB) (menorrhagia), which may lead to iron-deficiency anaemia, and painful menstruation (dysmenorrhoea). Fibroids which cause these problems are likely to be of the submucosal or intramural type. Fibroids also cause a variety of non-bleeding symptoms arising from their local mass effect, causing pelvic pain or pressure upon adjacent organs. An enlarged uterus may place pressure on the bladder, causing urinary symptoms such as urinary frequency/urgency. Subserosal fibroids may be large and the only symptom may be significant abdominal distension. Fibroids may also be a factor in sub-fertility and pregnancy loss. However, the relationship between presence of fibroids and lower fertility may be associative rather than causative. Rarely (in approximately 0.1% of cases) fibroids may undergo sarcomatous change into a smooth muscle malignant tumour or sarcoma.<sup>9</sup>

### Treatments for symptomatic fibroids

#### Medical

No pharmacological intervention is known to have a long-term effect on symptoms of fibroids.<sup>10</sup> Gonadotrophin-releasing hormone (GnRH) analogues which are administered by injection reduce oestrogen production, usually resulting in some shrinkage of fibroids and cessation of menstruation. However, the effectiveness of these hormones persists only for the duration of therapy and ceases upon stopping treatment. Fibroids re-grow to their original size within 4–6 months. This

therapy can only be used as a short-term measure because of its adverse effect on bone mass. In addition, many women dislike its associated menopausal side-effects. Rather than as a long-term therapy for fibroid symptoms GnRH analogues are often used prior to surgery to shrink fibroids and thus ease their removal. Other medical therapies used for treating menorrhagia, such as combined oral contraceptives, non-steroidal anti-inflammatory drugs (NSAIDs) and progestogens (including the Mirena coil) appear to be less effective where fibroids are the cause of symptoms.

### Hysterectomy

Surgical management has therefore been the mainstay of treatment for women with symptomatic fibroids. Hysterectomy, which removes the uterus, is the most established gold standard therapy for symptomatic uterine fibroids worldwide. Hysterectomy rates in the UK, however, have been declining during the last decade. In the 2004–5 financial year 37,926 hysterectomies were performed in England (31,424 abdominal and 6502 vaginal), compared with 56,856 (44,706 abdominal and 12,150 vaginal) in 1998–9.<sup>11</sup> Hysterectomy virtually eliminates both symptoms and the chance of further fibroid growth. Many women who suffer from fibroids, however, desire future childbearing or simply want to preserve their uterus. Furthermore, for women in whom fibroid symptoms are not severe, hysterectomy is an extreme treatment. It is a costly major surgical procedure requiring typically 5 days hospitalisation and several months to recover fully. As with all major surgery, it is not without risk of complications (major morbidity occurs in 3% of cases, minor morbidity in 14% of cases) and carries a mortality rate of 1–2 per 1000 women.<sup>12,13</sup> In the Vaginal, Abdominal or Laparoscopic Uterine Excision (VALUE) study,<sup>12</sup> there were two deaths in the women with fibroids from 5719 total abdominal hysterectomies and 256 sub-total hysterectomies (see below), approximately one per 3000 women. There is controversy as to whether hysterectomy causes longer term problems such as urinary incontinence, sexual dysfunction and psychological side-effects including a loss of femininity and depression.<sup>14–17</sup>

Although hysterectomy can be performed either laparoscopically or by the vaginal route, the uterus is usually significantly enlarged by the fibroids, so most are performed by the abdominal route. As the surgery may be technically difficult sometimes

the uterine cervix is not removed (sub-total hysterectomy) as this is likely to decrease the risk of bladder damage, shorten the operating time and reduce the blood loss.

### Myomectomy

A surgical alternative to hysterectomy is myomectomy, where only the fibroids are removed, with reconstruction and preservation of the uterus. Most myomectomies in the UK are performed by the open abdominal route, although small submucosal ones are removed preferably hysteroscopically.<sup>18</sup> The uterus is highly vascular with adhesiogenic tendency when damaged, so whichever method of myomectomy is used this procedure can lead to both short- and long-term complications. All methods are associated with a risk of bleeding and a transfusion rate of up to 20% following abdominal myomectomy has been reported.<sup>19</sup> Patients undergoing myomectomy have an unusually high incidence of fever occurring in the first 48 hours following surgery. Hysteroscopic myomectomy may incur a slight risk of uterine perforation and cervical damage. Laparoscopic myomectomy is associated with the usual risks of laparoscopy, particularly accidents during trocar (a surgical instrument) placement.<sup>20</sup> Short-term complications of abdominal myomectomy include bleeding, fever, infection, visceral damage and thromboembolism. In 2% of myomectomies conversion to hysterectomy is required.<sup>21</sup> Long-term complications of myomectomy include pelvic adhesions, recurrent myomas and risk of uterine rupture in subsequent pregnancies.<sup>20,22</sup> A review of 41 studies suggests that fibroids may re-occur in 20–50% of cases 5 years after myomectomy.<sup>23</sup>

### Uterine artery embolisation

Many women do not wish to undergo an operative procedure with its associated risks, but until recently effective non-surgical therapies for uterine fibroids have not been available. Uterine artery embolisation (UAE) was first reported as a 'stand-alone' treatment for fibroids in 1995.<sup>24</sup> Prior to this it was performed preparatory to surgical intervention for fibroids or for the management of other obstetric or gynaecological bleeding conditions such as postpartum haemorrhage.<sup>25</sup>

UAE is carried out by an interventional radiologist and involves complete occlusion of either one or both uterine arteries with particulate emboli to cause ischaemic necrosis of the uterine fibroids. The closure of the arteries is considered permanent, thereby blocking blood supply to the fibroid but without any permanent adverse effect



on the otherwise normal uterus. UAE is performed under local anaesthetic, sometimes with conscious sedation, epidural or spinal anaesthetic. Prophylactic antibiotics may also be administered. A vascular sheath of 4 or 5 French diameter is inserted directly into the woman's femoral artery and the contralateral uterine artery is then selectively catheterised. The catheter may then be manoeuvred to the ipsilateral uterine artery and the process repeated. The most commonly used embolic agent is poly(vinyl alcohol) (PVA), a non-biodegradable agent available in a variety of sizes suspended in a dilute contrast solution. In this study, the PVA particle size ranged from 250 to 710 µm; however, UAE now usually uses particles of 700–900 µm. Occlusion of the uterine vessels is confirmed by angiography and the catheter removed. The procedure generally takes between 45 and 135 minutes to complete, depending on the anatomy of the pelvic arteries. The woman is exposed to approximately 20 rad (20 cGy) of ionising radiation to the ovaries. Most patients in the immediate period post-UAE experience a post-embolisation syndrome (PES) of pain, nausea and high temperature and remain in hospital overnight, receiving narcotics and NSAIDs for pain relief. Successful UAE totally occludes both uterine vessels. The normal myometrium (muscle of the womb) rapidly establishes a new blood supply through collateral vessels from the ovarian and the vaginal circulations.<sup>26</sup>

## Status of UAE – evidence review

### Literature search

Literature searching was undertaken throughout the project, with the final update being carried out on 12 September 2006. All relevant references were downloaded to a bibliographic management database, Reference Manager Professional Edition Version 10.0 (ThomsonISI ResearchSoft).

The search strategy utilised both free-text and controlled-text subject headings wherever possible. It included all possible synonyms, variants of words, alternative spellings and abbreviations for the facets relating to the population/medical condition, the interventions/treatments and the outcomes being considered; for example, search terms for the population/condition included (fibroid\* OR leiomyoma\* OR myoma\* OR “Leiomyoma” [MeSH]). Search terms for the interventions/treatments included (uterine artery embolisation OR uterine artery embolization OR UAE OR uterine fibroid embolisation OR uterine

fibroid embolization OR UFE) (hysterectomy OR “hysterectomy” [MeSH]). Search terms for outcome included (treatment OR therap\* OR “Embolization, Therapeutic” [MeSH]). Searches were carried out on the following databases to include the publication dates 1995 to 2006: MEDLINE, EMBASE, CINAHL, PsycINFO and SIGLE and were supplemented with searches on PubMed ([www.pubmed.gov](http://www.pubmed.gov)).

Literature searching was undertaken using the platform ERLWebSPIRS Version 5.1 on SilverPlatter via the University of Oxford library services resource ([www.bodley.ox.ac.uk/oxlip](http://www.bodley.ox.ac.uk/oxlip)) prior to 1 March 2006. After this date, the platform OVID Web Gateway was used via the same resource.

In addition, the Current Controlled Trials metaRegister (mRCT) comprising public, charitable and commercial registers was also checked for any ongoing trials ([www.controlled-trials.com/mrct/](http://www.controlled-trials.com/mrct/))

Other sources searched included The National electronic Library of Health (NeLH) Guideline finder ([www.nelh.nhs.uk](http://www.nelh.nhs.uk)), The National Institute for Health and Clinical Excellence (NICE) ([www.nice.org.uk](http://www.nice.org.uk)) and The Cochrane Library ([www.thecochranelibrary.com](http://www.thecochranelibrary.com)).

Two systematic reviews<sup>27,28</sup> have examined the literature on UAE since the first observational reports of this alternative uterus-sparing treatment for fibroids.

The first of these<sup>27</sup> was commissioned by NICE as part of its Interventional Procedures Review Programme. The Interventional Procedures Advisory Committee (IPAC) reviewed the results of the systematic review and issued revised full guidance in October 2004.<sup>29</sup> The second is a Cochrane Review published in 2006 summarising randomised controlled trial (RCT) evidence on UAE.<sup>28</sup>

### UK clinical guidance (NICE)

The NICE guidance<sup>29</sup> issued in October 2004 for England, Wales and Scotland is as follows:

- “1.1 Current evidence on uterine artery embolisation (UAE) suggests that it is safe enough for routine use and that there is symptomatic benefit in the majority of patients in the short term. However, more evidence is required on the degree and duration of the procedure's benefits, and of its effects on fertility.

- 1.2 Clinicians wishing to undertake UAE should take the following actions:
- Ensure that patients understand the uncertainty about the degree and duration of the procedure's benefits and provide them with clear written information. Use of the Institute's Information for the Public is recommended.
  - Audit and review clinical outcomes of all patients having UAE. Data should be submitted to the British Society of Interventional Radiology registry ([www.bsir.org](http://www.bsir.org)).
- 1.3 Patient selection should be made with the involvement of a multidisciplinary team, which should include a gynaecologist and an interventional radiologist.
- 1.4 The Institute may review the procedure upon publication of further evidence."

This guidance was based upon the following conclusions of the systematic review<sup>27</sup> regarding efficacy and safety:

#### "2.3 Efficacy

2.3.1 The evidence from the studies included in the review indicated that after UAE, there was a reduction in mean fibroid volume of between 40 and 75%. Reductions in fibroid volume, however, did not correlate with changes in symptoms. Improvement in symptoms was reported in 62% (8/13) to 95% (19/20) of women who received UAE. Similar improvement was observed in a case series of 400 women, of which 73–90% reported symptom improvement. However, follow-up was short and, in the majority of studies, was limited to 6 months.

2.3.2 In three studies totalling 604 women, 24 women (4%) reported pregnancies following UAE. However, it was unclear how many women in these studies wished to become pregnant.

#### 2.4 Safety

2.4.1 There was a large variation in the reported rate of complications in the studies included in the systematic review. The most commonly reported complications were the need for hysterectomy in 0.5% (2/400) to 11.8% (6/51) of women, and the late expulsion of a fibroid in 2.2% (9/400) to 7.7% (2/26) of women. Other complications included infection and fever. One death was

reported in a small study of 21 patients. Pain is a normal sequela of UAE, but was reported as a complication in some studies.

2.4.2 Ovarian dysfunction (characterised by irregular or absent menses and menopausal levels of follicle-stimulating hormone) was reported in five studies and ranged from 2.5% (2/80) to 14% (9/66) of patients. In a further study of 555 patients, amenorrhoea following UAE was reported in 3% of women younger than age 40 years and in 41% of women aged 50 years and older."

The review assessed one RCT, two comparative studies, one patient questionnaire survey and 32 papers (one reporting baseline data only) from 25 case series of UAE patients. Most papers were from the USA. The number of patients in the series ranged from 11 to 555. The mean age of patients was 43 years. All the patients had symptomatic fibroids and were at the stage in their symptoms when some intervention was required. Beyond this, the criteria for inclusion in the UAE series varied between the studies.

The limitation of this evidence is that, with the exception of the one small Spanish RCT of moderate quality comparing UAE with hysterectomy,<sup>30</sup> it is mostly contained in uncontrolled case series of varying size. Case series are susceptible to population bias due to selection and loss to follow-up. Only one paper based on a small UK series ( $n = 21$ ) reported using a validated outcomes questionnaire. There were no consistent definitions or standard measures assessing clinical changes in symptoms following UAE. The resulting variation in the clinical data collection and reporting increases uncertainty in assessing the extent of any improvements. Consequently, from this evidence the true efficacy of UAE, particularly in the longer term, remains unknown.

In sum, although this review suggests promising results have been obtained with UAE over the short term with regard to symptom relief, it also points to several areas of possible concern regarding this treatment: management of post-procedure pain, post-embolisation syndrome, infection, premature ovarian failure (POF), secondary amenorrhoea and the unknown effect on future conception and pregnancy.

Longer term, larger RCTs that compare UAE with other treatments for managing symptomatic

fibroids in the UK population would provide data to clarify these uncertainties. Both NICE guidance IP094<sup>29</sup> and The Joint Working Party of the Royal College of Radiologists (RCR) and the Royal College of Obstetricians and Gynaecologists (RCOG)<sup>31</sup> have recognised this lack of medium- to long-term data comparing UAE with surgical options for symptomatic fibroids and have also emphasised the need for randomised comparisons. In the absence of this type of higher quality data, the Hysterectomy Or Percutaneous Embolisation For Uterine Leiomyomata (HOPEFUL) study was commissioned to provide longer follow-up on large numbers of women treated in the UK in a retrospective observational design.

Currently UAE is not routinely offered to women within the NHS due to this uncertainty about longer term outcomes. However, it is available in over 50 centres in the UK with patients' consent for audit or research, primarily in London and south-east England. Out of an estimated 2050 UAE procedures for fibroids performed in the UK to date [Fibroid Embolisation: Information, Support and Advice (FEMISA) data], 200 (10%) were performed outside London or south-east England. Of the 1850 carried out in London or south-east England, 1000 have been reported as being undertaken at one centre.

NICE guidance<sup>32</sup> published in January 2007 for the treatment of HMB makes recommendations for when HMB is due to uterine fibroids as follows:

- “1.1 Further interventions for uterine fibroids associated with HMB
- 1.1.1 For women with large fibroids and HMB, and other significant symptoms such as dysmenorrhoea or pressure symptoms, referral for consideration of surgery or uterine artery embolisation (UAE) as first-line treatment can be recommended.
  - 1.1.2 UAE, myomectomy or hysterectomy should be considered in cases of HMB where large fibroids (greater than 3 cm in diameter) are present and bleeding is having a severe impact on a woman's quality of life.
  - 1.1.3 When surgery for fibroid-related HMB is felt necessary then UAE, myomectomy and hysterectomy must all be considered, discussed and documented.
  - 1.1.4 Women should be informed that UAE or myomectomy may potentially allow them to retain their fertility.

- 1.1.5 Myomectomy is recommended for women with HMB associated with uterine fibroids and who want to retain their uterus.
- 1.1.6 UAE is recommended for women with HMB associated with uterine fibroids and who want to retain their uterus and/or avoid surgery.
- 1.1.7 Prior to scheduling of UAE or myomectomy, the uterus and fibroid(s) should be assessed by ultrasound. If further information about fibroid position, size, number and vascularity is required, MRI should be considered.
- 1.1.8 Pretreatment before hysterectomy and myomectomy with a gonadotrophin-releasing hormone analogue for 3 to 4 months should be considered where uterine fibroids are causing an enlarged or distorted uterus.
- 1.1.9 If a woman is being treated with gonadotrophin-releasing hormone analogue and UAE is then planned, the gonadotrophin-releasing hormone analogue should be stopped as soon as UAE has been scheduled.”

### **RCTs and large prospective studies of UAE with longer follow-up**

The current body of research is fairly limited. Literature searches found publications pertaining to only three RCTs of UAE versus hysterectomy and one RCT of UAE versus myomectomy.

### **RCTs of UAE versus hysterectomy**

There are two published RCTs, one from Spain<sup>30</sup> and one from Scotland (REST<sup>33</sup>) and one currently ongoing and partly published from The Netherlands (EMMY<sup>34-36</sup>). The Spanish study was included in the NICE systematic review<sup>27</sup> and the other two studies were included in the Cochrane Review.<sup>28</sup>

### **RCTs of UAE versus myomectomy**

There is one published Czech RCT<sup>37</sup> which was included in the Cochrane Review.

### **Large prospective studies with longer follow-up**

There are no RCTs of UAE versus surgical procedures under way in the USA. There is, however, a large multicentre prospective registry, the FIBROID registry.<sup>38-41</sup>

There is one published longer follow-up (5–7 years) observational study of 258 women in the UK.<sup>42</sup>

Results from these RCTs and prospective studies are outlined below.

### **UAE versus hysterectomy**

#### **Pinto study<sup>30</sup>**

Pinto and colleagues<sup>30</sup> reported a 6-month follow-up. Randomisation was stratified by blocks of six patients to yield a ratio of two UAE procedures to each hysterectomy. The study used a pre-consent design and was of moderate quality. The trial was powered for differences in length of hospital stay between the two arms. It was not powered to assess efficacy and safety.

Group 1 patients were randomised to be offered a choice of UAE if they wished ( $n = 37$ ) or hysterectomy if they did not ( $n = 1$ ). Two Group 1 UAE patients went on to have hysterectomy. Group 2 patients were intended to receive hysterectomy and were not informed of the alternative UAE treatment ( $n = 19$ ). However, three Group 2 patients refused hysterectomy and so were offered and had UAE.

An intention-to-treat (ITT) analysis was carried out to evaluate treatment efficiency (compare length of hospital stay). The 38 patients in Group 1 spent a mean of  $1.71 \pm 1.59$  days in the hospital, compared with the mean of  $5.85 \pm 2.52$  days that the patients in Group 2 ( $n = 19$ ) spent in the hospital {difference of 4.14 days [95% confidence interval (CI), 3.06 to 5.22,  $p < 0.001$ ]}.}

For efficacy and safety outcome measures a 'treatment-received-analysis' was used because not all patients received the treatment intended at randomisation. After 6 months of follow-up, the overall clinical success rate (cessation of bleeding problems) for the 36 patients who underwent UAE was 86%. Twenty of 36 patients had a full recovery, five a partial recovery and six amenorrhoea. The mean dominant fibroid volume decreased by 46% (95% CI, 27 to 66%) at 6 months of follow-up. The mean uterine fibroid volume was  $84.42 \text{ cm}^3$  (range, 1.8–408.0  $\text{cm}^3$ ) pre-embolisation and  $45.46 \text{ cm}^3$  (range, 0.53–408.0  $\text{cm}^3$ ) post-embolisation. It is difficult to make meaningful comparisons between the efficacy of hysterectomy, which has 100% effect on related symptoms and fertility, and UAE, which does not.

With regard to overall safety, 32% (13/40) of patients made emergency department visits following UAE, predominantly for post-embolisation syndrome ( $n = 6$ ) or severe pelvic pain ( $n = 3$ ), compared with 20% (4/20) of the patients who had hysterectomy. Two of 40 patients

were re-admitted post-UAE versus one of 20 patients post-hysterectomy. Some 25% (10/40) of the UAE patients had minor intra-procedural complications. In contrast, 20% (4/20) of the hysterectomy patients experienced major complications during the procedure necessitating blood transfusions. At 30 days post-procedure, 72% (29/40) of patients who had UAE had complications (primarily minor–moderate) versus 45% (9/20) of the patients who had a hysterectomy ( $p = 0.05$ ). The complications experienced by hysterectomy patients tended to be more major.

The patients who underwent UAE resumed their routine daily activities after a mean of  $9.50 \pm 7.21$  days, compared with the patients who underwent hysterectomy, who required a mean of  $36.18 \pm 20.47$  days [difference 26.68 days (95% CI, 18.85 to 34.50,  $p < 0.001$ )].

After 6 months of follow-up, the patients were asked whether they would undergo the same treatment again. Of 36 patients who underwent UAE, 28 (78%) answered yes, five (14%) no and three (8%) maybe. Of 17 patients who underwent hysterectomy, 15 (88%) answered yes and two (12%) no.

#### **EMMY trial<sup>34–36</sup>**

The EMMY trial is a multicentre 1:1 ratio ITT RCT. Patients from 28 hospitals in The Netherlands were recruited and randomised to UAE ( $n = 88$ ) or hysterectomy ( $n = 89$ ). Inclusion criteria were (1) uterine fibroids had been diagnosed clinically and confirmed by ultrasonography, (2) menorrhagia was the predominant complaint, (3) patients were to be scheduled for a hysterectomy, (4) were premenopausal, (5) preservation of the uterus was not warranted for future pregnancy and (6) the following disorders were absent: moderate/severe renal failure (creatinine  $> 150 \text{ mmol/l}$ ), active pelvic infection, clotting disorders, contrast medium allergy, (suspected) uterine malignancy, submucosal fibroids with  $> 50\%$  of their diameter within the uterine cavity or pedunculated serosal fibroids.

The primary end-point of EMMY was stated as "the elimination of menorrhagia after a follow-up period of two years, with UAE considered equivalent to hysterectomy if menorrhagia resolved in at least 75% of patients with no significant differences in major complications between the two procedures". A power calculation suggested a requirement of 120 total patients to be included for this outcome. Two initial publications from EMMY have reported on short-

term outcome measures (peri- and post-procedural complications, length of hospital stay, unscheduled visits and readmission rates up to 6 weeks post-intervention),<sup>34,35</sup> for which no separate power analysis was described. A third publication reports on pain and return to daily activities.<sup>36</sup>

Following randomisation, bilateral UAE was impossible in four patients. These patients subsequently underwent hysterectomy, but were analysed in the UAE group. In the UAE-allocated group 81 patients underwent the procedure. Seventy-five women allocated hysterectomy underwent the surgery; the remaining patients refused the allocated treatment and withdrew from the trial.

The first publication<sup>34</sup> reported a follow-up period of 6 weeks. The technical failure rate for the procedure was significantly higher with UAE, bilateral UAE failed in 4.9% of patients, and an additional 6.2% of patients had a unilateral technical failure. All hysterectomy operations were technically successful.

Major complications occurred in 4.9% of patients in the UAE group and 2.7% in the hysterectomy group, incidences that were not significantly different ( $p = 0.68$ ). Complications were classified as “major” when the events were potentially life-threatening, could lead to permanent sequelae or required surgical intervention. Other complications were listed as “minor”. Nausea, pain, and fever were considered “general” complications. The minor complication rate from discharge until 6 weeks was significantly higher in the UAE group than in the hysterectomy group [58.0% versus 40.0%; versus relative risk (RR) 1.45 (95% CI 1.04 to 2.02),  $p = 0.024$ ]. UAE patients were more often readmitted (11.1% versus 0%,  $p = 0.003$ ) with most readmissions within the first few days after discharge. However, total length of hospital stay was significantly shorter in UAE patients [mean standard deviation (SD): 2.5 (2.7) versus 5.1 (1.3),  $p < 0.001$ ].

The authors concluded, “UAE is a procedure similar to hysterectomy with a low major complication rate and with a reduced length of hospital stay. Higher readmission rates after UAE stress the need for careful post-procedural follow-up.”

Additional analysis is provided in EMMY’s second publication,<sup>35</sup> including an attempt to identify risk factors for technical failure, fever after UAE, pain

and other complications. Univariate and multivariate analyses were used to identify predictors for technical failure, post-procedural fever, complications [Society of Interventional Radiology (SIR) definitions<sup>43</sup>] and pain scores.

The technical failure rate of UAE according to SIR guideline definitions<sup>43</sup> was 5.3% (95% CI, 2.3 to 10.1%). The procedural failure rate was 17.3% (95% CI, 9.8 to 27.3%). Bilateral failure occurred in four of 81 patients and unilateral failure occurred in 10 of 81 patients. Technical failure occurred mainly as a result of difficult anatomy (3.7%) or absence of the uterine artery (3.1%). This high frequency of incomplete embolisation is likely to affect the clinical outcomes that will be noted 2 years after therapy when the trial is concluded. The overall complication rates were 28.4% during the patients’ hospital stay and 60.5% for the 6 weeks after discharge.

The following results were reported regarding risk factors. The risk of technical failure was found to increase in the presence of a single fibroid tumour [odds ratio (OR), 6.21; 95% CI, 1.65 to 23.41,  $p = 0.007$ ] and/or a small uterine volume (<500 cm<sup>3</sup>; OR, 10.8; 95% CI, 1.25 to 93.36,  $p = 0.03$ ). The amount of embolisation material used was associated with the onset of fever after UAE (OR, 2.05; 95% CI, 1.09 to 3.87,  $p = 0.027$ ), major complications (OR, 5.68; 95% CI, 2.05 to 15.75,  $p = 0.001$ ), and high pain scores (OR, 1.97; 95% CI, 1.08 to 3.58,  $p = 0.027$ ).

The authors concluded, “The procedural failure rate for UAE was higher than those reported by others, mainly as a result of difficult anatomy. The risk of procedural failure was increased for patients with single fibroid tumours and/or small uterine volumes. A clear dose–effect response was revealed between the amount of embolisation material used and the risk for post-procedural fever, major complications and severe pain.”

Based on these two publications, the authors drew the following initial conclusions:

1. There is a higher than previously reported technical failure rate for UAE.
2. Post-discharge complications are more likely for patients treated with UAE (than hysterectomy).
3. There is a higher readmission rate among patients treated with UAE (than hysterectomy).

They suggest that their results reflect a more realistic view of outcome in general clinical practice in contrast to observational reports which

have often been from specialised centres. They also suggest that, because their results are from a randomised study, they are more valid than those with non-randomised designs which are more prone to “publication bias and patient selection criteria”. The implication is that the poorer results they found for UAE are the ‘true’ rate of these occurrences and that earlier studies have been misleading as a result of incomplete or biased data reporting or study design flaws.

It is acknowledged that an RCT design is the gold standard for any attempt to determine the relative effectiveness of two therapies; however, this is dependent on the quality of the trial methodology. Spies<sup>44</sup> highlights a number of flaws in the EMMY trial that outweigh some of the strengths of its randomised design:

“First, the power of this study to detect differences in short-term outcomes was not calculated. A very large number of variables were evaluated in a relatively small sample size and the likelihood of erroneous interpretation increases with each additional analysis.

“Second, the patients included may have had a preference for hysterectomy, as they had already agreed to undergo that procedure.

“Third, based on the information provided in the two articles, the management plan for post-procedural pain, the manner of patient instruction, and follow-up of the patients treated with UAE do not meet the accepted practice standards at the time of the study. The patients were told to call their gynecologists if their pain was not controlled. The radiologists had no role in caring for the patients.

“Finally, and perhaps most importantly, the operators in this study were inexperienced with UAE and the gynecologists who provided all post-procedural care had essentially no experience with UAE. An average of three patients were provided per hospital. For many of these centers, these were the first patients ever treated with UAE. This degree of inexperience may explain the very high rate of procedural failure. In addition, the gynecologists were ill equipped to manage these patients and yet were responsible for deciding whether patients required readmission and whether a patient’s post-procedural problems represented a complication.”

Conclusions drawn from the EMMY trial need to consider the influence of these limitations. The same is true of their third publication examining pain and return to daily activities. No power calculation was done for the analysis presented in this paper.<sup>36</sup> Analysis was by ITT.

Pain was assessed during admission and after discharge, both quantitatively and qualitatively,

using a numerical rating scale (NRS) and questionnaires. Time to return to daily activities was assessed by questionnaire at 6 weeks after discharge asking for how many days after hospital discharge women had refrained from the following: paid work, voluntary work, buying groceries, usual household activities, heavy household activities, leisure time activities and activities with children.

Pain scores were available for 135 patients (UAE,  $n = 77$ ; hysterectomy,  $n = 58$ ). UAE patients reported experiencing significantly less pain during the first 24 hours after treatment ( $p = 0.012$ ). The majority of patients in both groups needed opiates at some point during the first 24 hours. Six weeks after discharge, 57 UAE patients reported having experienced pain after discharge compared with 52 hysterectomy patients (70.4% versus 69.3%,  $p = 0.89$ ). After 6 weeks, eight patients (10%) still reported pain in the UAE group compared with 12 patients (16%) in the hysterectomy group ( $p = 0.25$ ). In the UAE group, 10 patients (12%) still used analgesics compared with 14 patients (19%) in the hysterectomy group ( $p = 0.27$ ). The time for 50% of patients to become free from pain after discharge was 7 days (95% CI, 5 to 9 days) for UAE patients compared with 10 days (95% CI, 6 to 14 days) for hysterectomy patients. When only bilateral UAE and abdominal hysterectomy were compared, no different results were obtained for the evaluation of pain.

UAE patients returned significantly sooner to daily activities than hysterectomy patients (for paid work: 28.1 versus 63.4 days;  $p < 0.001$ ).

A major limitation of this analysis is that no standard medication regimen was used due to the large number of participating hospitals, each with their own pain medication protocols.

### REST study<sup>33</sup>

REST<sup>33</sup> is an RCT involving 25 Scottish Health Boards plus two English centres. Computer-generated randomisation used a 2:1 allocation of patients to UAE ( $n = 106$ ) and surgery ( $n = 51$ ), respectively. The women who had fibroids  $> 2$  cm causing symptoms that would justify surgical treatment were randomised over a 30-month period (November 2000 to May 2004). Quality of life (QoL) measured at 12 months was the primary outcome measure [Short Form with 36 Items (SF-36)]. Secondary outcome measures included morbidity, pain scores, time to achieve various lifestyle events, hospital stay and re-intervention rates. Analysis was by ITT. Key results reported by

the trialists on the CSO (Chief Scientist Office) website and at CIRSE (Cardiovascular and Intervention Radiological Society of Europe) conference in September 2006 are as follows: 95% of patients underwent their allotted treatment (UAE 101, hysterectomy 40, myomectomy 8). There was no statistically significant difference in any of the eight components of the SF-36 scores at 1 year. Length of hospital stay was significantly shorter in those having UAE compared with surgery (median 1 day versus 5 days). The time to performing routine tasks was significantly shorter in the UAE group. Symptom scores were significantly better in the surgical arm at all time points. Ten (9%) of patients in the UAE arm required further invasive treatment for symptom control. At 1 year, women randomised to UAE had a 4% probability of having a repeat UAE and an 8% chance of hysterectomy. There were 33 (31%) serious adverse events (SAEs) in the UAE arm and nine (18%) in the surgical arm at latest follow-up (maximum 56 months). Economic analysis showed a significant difference in cost in favour of UAE (UAE £1757 versus surgery £2702).

The authors' conclusions are as follows. Both surgery and UAE provide a successful outcome for a majority of women with symptomatic fibroids.

No difference in the primary outcome measure (QoL) at 1 year was detected. Faster recovery following UAE must be weighed against the need for further treatment, in a minority of patients, following UAE. UAE appears more cost-effective than surgery at 1 year. There is, however, a continued need for follow-up beyond 1 year, particularly because a number of major complications occurred many months after treatment. The study was not big enough to show the effect of UAE on fertility or pregnancy.

This is the first RCT to report 12-month outcomes comparing UAE with the traditional surgical remedies for fibroids and suggested no difference in QoL between the treatment groups at 1 year.

#### **UAE versus myomectomy**

There is one published RCT from the Czech Republic.<sup>37</sup> This was a 1:1 trial of 63 women, 30 of whom randomised to UAE and 33 to myomectomy (18 open abdominal, 15 laparoscopic). The average age of participants was identical in both groups (32.3 years). The inclusion criteria were age up to 40 years, planned future pregnancy, US-verified intramural fibroid of at least 4 cm in greatest diameter and serum concentration of follicle-stimulating hormone under 30 IU/l (on the

third day of the menstrual cycle). Their stated elimination criteria: other than intramural localisation of fibroids (type 0 and type I submucous myomas, according to the classification of the European Society for Hysteroscopy, and subserous myomas were excluded), size of largest fibroid greater than 12 cm in greatest diameter (by US) or a uterus greater than the fourth month of pregnancy (on palpation), previous treatment of fibroids (myomectomy, medical treatment with GnRH agonists or danazol), suspected uterine sarcoma [by palpation, Doppler US, magnetic resonance imaging (MRI) and/or strikingly rapid tumour growth], significant illness that would contraindicate pregnancy, lack of consent in participating in the study or wish to withdraw from the study.

No sample size calculation was performed. Outcome measures reported were procedure duration, length of hospital stay, technical success, fibroid-related symptom relief, early and late complications, recurrences and re-interventions. Minimum follow-up was 6 months with a mean of 17 months (range 6–36 months).

Technical success rate was similar in both groups. Bilateral occlusion of uterine arteries was successfully performed in nearly 87% of cases. In four patients embolisation was unilateral. Total surgical extirpation of all significant fibroids was successful in 31/33 cases (94%). The average duration of myomectomy was significantly ( $p < 0.0001$ ) longer (104.8 minutes, range 48–173 minutes) than the length of embolisation (70.3 minutes, range 45–140 minutes).

In the early post-procedural period, no significant difference between the groups was found in febrile morbidity, count of leucocytes, necessity of administering antibiotics or frequency of prolonged hospitalisation or re-hospitalisation. On the other hand, the durations of hospitalisation and sick leave were markedly longer after myomectomy. Similarly, serum levels of some laboratory markers significantly differed: they showed higher C-reactive protein and lower haemoglobin the second day after procedure in the myomectomy group.

The frequency of early postoperative adverse events was relatively high in both groups: 23% in the UAE group and 27% in the myomectomy group. Complications were generally mild and temporary.

Both methods were highly effective in treating symptoms; 21 out of 24 women (87.5%) with

previous symptoms had significant relief 6 months after embolisation and 28 out of 30 women (93.3%) after myomectomy. There was a higher proportion of completely asymptomatic patients after myomectomy (70%) than after UAE (46%), but the difference was not significant ( $p < 0.1$ ).

The US evaluation of the uterus 6 months after procedure in terms of its readiness for planned gestation revealed no significant pathology in 43% of women after embolisation and in 82% of patients after myomectomy ( $p < 0.01$ ).

Groups differed significantly in the frequency of re-interventions. Eleven women in the UAE group (37%), including four with only unilateral embolisation, underwent secondary myomectomy for a persisting significant fibroid. In the myomectomy group only two patients (6%) underwent re-operation for fibroid recurrence.

No significant difference between the groups in the frequency of late complications was found. All late events related to myomectomy were mild but there were three complications after embolisation regarding ovarian functions. There were no reports of life-threatening complications, hysterectomy or other urgent surgery.

The authors report that 38 women of 63 were attempting to conceive and at the time of their report 18 gestations in 17 women, eight live newborns and five ongoing uncomplicated pregnancies were observed in the study population.

The authors conclude: “We can summarise that in the great majority of cases both methods of fibroid treatment were technically successful and not burdened with a great number of serious complications. Less invasiveness and its resulting shorter hospitalisation and recovery period speak in favor of embolisation. Certainty of definite eradication of the fibroid(s) and thus a smaller frequency of further invasive therapy, at least in the short-term one–two years, speak in favor of surgical therapy (myomectomy). We need to wait a while longer for the long-term results of the various methods of treating uterine fibroids, especially on their effect on reproductive and perinatal outcomes.”

### **Large prospective observational studies with longer follow-up**

#### **US FIBROID Registry**

The US FIBROID Registry ([www.fibroidregistry.org/](http://www.fibroidregistry.org/)) was set up following an evidence report

commissioned by the SIR Foundation.<sup>45</sup> The report identified four important research needs: (1) to develop a disease-specific QoL instrument, (2) to establish a registry for prospective collection of outcomes data, (3) to carry out a randomised trial and (4) to carry out a comparative cost analysis.

The SIR Foundation subsequently funded the development of the first two of these.

Spies and colleagues developed and validated a disease-specific QoL instrument for symptomatic fibroids, the Uterine Fibroid Symptom and Quality of Life Questionnaire (UFS-QoL).<sup>46</sup> The UFS-QoL was developed from focus groups, clinician opinion and literature review, using standard instrument development techniques. The validation study was conducted in both non-symptomatic volunteers and women with uterine fibroids. The final instrument yielded a questionnaire with 37 questions, including eight symptom questions and 29 QoL questions. There are six QoL subscales: Concern, Activities, Energy/Mood, Control, Self-consciousness and Sexual function. The questionnaire can be scored by hand and yields both a symptom and QoL score. Each of these scores ranges from 0 to 100, but in an inverse manner. For the symptom scale, a lower score is better because it indicates lower symptoms, whereas a higher QoL score indicates better QoL status. These scores are the primary outcome measure of the FIBROID Registry.

The FIBROID Registry was designed to answer several key questions about UAE:

- Is UAE a safe treatment? What is the incidence of minor and serious short-term complications?
- Is UAE an effective treatment? What is the likelihood of symptom relief?
- How durable is the treatment? What is the likelihood of subsequent therapy to treat recurrent symptoms?
- What is the likelihood that a woman who undergoes UAE will be able to conceive and deliver a subsequent pregnancy?
- Is there a differential outcome based on device (product size, primary and secondary embolic material) used?
- Are there certain patient subgroups at higher risk or that have an increased likelihood of treatment benefits?
- What number of procedures should be recommended for training interventional radiologists and for maintaining skills?



The Registry is a collaboration between the SIR Foundation and the Duke Clinical Research Institute (DCRI), Washington, DC. It is a voluntary registry of patients treated with UAE at participating hospitals.

Following consent, patients' baseline demographic data, reproductive and gynaecological history and medical history were recorded. Each patient completed the UFS-QOL questionnaire. The interventional radiologist recorded details of pelvic imaging (US or MRI). At the time of the procedure, technical details (including data about perioperative care and embolic material used) were recorded.

Thirty-day follow-up data were obtained for each patient and recorded via the Web-based reporting system. Recovery and adverse events were the primary focus of the 30-day follow-up. Adverse events were scored according to the SIR scale for severity,<sup>47</sup> and a system of complication definitions derived from American College of Obstetricians and Gynecologists (ACOG) quality indicators.<sup>48</sup>

Longer-term follow up data were gathered by DCRI via mailed questionnaires. Non-responders were contacted by telephone and given a choice of completing the questionnaire via interview or having another questionnaire set mailed to them. The long-term follow-up schedule was 6, 12, 24 and 36 months after treatment. The 6- and 12-month data collections are complete, and the initial analysis of these data has been reported.<sup>38-41</sup>

Eighty-five sites completed the process for participation in the Registry. The first patient was enrolled 13 December 2000 and, at closure on 31 December 2002, 3319 patients had been logged into the Registry by 72 sites. Of the eligible patients (3180), complete data on core variables were available for 3005 (94.9%). The mean age of these 3005 women was  $43.5 \pm 5.6$  years (SD), 48% were African-American and 44.4% were white (non-Hispanic), 9.5% were definitely planning to attempt conception within 2 years and 17.3% wanted to retain the option. HMB was the predominant symptom in 64.7% of cases. In-hospital data were obtained on 3005 patients and complete 30-day data were received on 2729 (90.8%) cases. At the 6-month follow-up 2112 patients qualified for further follow-up. Follow-up data were received on 1797 of these (85.1%) cases, and 12-month data were received on 1701 (80.5%) cases. A small percentage of cases at each time point were lost to follow-up.

The following data are reported.

#### **Is UAE a safe treatment? What is the incidence of minor and serious short-term complications?**

Overall, the incidence of complications was low and recovery was rapid. Patients returned to normal activities in a mean of 14 days. Of those women who worked outside the home ( $n = 2404$ ), the mean number of days lost from work (including the day of the procedure) was 10.

There were no deaths and only two events that resulted in permanent patient injury. These were bilateral oophorectomy 3 weeks after embolisation for pelvic pain in one patient and a puncture site femoral nerve injury in another.

Ninety of 3005 patients reported a total of 94 adverse events during hospitalisation for UAE (3%).

Of the 94 adverse events, 20 were in-hospital major adverse events (0.66% of patients). These were primarily for prolonged pain or nausea (10 events) requiring hospitalisation longer than 48 hours.

Adverse events (major or minor) occurred between hospital discharge and 30 days in 710 women (26%), of whom 191 (7%) had more than one adverse event.

Major events occurred in 111 of 2729 patients (4.1%) within 30 days of hospital discharge. The most common major event was emergency room care or readmission for recurrent pain (65 patients, 2.4%).

During the period between discharge and 30 days after UAE, 32 (1.2%) patients required a surgical intervention for an adverse event. The most common intervention was dilatation and curettage (D&C) for management of a fibroid being expelled from the uterus. Three hysterectomies were performed in the first 30 days after the procedure.

#### **Is UAE an effective treatment? What is the likelihood of symptom relief?**

Of the 2112 patients eligible for 6- and 12-month follow-up, complete data were available on 1797 patients at 6 months and 1701 patients at 12 months. UFS-QOL scores are reported as the primary outcome measures.

For total health-related quality of life (HRQoL) scores, 85.4% had at least a 10% improvement by

6 months and 87.5% had this degree of improvement by 12 months. The Registry is assessing what degree of improvement should be considered 'clinically successful'.

There were large improvements in symptom scores. The mean score improved from a baseline of 58.0 (SD 20.81) to 19.9 (SD 18.6) at 6 months and 19.2 (SD 17.9) at 12 months, both within the range seen among normal subjects in the original validation study.

Similarly, there were large improvements in HRQoL scores. The mean score improved from a baseline of 47.3 (SD 22.9) to 85.1 (SD 20.1) at 6 months and 86.7 (SD 18.2) at 12 months; again, both scores are in the range for normal subjects in the original validation study.

Patient satisfaction with treatment outcome was measured by whether the patient would recommend the procedure to family or friends. At 12 months, 82% of women would recommend the procedure. However, data were not available for almost 20% of women eligible for longer-term follow up. If these women were more likely to have had poor outcomes, both overall success rates and mean improvements in QoL scores would be lower.

#### **How durable is the treatment? What is the likelihood of a subsequent therapy to treat recurrent symptoms?**

The Registry defines recurrence as a return of initially controlled fibroid-related symptoms greater than 12 months after embolisation. Determination of the recurrence rate will thus require analysis of the data from 24 and 36 months.

Women who did not have symptom improvement sustained for 1 year were defined as clinical failures. For these analyses, the denominators were 1797 patients at 6 months and 1701 patients at 12 months. Additional procedures for symptoms were performed in 4.5% of patients within 6 months of UAE and another 5.0% of patients by 12 months. These included hysterectomy, myomectomy, D&C and repeat embolisation. There were 49 hysterectomies in the first year of the Registry (2.9% of patients), primarily for symptoms not controlled by the embolisation procedure. Within 6 months after embolisation, 7.4% of patients needed additional hormonal or medical therapy, and between 6 and 12 months, 3.5% of patients needed additional medical therapy.

#### **What is the likelihood that a woman will be able to conceive and deliver a subsequent pregnancy post-UAE?**

The data from the Registry are insufficient to determine this likelihood currently since the post-procedure interval has been too short. There were, however, 12 pregnancies during the first 12 months of the Registry.

Based on the advanced mean age (37 years) of women who have expressed an interest in pregnancy and their high proportion of prior infertility, it is unlikely that the Registry will generate sufficient pregnancies to make meaningful generalisable estimates of embolisation impact on pregnancy rates or outcomes. This would require clinical trials in this patient population designed to answer this question.

#### **Is there a differential outcome based on device (product size, primary and secondary embolic material) used?**

Registry results suggest that there does not appear to be any differential impact of UAE related to the embolic type, embolic particle type, or other technical aspects of the procedure on adverse events at least up to 1 year.

#### **Are there certain patient subgroups at higher risk or that have an increased likelihood of treatment benefits?**

No subgroups have been identified that had a poor outcome or for whom the procedure would not be recommended in the 6 and 12-month follow-up data. The one strong predictor of clinical failure was unilateral embolisation, which was defined at the outset as a technical failure. The patients with a technically failed procedure were significantly more likely to be clinical failures at 12 months (hazard ratio 2.56, 95% CI [1.48 to 4.42]). The only demographic factors that predicted a minor increase in adverse events was African-American race (OR 1.129,  $p = 0.02$ ) and current or recent smoking status (OR 1.141,  $p = 0.04$ ). Patients who had prior fibroid-related procedures at baseline were slightly more likely to have an adverse event (OR 1.235,  $p = 0.0003$ ). Prophylactic antibiotics did not influence the frequency of adverse events, although only 5% of patients did not have prophylaxis. The small proportion of patients without prophylaxis limited the ability to predict adverse events related to this factor. Use of deep vein thrombosis (DVT) prophylaxis decreased the risk of adverse events (OR 0.76,  $p = 0.005$ ). It is expected that analyses of the 24- and 36-month data will provide better

insight into the predictors of long-term success or failure.

### **What number of procedures should be recommended for training and for maintaining skills?**

There were no predictors of adverse events or symptomatic outcome that related to site experience, enrollment rates in the Registry, or site type. However, only members of the SIR (or their international equivalent) were participants in this Registry. Most investigators in the Registry therefore had considerable angiographic and embolisation experience. It is unlikely that uniformity of outcomes noted in this study can be duplicated for those without the requisite background. Consequently, as with training for the procedure, the number of procedures that would ensure maintenance of skills cannot be estimated based on this dataset.

### **Prospective observational study**

A prospective observational study to evaluate the long-term efficacy and complications of UAE carried out in a district general hospital and two private hospitals in south-east England has been reported.<sup>42</sup> This study used its own unvalidated postal questionnaire follow-up at 5–7 years to assess long-term clinical effects. The main outcome measures were menstrual flow, amenorrhoea and menopause, fibroid-related symptoms, fertility, vaginal discharge, sexual function, subsequent treatments for fibroids and satisfaction with the procedure. Questions regarding menstrual bleeding, fibroid-related symptoms, vaginal discharge and sexual function were subjective.

A total of 258 women were identified as being between 5 and 7 years post-UAE and suitable for long-term follow up in October 2004, and 172 completed questionnaires were analysed (67% response rate). The mean age of women in the sample was 43 years; 19% were older than 50 years, 22% between 45 and 50 years and 58% between 30 and 44 years old. About 87% were white women and 8% were black women. Four of the women received unilateral UAE. The remaining 168 all underwent a bilateral procedure. Eleven women required more than one session to complete the procedure. Imaging and clinical evaluation were carried out both pre- and post-UAE.<sup>49</sup>

About 75% of women still had either a return to normal or an improvement in menstrual flow compared with how they were prior to UAE. More

than 80% of fibroid-related symptoms were still resolved or improved; 16% of women required further treatment for fibroids. Nine had hysterectomies, six had myomectomies (one woman had two separate myomectomies), nine had hysteroscopic resections of fibroids (one woman also had an ablation procedure) and three had hysteroscopies for vaginal discharge. One woman had *Escherichia coli* septicaemia that developed rapidly after UAE, necessitating hysterectomy at 2 weeks post-UAE. Premature menopause directly following UAE occurred in only one woman in the study group. A total of 88% of women were satisfied with the outcome of the procedure 5–7 years later and would choose it again or recommend it to others.

The authors conclude, “Our results show that fibroid embolisation as we were performing it five–seven years ago is a viable alternative to hysterectomy. It carries high success and low complication rates that are sustained in the long term. We anticipate even better future results with our current technique.” The improved current technique includes carrying out a planned second UAE in cases of initial under-embolisation.

The Cochrane Review<sup>28</sup> included the Pinto and EMMY trials comparing UAE with hysterectomy and the Mara trial comparing UAE with myomectomy. The review summarises the evidence from these three studies with up to 6 months’ follow-up as follows.

The trials show a reduction in total length of hospital stay and quicker resumption to daily activities with UAE. Patient satisfaction rate is similar between UAE and surgery (hysterectomy/myomectomy) groups. With respect to safety, there seems to be more minor intra-procedural and post-procedural complications associated with UAE. Technical failure to accomplish bilateral UAE (up to 12%) results in a higher surgical intervention rate, particularly myomectomy, when fertility is desired.

The REST study, which reports 12-month follow-up, concurs with these results for the short-term variables. In addition at 12 months, “both surgery and UAE provide a successful outcome for a majority of women with symptomatic fibroids. There was no difference in quality of life at one year. Complications after surgery usually occurred in the early post-operative period whereas some of those occurring after UAE did so after a prolonged period of time”.

The FIBROID Registry also provides data on 12-month follow-up after UAE. The authors conclude that UAE is a low-risk procedure with little variability in adverse events based on patient demographics or practice setting. The procedure results in substantial improvement for most patients with hysterectomy required in only 2.9% of patients in the first 12 months after therapy.

### Conclusion

There is a continued need for further longer term and larger RCTs of UAE versus medical or surgical treatments for managing symptomatic fibroids, particularly with regard to future fertility (Table 1).

**TABLE 1** Summary of main evidence from RCTs and large prospective study on the safety and efficacy of UAE

Study	Study details: randomisation/ power/reported follow-up	Main significant results
<b>RCTs of UAE vs hysterectomy</b>		
Pinto, <sup>30</sup> 2003 (Spain)	2:1 intended, 38 UAE:19 Hyst Actual treatment received, 40 UAE:20 Hyst  Powered for length in hospital stay, “we determined that a minimum of 54 patients ... were needed” Not powered for efficacy and safety analyses  6 months follow-up	ITT analysis re. hospital stay was shorter for UAE (by 4.14 days – 1.71 vs 5.85) Treatment received analyses re. safety and efficacy Resumption of normal activities shorter in UAE (by 26.68 days – 9.5 vs 36.18) <b>Safety:</b> Emergency room visit after procedure – 32% UAE vs 20% Hyst During procedure complications – 25% UAE (minor) vs 20% Hyst (major requiring blood transfusion) 30-day post-procedure complications – 72% UAE (minor–moderate) vs 45% Hyst (moderate–major) <b>Efficacy:</b> UAE only (cannot compare vs Hyst) 86% successful (cessation of bleeding problems), fibroid shrinkage by 46%
EMMY, <sup>34–36</sup> 2005–6 (The Netherlands)	1:1 randomisation, 88 UAE:89 Hyst Actual treatment received, 81 UAE:75 Hyst  Primary end-point (SF-36) UAE equivalent to Hyst if elimination of menorrhagia after 2 years in 75% of UAE patients with no significant safety differences. <i>n</i> = 120 required  Follow-up to 6 weeks post- procedure, pain and return to daily activities	ITT analysis carried out for all analyses Technical failure greater in UAE: 4.9% bilateral failure (2nd report states 5.3%) vs zero Hyst failures Hospital stay shorter in UAE 2.5 vs 5.1 days. UAE experienced less pain than Hyst 24 hours post- procedure UAE returned to normal activities sooner – for paid work 28.1 vs 63.4 days <b>Safety:</b> No difference in major complication rates: 4.9% UAE vs 2.7% Hyst Minor complications higher in UAE: 58% vs 40% Hyst UAE more often readmitted: 11.1% vs 0% <b>Efficacy:</b> not yet reported
REST, 2007 <sup>33</sup> (Scotland)	2:1 randomisation, 106 UAE:51 surgery Treatment received, 101 UAE:40 Hyst:8 myomectomy  Primary outcome: QoL (SF-36)  12 months follow-up	95% patients underwent allotted treatment Length of hospital stay shorter in UAE than surgery, Time to return to routine tasks shorter in UAE than surgery <b>Safety:</b> At 12 months UAE patients had 4% risk of repeat UAE and 8% risk of Hyst SAEs occurred in 31% UAE and 18% surgical patients. <b>Efficacy:</b> No difference in QoL at 12 months between treatments Symptom scores better in surgical arm at all points (9% UAE required further invasive treatment for symptoms) <b>Economic analysis:</b> UAE cheaper, £1757 vs £2702 for surgery

continued

**TABLE 1** Summary of main evidence from RCTs and large prospective study on the safety and efficacy of UAE (cont'd)

Study	Study details: randomisation/ power/reported follow-up	Main significant results
<b>RCTs of UAE vs myomectomy</b>		
Mara, <sup>37</sup> 2006 (Czech Republic)	1:1 randomisation, 30 UAE:33 myomectomy  No sample size calculation described  Minimum follow up 6 months, mean 17 months, range 6–36 months  All subjects were planning future pregnancy	Technical success similar in both 87% UAE vs 94% myomectomy Average myomectomy longer (104.8 vs 70.3 minutes), Duration of hospitalisation and sick leave markedly longer after myomectomy <b>Safety:</b> Frequency of early post-operative adverse events relatively high in both groups, 23% UAE vs 27% myomectomy, but mostly minor and temporary. No difference in infections or in frequency of late complications – all mild <b>Efficacy:</b> Both methods effective in treating symptoms: after 6 months 87.5% UAE had significant symptom relief vs 93.3% myomectomy. Groups showed a difference in re-interventions, 37% in UAE vs 6% in myomectomy.
<b>Large observational prospective study of UAE with longer follow-up</b>		
FIBROID Registry, <sup>38–41</sup> 2005 (USA)	3319 patients at 72 sites treated with UAE in 2 years to December 2002  Mean age 43.5 ± 5.6 years, 48% African-American/44.4% white/ non-Hispanic  Developed and validated UFS-QOL instrument  6, 12, 24 and 36 month follow-ups scheduled  Data reported for 12-month follow- up (6-month data on 1797 patients, 12-month data on 1701) 20% loss at 12 months	Return to normal activities in mean of 14 days <b>Safety:</b> No deaths, only two events resulted in permanent injury 3% experienced adverse events while inpatient for UAE 26% experienced adverse event between discharge and 30 days. Major events in 4.1% (generally readmission for recurrent pain). 1.2% required re-intervention (D&C) <b>Efficacy:</b> 87.5% had at least 10% improvement in total HRQoL scores by 12 months. Mean HRQoL score improved from 47.3 at baseline to 86.7 at 12 months. Mean symptom score improved from 58.0 at baseline to 19.2 at 12 months. At 12 months 82% of women would recommend UAE to a friend. Within 12 months there were 49 hysterectomies (2.9%). Additional gynaecological procedures for symptoms in 4.5% of patients within 6 months and an additional 5.0% of patients by 12 months (included hysterectomy, myomectomy, D&C and repeat embolisation). Within 6 months, 7.4% of patients needed additional hormonal/medical therapy, and between 6 and 12 months, 3.5% of patients needed additional medical therapy  No subgroups have been identified that had a poor outcome or for whom the procedure would not be recommended One strong predictor of clinical failure was unilateral embolisation, defined at the outset as a technical failure Patients with a technically failed procedure were significantly more likely to be clinical failures at 12 months (hazard ratio 2.56, 95% CI 1.48 to 4.42) Few predictors of adverse events, none substantially increased the OR for an event. The only demographic factors that predicted a minor increase in adverse events was African- American race (OR 1.129, <i>p</i> = 0.02) and current or recent smoking status (OR 1.141, <i>p</i> = 0.04) Prophylactic antibiotics did not influence adverse events; only 5% of patients did not have prophylaxis



# Chapter 2

## Methods

### Study design and objectives: introductory remarks

The HOPEFUL study is a multi-centre retrospective cohort design comparing the experiences of two cohorts of women who received one of two alternative treatments for symptomatic fibroids according to routine practice and availability within the UK from the mid-1990s.

NICE<sup>29</sup> and RCOG<sup>31</sup> have identified a lack of longer term data on the efficacy and safety of UAE. This observational study examines the experience of two cohorts of women who underwent either hysterectomy or UAE for symptomatic uterine fibroids, in particular their experience over several years following their treatment. Direct comparisons in outcomes are made between the two cohorts wherever possible.

The limitations of an observational retrospective cohort study design are acknowledged. A prospective RCT of the two treatments would clearly provide the highest quality evidence to examine this question by minimising biases and allowing more direct pre- to post-treatment comparisons to be made. However, recruitment to such trials in these circumstances is difficult and it would require a decade to achieve several years' follow-up on patients prospectively. The advantage of the current design is that it enables a large number of patients' longer term experiences to be examined in order to contribute valuable data for informing decisions on recommendations for practice.

There are important methodological considerations to be addressed due to the retrospective study design. These are fully considered in the analyses.

The first consideration concerns the comparability of the women in the two treatment cohorts at baseline. Without randomisation it is likely that the patients in the two treatment cohorts will differ in any of a number of ways that may have a confounding influence on outcome measures, for example, their demographic characteristics, physical and health characteristics, clinical indications, treatment preferences and

expectations. Possible confounders examined include age, ethnicity, educational level, body mass index (BMI), smoking history, age at menarche, menstrual status, parity, time since index treatment, high blood pressure and other co-morbidity, prior surgery, previous fibroid treatments, fibroid symptoms, fibroid characteristics, fertility aspirations, treatment preferences and treatment-related variables including prophylactic antibiotic use.

A second important consideration concerns the identification of relevant outcome measures which can be assessed in both cohorts retrospectively to allow a direct comparison between the two treatments.

Clinical outcomes of relevance relate to both safety of the procedures and the efficacy of the treatment to resolve or reduce symptoms. Because hysterectomy surgically removes the uterus and therefore the source of all fibroid symptoms it is difficult to compare directly improvements in symptoms between the two interventions as the primary study outcome. Furthermore, the retrospective design means that no pretreatment measures of QoL/symptoms are available to compare with post-treatment values in both groups.

Primary outcome therefore was a comparison of safety. Data were collected on complications arising as a consequence of the index procedure. To overcome the issue of different treatment-specific complications, safety was assessed by clinical severity. Events were categorised into severe/major/minor *a priori* by the project team. The general side-effects (GSEs) of treatment in the UAE group that may be anticipated were also investigated.

Secondary outcomes relate to treatment efficacy. Data were gathered retrospectively, primarily by patient questionnaire on resolution of fibroid symptoms and satisfaction with treatment compared between treatment groups. In addition, further measures of efficacy in the UAE group only including fibroid/uterine size shrinkage, resolution of menstrual symptoms and any further treatments for fibroid symptoms were investigated.

Additional issues of relevance to the UAE treatment group only were investigated, including factors influencing choice of treatment, factors influencing outcome of UAE treatment and fertility post-UAE.

The cost-effectiveness analysis utilised data constructed in the primary outcome analysis. This included probabilities derived from the multiple regression analysis (minimum model) for primary outcome [1], primary outcome [2] and GSEs. Further probabilities, costs and utilities were taken from the literature where possible or using expert opinion.

Due to the complexity of the clinical issues being addressed by HOPEFUL, free-text analysis was utilised to add further understanding to the quantitative data. The patient questionnaire contained 34 questions, some with subsections, and all with precoded responses. This highly structured format allowed the collection of large amounts of quantitative information efficiently from the large number of respondents. In recognition of the inherent interpretative limitations of collecting only precoded material, and in appreciation of possible frustration among respondents if they were not invited to tell us anything extra, space was provided at the end of the questionnaire where respondents were asked to record "anything else about your treatment/s for fibroids and your health which is important to you".

Two precoded questions within the questionnaire were also allocated space for free-text comment. These were:

**Q24 (a)** My expectations about my <sub>1</sub> yes  <sub>2</sub> no   
treatment have now been fulfilled  
If no, please tell us why:

**Q24(f)** I have suffered from <sub>1</sub> yes  <sub>2</sub> no   
problems caused by the treatment  
If yes, please give details about the problems:

Space was included for Q24(a) to collect data on the particular expectations and disappointments that people had, rather than simply the fact that expectations had not been fulfilled. Space was provided for Q24(f) in preference to a long precoded list of all possible problems that might have been caused by treatment, and to allow people to record the most important problems as they perceived them, and in their own words.

## Participant recruitment

The eligibility criterion for HOPEFUL was that the index treatment (first UAE or hysterectomy) was for symptomatic fibroids. There were no exclusions by age, other medical conditions or any other variable as the study population was intended to represent UK experience at time of treatment. Identification of patients for the study was as follows.

Interventional radiologists offering the newer UAE procedure to treat fibroids who had been carrying out this procedure on a significant number of women since the late 1990s were invited to collaborate in the study. Nine patron radiologists, pioneers of this procedure for fibroids, agreed to provide a complete list of their patients from undertaking their first procedure up to the end of December 2002. One centre provided their first 100 patients which dated to September 1998 and another centre provided their patients until they discontinued embolisation procedures in March 2000. After tracing current addresses, this provided the potential opportunity to collect clinical data on up to 972 UAE patient procedures with follow-up of more than 2 years. UAE collaborators are listed in Appendix 1.

The control/hysterectomy cohort comes from the VALUE study,<sup>50</sup> which is investigating long-term effects of 37,000 unselected consecutive hysterectomies carried out between October 1994 and September 1995 in centres in the UK, except Scotland. This group was initially recruited as a control group for women treated with transcervical endometrial ablation or resection for dysfunctional uterine bleeding (DUB). Amongst them, there were about 6000 women with uterine fibroids as the first indication for hysterectomy. From this database of 6000 women held by one of the HOPEFUL co-investigators (MM) on behalf of RCOG, the ten centres that had performed the most hysterectomies for uterine fibroids were invited to take part in HOPEFUL in order to maximise patient numbers and for pragmatic reasons to minimise the number of centres for data collection from hospital records. These patients are not part of the existing VALUE follow-up protocol, which is concerned with patients with menorrhagia as the main indication. Nine centres agreed to collaborate in the study and were provided with a list of their eligible patients from the VALUE database by MM.

After tracing current addresses of these patients via the NHS Tracing Service, a possible 762



**TABLE 2** Number of eligible patients per collaborating centre and per cohort

Centre code	Collaborating NHS Trust/Hospital centre	No. of eligible patients
<b>Hysterectomy cohort</b>		
01	Blackpool, Fylde and Wyre Hospitals NHS Trust, Blackpool Victoria Hospital	65
02	Countess of Chester Hospital NHS Foundation Trust, Countess of Chester Hospital	57
03	Derby Hospitals NHS Foundation Trust, Derby City Hospital	87
04	Gloucestershire Hospitals NHS Trust, Gloucestershire Royal Hospital	64
05	Barking, Havering and Redbridge Hospitals NHS Trust, King George Hospital, Ilford	108
06	University Hospitals of Leicester NHS Trust, Leicester General Hospital	70
07	Norfolk and Norwich University NHS Trust, Norfolk and Norwich Hospital	166
09	Chesterfield and North Derbyshire Royal Hospital NHS Trust, Royal Hospital, Chesterfield	75
12	Bradford Teaching Hospitals NHS Foundation Trust, Bradford Royal Infirmary	70
	<i>Hysterectomy total</i>	762
<b>UAE cohort</b>		
21	Greater Glasgow Health Board (North Glasgow University Hospitals Division), Glasgow Royal Infirmary and Gartnavel General Hospital	73
22	The Guy's and St Thomas' NHS Trust, Guy's and St Thomas' Hospital (London)	154
23	Hull and East Yorkshire Hospitals NHS Trust, Hull Royal Infirmary and York Hospitals NHS Trust, York Hospital	92
24	Royal Berkshire and Battle Hospitals NHS Trust, Royal Berkshire Hospital (Reading)	194
25	Royal Free Hospitals NHS Trust, Royal Free Hospital (London)	101
26	St George's Healthcare NHS Trust, St George's Hospital (London)	43
27	Southampton University Hospitals NHS Trust, Southampton General Hospital	86
28	Oxford Radcliffe Hospitals NHS Trust, The Churchill Hospital (Oxford)	120
29	Royal Surrey County Hospital NHS Trust, Royal Surrey County Hospital (Guildford)	100
30	Countess of Chester Hospital NHS Foundation Trust, Countess of Chester Hospital	9
	<i>UAE total</i>	972
	<i>Total eligible patients</i>	1734

hysterectomy patients were identified. For the HOPEFUL study the surgery referenced in the VALUE database is the index treatment. VALUE/hysterectomy collaborators who agreed to participate are listed in Appendix 2.

Table 2 shows the number of eligible patients identified per centre in both treatment cohorts.

The HOPEFUL study population comprised 1734 traceable women, 972 of whom were treated with embolisation as their index treatment for symptomatic fibroids and 762 with hysterectomy.

## Treatments

The hysterectomy treatment cohort may have undergone any method and extent of hysterectomy including abdominal, vaginal or laparoscopic methods with or without removal of ovaries.<sup>44</sup> The majority of patients underwent total abdominal hysterectomies [ $n = 398$  (86.7%)]. Twenty-three (5.0%) had subtotal abdominal hysterectomies, 24 (5.2%) vaginal hysterectomy and 12 (2.6%) laparoscopically assisted vaginal

hysterectomy. There is a greater risk of complications from laparoscopically assisted vaginal hysterectomy,<sup>12</sup> but with such small numbers this should not affect the primary outcome analysis.

The majority of patients underwent bilateral oophorectomy at the same time as their hysterectomy (59.0% of patients had no ovaries remaining after their hysterectomy, 7.4% had only one ovary remaining and 31.8% had both ovaries remaining).

The UAE group all underwent a standard uterine artery embolisation procedure as described in Chapter 1. All UAE centres used traditional PVA embolic particles (sizes were in the ranges 250–355, 355–500 and 500–710  $\mu\text{m}$ ) during the period covered by the study. In addition to PVA particles, some of the centres used gelfoam or coils, either routinely or for specific cases. Exclusion criteria for embolisation treatment at centres included active pelvic infection/pelvic inflammatory disease, pedunculated fibroids and a wish to improve fertility status. Table 3 shows the inclusion/exclusion criteria details by centre.

**TABLE 3** Details of embolisation per centre

Centre	Embolic agent	First UAE procedure	Last UAE procedure	Inclusion criteria	Exclusion criteria
21	500–710 PVA only	23/02/1999	20/12/2002	Symptomatic fibroids Fibroids > 2 cm in diameter and adequately imaged	Pedunculated subserosal Active infection (PID, UTI, etc.) Allergic to contrast medium Contraindication or unable to tolerate MRI
22	500–700 PVA + gelfoam	08/07/1996	31/10/2002	Significant symptomatic fibroids, as seen and assessed by a gynaecologist	Active infections Pedunculated subserosal Asymptomatic for fertility reasons
23	355–500 PVA only	07/11/1997	09/12/2002	Symptomatic fibroids	Pelvic infection/inflammatory disease Pedunculated fibroids Infertility Cosmetic symptoms
24	355–500 PVA + coils	09/10/1997	22/10/2002	Symptomatic fibroids	Pedunculated fibroids Wishing to retain fertility
25	355–500 PVA only	16/12/1998	23/12/2002	Symptomatic fibroids (identified by MRI or US)	Wishes to improve fertility status Asymptomatic Pedunculated
26	355–500 PVA only	15/06/1998	20/03/2000	Symptomatic fibroids	Subserosal pedunculated
27	355–500 PVA ≤ 1998 500–710 PVA ≥ 1999 Occasional use of coils or gelfoam only ≥ 2000	07/04/1998	15/11/2002	Symptomatic fibroids	Active pelvic infection Pregnancy wishes Thin-stalked pedunculated fibroids
28	PVA (varying size) Occasional use of coils	09/12/1997	10/11/2002	Symptomatic fibroids	
29	PVA (355–500) Usually with coils	24/12/1996	16/09/1998	Symptomatic fibroids	Large pedunculated fibroids Pelvic infection/pelvic inflammatory disease
30	PVA (250–355 or 300–500)	06/07/1999	17/09/2002	Symptomatic solitary fibroid	Pelvic infection/inflammation Multiple small fibroids Desire for future pregnancies Very large fibroids

PID, pelvic inflammatory disease; UTI, urinary tract infection.

Information was available on embolisation technique in 590 cases (90.9%), 540 (83.2%) had a single-stage embolisation procedure and 50 (7.7%) had a preplanned two-stage procedure, usually on two consecutive days. In the UAE cohort, 27 (4.2%) of the patients were unable to have both their uterine arteries embolised, usually because of absent or tortuous arteries. Two had their left ovarian artery embolised with prior consent, one in addition to bilateral embolisation of the uterine arteries and the other as a single ovarian

embolisation due to the fibroid being fed by the ovarian artery.

## Study procedures

### Central project management

The Oxford Project Coordinating Team responsible for overall project management was based in the University of Oxford, Nuffield Department of Obstetrics and Gynaecology, John

Radcliffe Hospital, Oxford. The team comprised Professor Klim McPherson (Chief Investigator), Allison Hirst (Project Manager/Researcher December 2003–December 2006), Susan Dutton (Project Statistician/Data Manager April 2004–December 2006), Sue Boyt (Personal Assistant to Professor McPherson and Project Research Secretary January 2004–July 2005) and Lara Waldenmaier (Research Secretary/Qualitative Researcher November 2005–November 2006).

In addition to the Oxford staff, two other grant-holders functioned as representatives for the two treatment cohorts of women and advised on clinical issues. The hysterectomy cohort was represented by Mike Maresh (Consultant in Obstetrics and Gynaecology, St Mary's Hospital for Women and Children, Manchester, Principal Investigator (PI) for the VALUE study) and the UAE cohort by Tony Nicholson (Consultant Vascular Radiologist, Leeds General Infirmary).

### Local collaborators

All consultants responsible for the patients identified in either the hysterectomy or UAE cohorts agreed to a formal collaboration and acted as local PIs for the study. A formal participation agreement was signed for each centre between the local PIs, the participating NHS Trust R&D Directors and the University of Oxford.

Temporary researchers/nurses were employed within each of the collaborating hospitals to collect clinical data according to the study protocol.

### Trial Steering Committee

The running of the project was under the supervision of a Trial Steering Committee which was constructed for that purpose and met on three occasions during the lifetime of the project. (Appendix 3).

### Ethics and research governance (including changes to study protocol)

Overall ethical approval for the HOPEFUL study was obtained from the Multi-Centre Research Ethics Committee (MREC) for Scotland, Edinburgh (REC reference MREC/03/10/49). Full approval was received on 23 February 2004.

Subsequent approvals for small amendments to the protocol were sought and obtained as follows:

- Amendment No 1: approved 2 June 2004. This amendment related to making changes to improve the patient-friendliness of the initial contact letter and patient questionnaire following piloting of study documentation with

a UAE patient group (FEMISA ([www.femisa.org.uk](http://www.femisa.org.uk))) and personal communication with Ginette Camps-Walsh (Voluntary Coordinator of FEMISA Patient Support Group). This amendment also included a reallocation of tasks to reduce workload on research nurses at local sites. The Oxford Project team took over the responsibility of tracing status/current addresses of patients using the NHS Strategic Tracing Service (NSTS) (with Caldicott Permission from Oxford) and sending out all patient questionnaires and questionnaire reminders. It was also agreed not to collect follow-up data from GPs as had been initially planned due to logistical difficulties and the likelihood that little additional information would be obtained.

- Amendment No 2: approved 15 December 2004. This amendment related to contacting patients again who had not responded at 4 weeks after the initial contact letter in order to provide a further opportunity to consent. This action was requested by the Trial Steering Committee in order to maximise patient consent rates.
- Amendment No 3: approved 21 April 2005. This was requested by the Trial Steering Committee concerned about possible biases between cohorts in which patients were consenting to participate. This amendment gave HOPEFUL permission to contact all non-consenters a further time asking them to complete a form containing tick boxes with reasons why they did not wish to consent.

In addition to the overall MREC approval for the project, each local centre obtained their Local Research Ethics Committee (LREC) site-specific approval and local NHS Trust R&D Management approval prior to starting the study.

*Figure 1* outlines the study processes.

### Patient contact/consent and deceased patients

Prior to seeking consent from eligible patients, it was necessary to establish their status and current address. It was likely, particularly for the hysterectomy cohort who had had their surgery 10 years previously, that addresses in treatment records were out of date. The research nurse in each centre provided a list of their eligible patients including the patient's NHS number or last known contact details at the time of the treatment (if no NHS number was available). Using this information, the Oxford team attempted to establish the current status of the

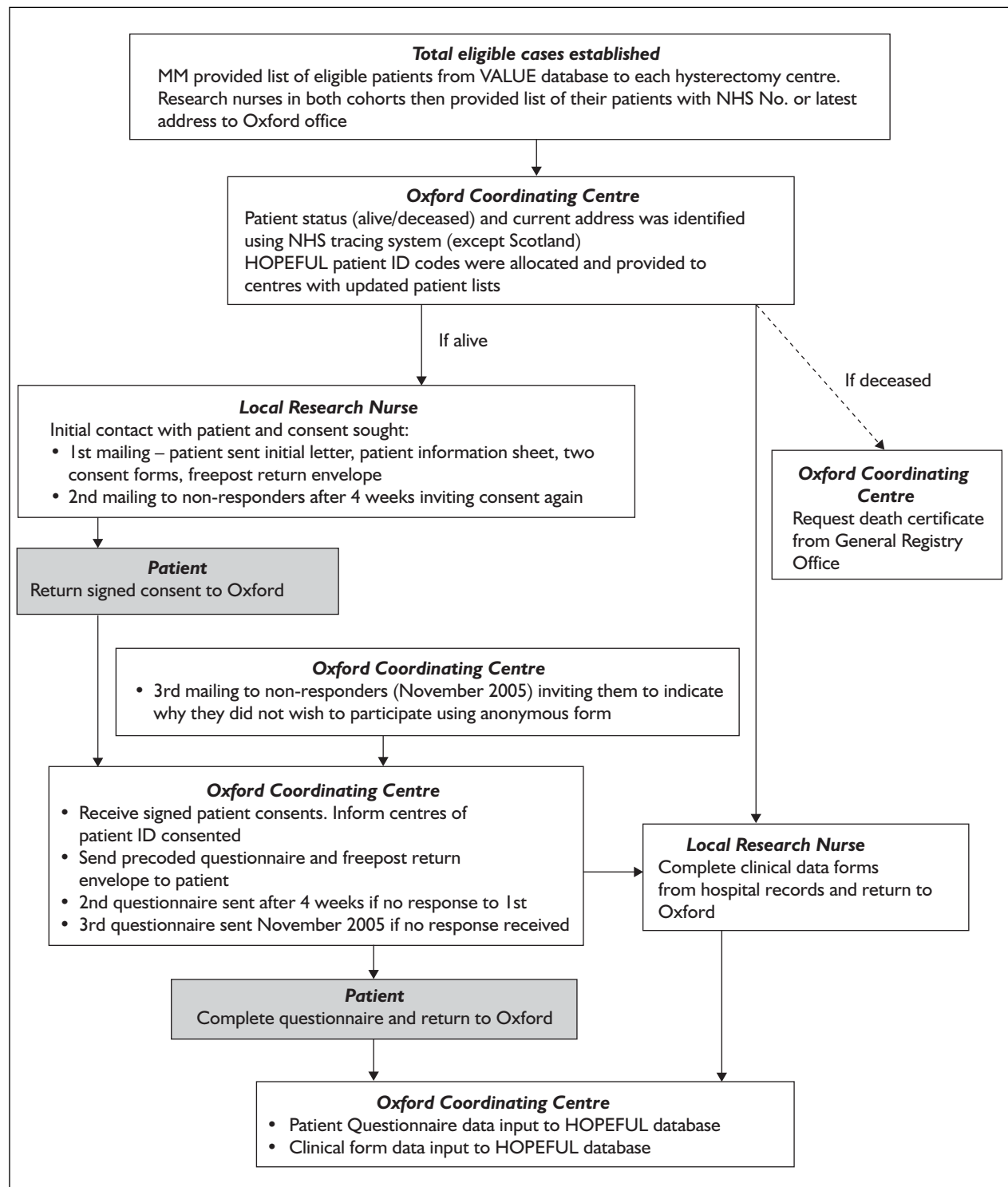


FIGURE 1 HOPEFUL study process flowchart

eligible patients (deceased or living, and if living, their current address). The Oxford office utilised the NSTS to establish this information (<https://nww.nsts.nhsia.nhs.uk/>). Permission was obtained from the Caldicott Guardian at the Oxford Radcliffe Hospitals NHS Trust for Oxford

HOPEFUL project staff to utilise this service for this purpose. The NSTS is not available in Scotland so the research nurse in the Glasgow collaborating centre was responsible for ascertaining the status and location of her own patients.

Twenty-six patients could not be traced and had no previous address, so could not be included. Of those included in the HOPEFUL study population, 113 women could not be found using the NSTS and so their last known address was used (94 in the UAE cohort and 19 in the hysterectomy group). The higher number of untraceable patients in the UAE group using the NSTS may have been due to women having this treatment privately and possibly travelling from abroad to do so.

After establishing the status and current address of each eligible patient, this information was supplied back to each centre on an updated database and in addition each patient was allocated a unique five-digit ID number based on a collaborating centre ID number combined with a patient number. The updated password-protected patient databases were maintained on a separate PC to maintain patients' confidentiality. Patient ID numbers only were used in the HOPEFUL database.

Each research nurse made the initial contact with their living patients for the HOPEFUL study by sending them the MREC-approved initial contact letter (Appendix 4) signed by the relevant local hospital consultant PI on the appropriate local hospital headed paper. The letter explained the purpose of the study, invited the patient to consent to take part and invited them to telephone a dedicated Freephone number with any questions if uncertain about the project. This initial contact mailing also included the MREC-approved patient information sheet (Appendix 5) and two copies of the MREC-approved consent form (Appendix 6). The consent forms were precoded with the patient's ID number and signed by the research nurse prior to sending out. The patient was asked to sign both copies of the

consent form, to retain one for her own records and return the other copy to the Oxford Office in the freepost envelope provided.

In the cases where the patient had been identified as deceased since their index treatment, this initial contact letter seeking consent was not appropriate. The study protocol ethics approval allowed the research nurse to obtain clinical data for HOPEFUL from hospital notes for these cases. There were 28 deceased patients (hysterectomy  $n = 21$  and UAE  $n = 7$ ). For 10 of these patients clinical records were not available. For the six patients in the hysterectomy cohort, basic information on the patients and their procedures was available from the VALUE study, but no information was available for the four patients from the UAE cohort. Details of cause of death were obtained from the clinical notes for 16 of the remaining patients.

In addition, death certificates were requested from the General Registry Office, Southport, in order to establish exact causes of death. Twenty-seven death certificates were applied for using either the date of death where it was available or a range of possible years where the date was unknown. One patient died during 2005, which was outside the range of years that could be supplied. The nursing home was contacted by the research nurse seeking information about this patient and they reported that she had died of 'general old age and heart failure' at the age of 82 years.

All 27 death certificates were supplied. The certificated cause of death confirmed the cause of death reported in the clinical notes in all cases where it was available. A summary of the cause of death is shown in *Table 4*. Further details are presented in Appendix 7.

**TABLE 4** Cause of death for those patients deceased at time of HOPEFUL study

Cause of death	Hyst	UAE	Total
Cancer	12	6	18
Cardiovascular disease	7	0	7
Respiratory	1	0	1
Open verdict	1	1	2
<b>Total</b>	<b>21</b>	<b>7</b>	<b>28</b>
Number in cohort	459	649	1108
Average length follow-up (years)	9.9	4.9	6.9
Average person-years at risk	4553	3206	7700
<b>Death rate per 1000 person-years (not adjusted for age)</b>	<b>4.61</b>	<b>2.18</b>	<b>3.64</b>
Hyst, hysterectomy cohort; UAE, UAE cohort.			

Where there was any possible association between the index treatment for fibroids and subsequent death, the PI at the relevant centre was requested to provide a medical summary for the patient from the time of their index treatment up to their death. One UAE patient who died from metastatic uterine sarcoma was further investigated in this way. The undiagnosed sarcoma was developing inside the fibroid and was diagnosed when instead of the UAE procedure causing a reduction in the size of the fibroid, the fibroid continued to grow. Uterine sarcomas are very rare and difficult to diagnose. The sarcoma itself was not caused by the UAE procedure and is not therefore attributed as a death caused by the treatment.

The cause of death in one of the hysterectomy patients was metastatic carcinoma of the endometrium. Endometrial cancer was diagnosed in the pelvis 5 years after hysterectomy. Endometriosis had been noted at the time of the hysterectomy. VALUE data at the time of her total hysterectomy records "Stage 4 endometriosis and fibroids".

Table 5 provides details of the elapsed time between the procedure and the date of death. The cause of death for the two patients who died within a year of their treatment were myocardial infarction [hysterectomy cohort (Hyst)] and death by hanging (open verdict) (UAE) and were not thought to be associated with their treatment. Most of the excess deaths in the hysterectomy cohort occurred after 5 years. The average follow-

**TABLE 5** Time elapsed between procedure and death

Elapsed time since procedure (years)	Hyst	UAE	Total
<1	1	1	2
1-3	5	1	6
3-5	4	1	5
5-10	11	0	11
Missing	0	4	4
Total	21	7	28

**TABLE 6** Age of deceased patients at death

Age at death (years)	Hyst	UAE	Total
<40	1	0	1
40-44	0	3	3
45-49	4	2	6
50-54	8	2	10
≥55	8	0	8
Total	21	7	28

up time for the UAE cohort was 4.9 years (SD = 1.66) and that for the hysterectomy cohort was 9.9 years (SD = 0.38).

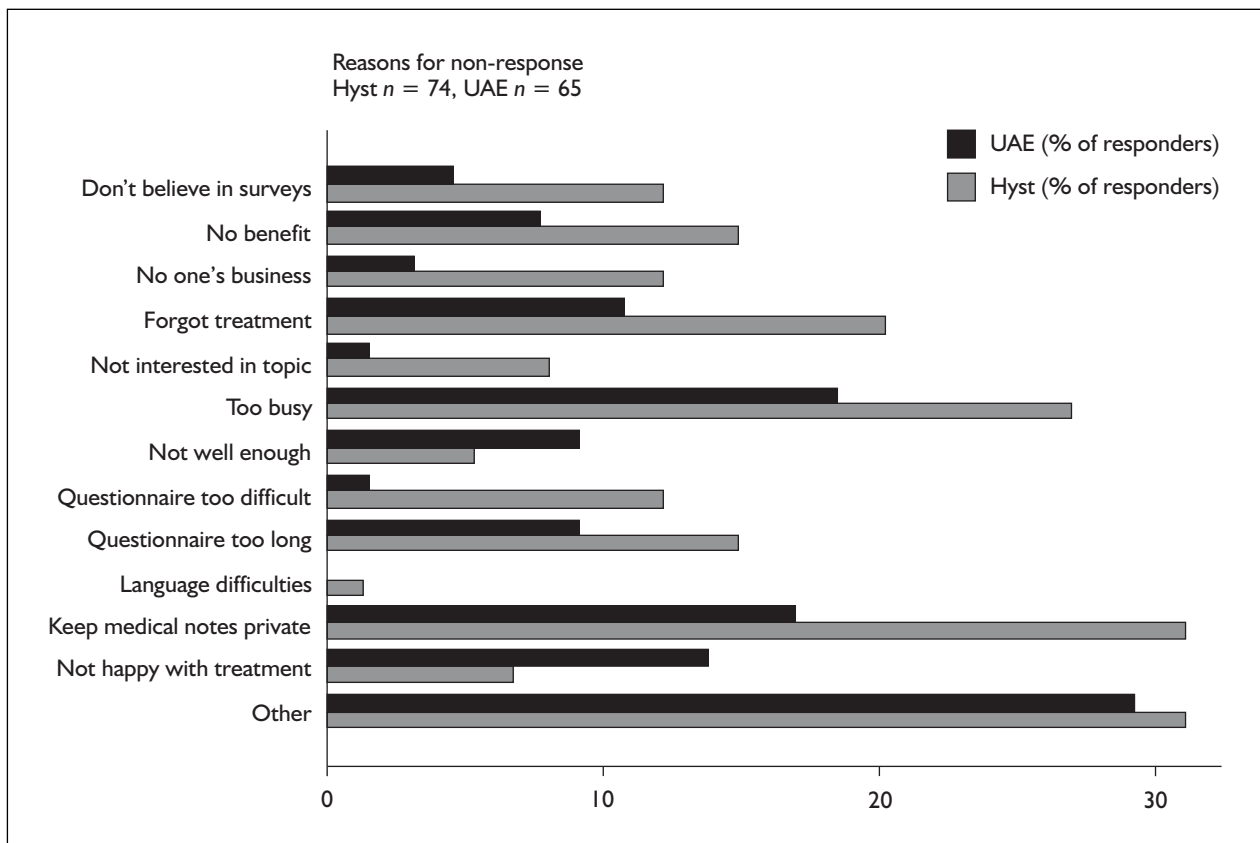
Table 6 shows details of the age of these patients at the time of death. The four patients aged under 45 years at death died of an overdose (Hyst,  $n = 1$ ) and various cancers (UAE,  $n = 3$ ).

After receiving MREC permission to do so, we pursued non-responders 1 month after the first contact letter was sent to invite participation again. This second letter (Appendix 8) was sent out from the collaborating centres with accompanying documentation as previously. Any patients consenting at this opportunity were included in the study. In total 772 second letters were sent out (Hyst,  $n = 360$ , UAE,  $n = 412$ ). This process encouraged 160 further patients to participate (Hyst,  $n = 60$ , UAE,  $n = 100$ ), a response rate of 20.7% (Hyst 16.7%, UAE 24.3%).

### Non-consenters

In order to investigate possible biases between patients agreeing to consent and those not wishing to participate after a second invitation, we sought and obtained permission from MREC to contact all non-consenters again with a simple anonymous form seeking their reasons for not wishing to consent (Appendix 9). The form provided a list of 13 options and patients were asked to tick as many boxes as they thought applied to them. This was sent to all 613 non-responding patients on 4 November 2005. Seventy-four out of 303 sent to the hysterectomy cohort were returned (24.4%) and 65 out of 310 sent to the UAE cohort were returned (21.0%), an overall return rate of 22.7%. The respondents indicated a wide variety of reasons for not wishing to participate. These are shown in Figure 2.

The most commonly ticked options in the hysterectomy non-consenters group were 'other', 'wanting to keep medical notes private', 'too busy' and 'had forgotten about their treatment'. The most commonly ticked options in the UAE non-consenters group were 'other', 'too busy', 'wanting to keep medical notes private' and 'not happy with treatment'. Hysterectomy non-consenters appeared to tick more options overall. Of those who ticked they 'had forgotten their treatment', 15 (20.3%) were from the hysterectomy non-consenters and seven (10.8%) were from the UAE non-consenters. This difference may have arisen due to the shorter length of follow-up in the UAE cohort. Of those who were 'not happy with their treatment' five (6.8%) were from the hysterectomy



**FIGURE 2** Frequency of items ticked in response to asking about reasons for not wishing to consent

cohort and nine (13.9%) were from the UAE cohort. This difference may have occurred because the UAE cohort had to be more proactive in order to receive UAE and therefore possibly had higher expectations of a successful outcome.

The 'other' category arises from comments written in the space provided on the form for further comments. From these comments, additional information was obtained which had not already been covered in the options provided. These included reasons such as 'moved address', particularly in the UAE group, suggesting the initial contact letters had not reached them. Conversely, several women indicated they had consented but had no further response, indicating their response had not reached the HOPEFUL Centre. This may have been a result of a major postal strike in Oxford during this period.

Although this form had been designed to be anonymous, 33 non-consenters volunteered their names and 19 included their contact details. Of these, 18 women (three Hyst and 15 UAE) clearly indicated that (1) they would still like to participate in the study, (2) their previous forms

may have been lost in the post and (3) they could be contacted by their current name and contact details. Consequently, these 18 women were given a further opportunity to consent and complete a patient questionnaire. Nine of the 18 consented at this point (three Hyst and six UAE) and all nine returned completed questionnaires. Unfortunately, the local research nurses had ceased their employment on the project by this time and clinical data could not be obtained from the local sites. Limited clinical data were available, however, for the three hysterectomy patients from the VALUE database and we were also able to obtain clinical data for the two UAE patients from the Oxford collaborating site.

Figure 3 summarises the different stages of entry to the HOPEFUL study. Of the 1734 eligible patients a total of 1094 (63.1%) consented to participate [Hyst n = 438 (57.5%), UAE n = 656 (67.5%)] and a further 28 (1.6%) deceased patients were also included [Hyst n = 21 (2.8%), UAE n = 7 (0.7%)]. In total 1122 (64.7%) (Hyst 60.2%, UAE 68.2%) of eligible patients were enrolled into the study. A breakdown of these participation rates per centre is presented in Figure 4.

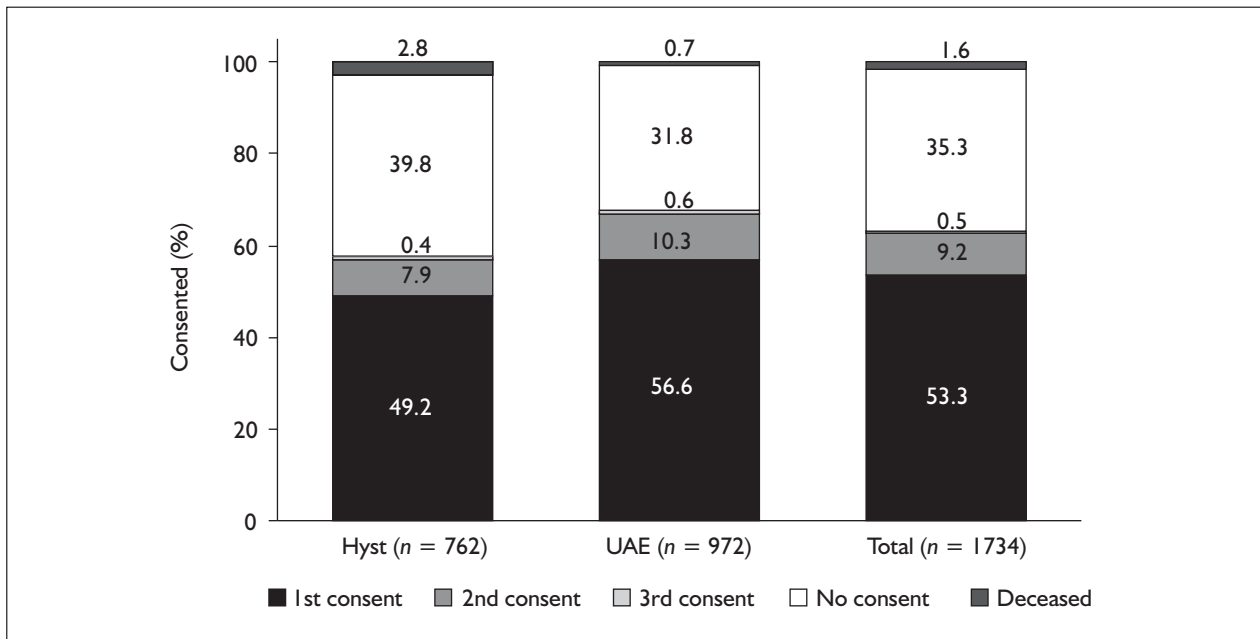


FIGURE 3 Summary of participants consenting at each stage

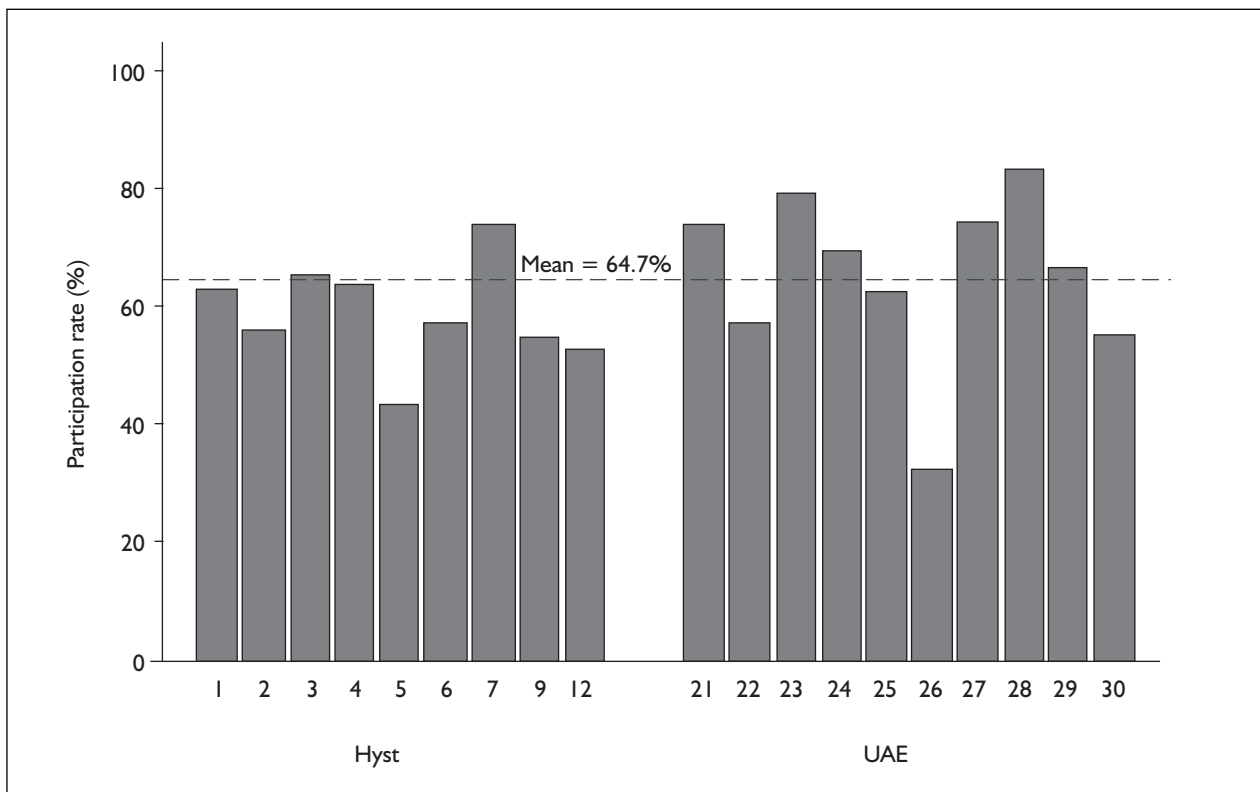


FIGURE 4 Participation rate by centre ID

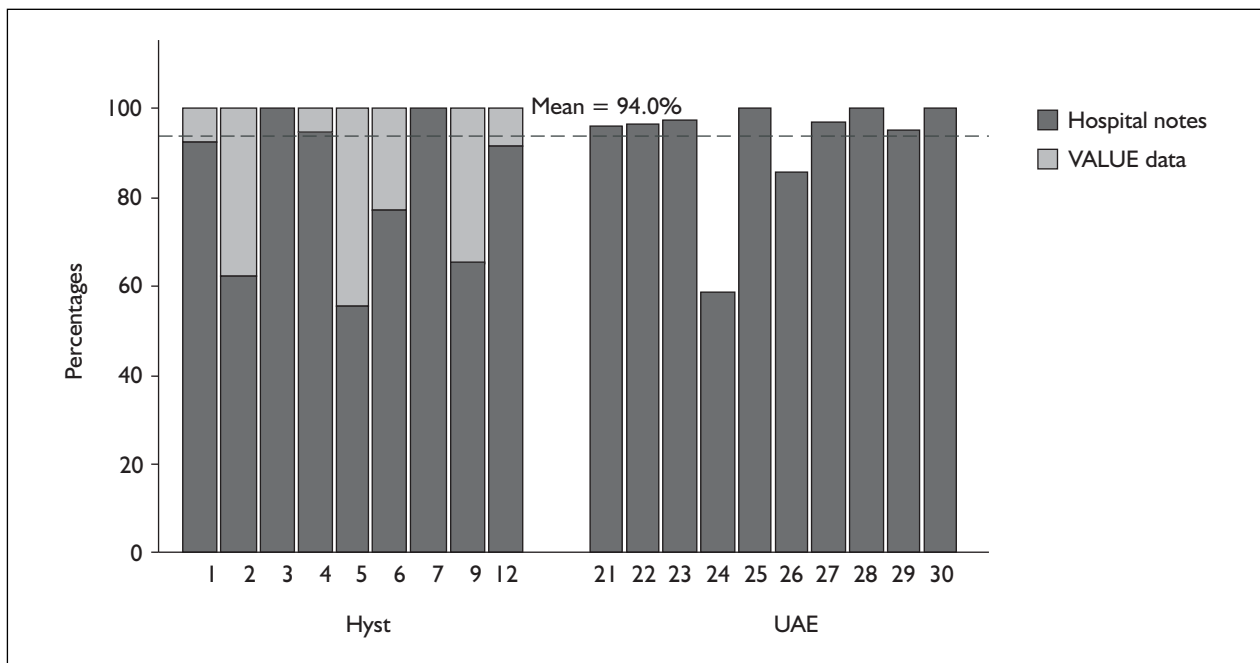
**Data collection**

**Clinical data forms**

Following receipt of each patient’s signed consent by Oxford, the relevant research nurse was informed of the consenting patient ID, so giving

permission for clinical data collection from the patient’s hospital notes on to the HOPEFUL data collection forms. Sufficient copies of clinical data collection forms were provided to centres from Oxford with an instruction sheet (UAE Form,





**FIGURE 5** Clinical form completion rate by centre ID

Appendix 10; Hysterectomy Form, Appendix 11). The clinical data forms included details confirming the diagnosis, full details of the surgery or embolisation techniques used, relevant treatment outcomes and complications and further investigations or treatments over a period of several years follow-up. Additional parts of the data forms were provided to collect data on any post-UAE pregnancies or any post-treatment deaths.

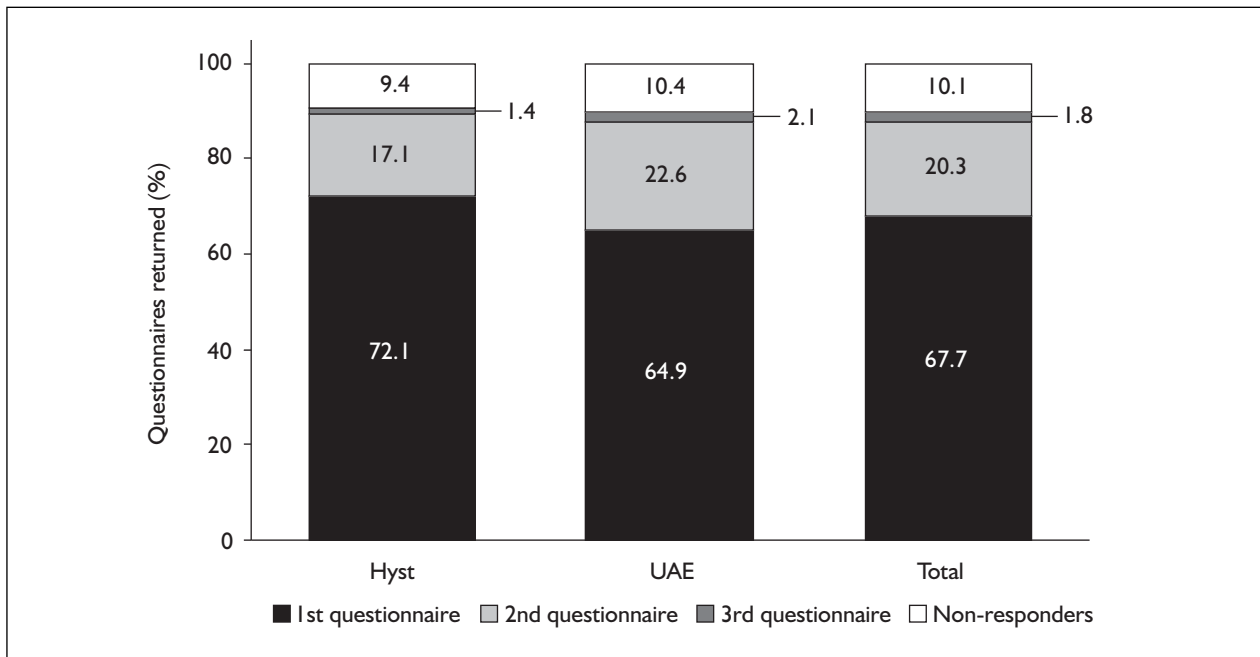
Issues of non-standard data collection across centres and missing data due to local variations in hospital record keeping were identified. There were 136 patients whose hospital notes could not be retrieved; 66 of these were in the hysterectomy cohort and for these patients we were able to merge basic clinical data from the VALUE database. The large number of unavailable notes in this group was due to the fact their treatment had been 10 years ago and many NHS hospital notes are destroyed after 8 years of inactivity. Also, for some centres, the hospital records had been archived on microfiche, causing difficulty in accessing information. Seventy UAE patients' hospital notes were not able to be examined in the time available for the study. These were primarily from centre 24, which had almost twice as many eligible patients as the other UAE centres. We had patient questionnaire data for 56 of these UAE patients but no data at all on 14, four of whom are now deceased. *Figure 5* shows the clinical form completion rate by centre; 94% of the clinical forms were completed.

#### **Patient postal questionnaires**

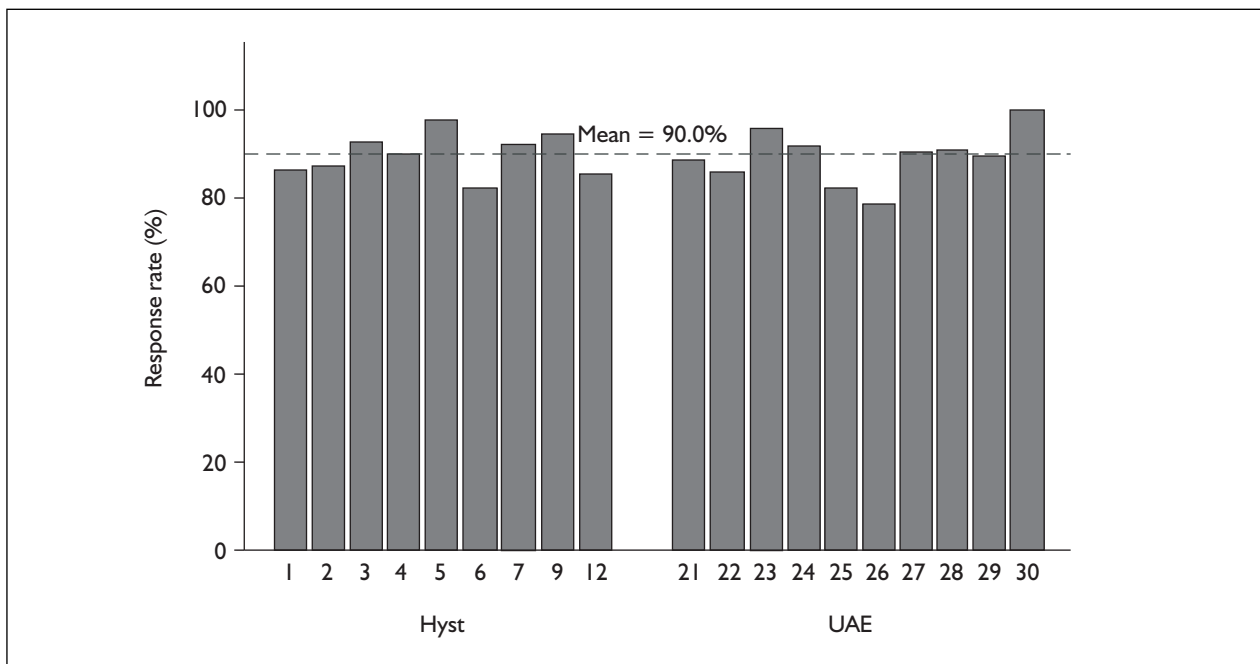
At receipt of consent, Oxford also sent out a simple follow-up patient questionnaire (Appendix 12) to the consenting patient with a freepost envelope for return to Oxford. The patients were assured of their confidentiality and provided with a freephone telephone number to the Project Manager should they have any concerns or questions whilst completing the questionnaire. Reminder letters and additional questionnaires were sent to patients who had not returned questionnaires after 4 weeks following the first questionnaire being sent (Appendix 13). A third questionnaire was sent to all patients who had not responded to the second questionnaire reminder in November 2005.

*Figure 6* provides a summary of numbers of patients returning questionnaires at each stage and *Figure 7* breaks down questionnaire return by centre; 90% of questionnaires sent out were returned.

The self-completion questionnaire was designed to be comprehensive in covering all the information needed for the study and all the main areas women may wish to comment on (Appendix 12). There were 34 precoded questions, many of which had subsections. They asked women about themselves, their general health, their fibroid symptoms pretreatment, treatment choices and subsequent health following treatment. Outcomes such as resolved symptoms, specified



**FIGURE 6** Summary of questionnaire return at each stage



**FIGURE 7** Questionnaire return by centre ID

complications, residual symptoms, subsequent treatments and pregnancies were asked about. The questionnaire also asked the women about their satisfaction with the treatment procedure they received. In acknowledgement of the limitations of even the most comprehensive questionnaire in providing the opportunity for feedback solely within a tick box system, several of the questions gave space for free-text comments. A final

question, number 35, was also included asking respondents to write about “anything else about your treatment/s for fibroids and your health which is important to you”.

The purposes of the option to contribute free text were (1) to allow clarification or expansion of material that the respondent had recorded via the tick box responses and (2) in case a respondent

had something to tell us that had not been covered specifically anywhere in the questionnaire.

In line with these two purposes, the results of the free-text analysis relating to specific questions are reported close to the quantitative statistical analysis to which it relates. Comments that refer to completely different issues or emergent themes are presented in Chapter 9.

The term 'free-text comments/data' rather than 'qualitative data' is used to reflect the limitations inherent in data collected in this way. Compared with qualitative research practice,<sup>51</sup> using the self-completion free-text option means that:

- The researcher has no influence on the data creation process.
- The choice of topic within the overall field of the study (sometimes not) is left to the respondent.
- There is limited space to write, although could use extra sheet.
- There is no facility for the researcher to follow up and probe into rationale.
- There is no opportunity to test developing theories with participant, or with other participants, as would be done in an interview study or a focus group.
- There is no opportunity to clarify points.
- There is no opportunity to focus on particular slants, e.g. experiences, constructs and interactions, so data will be mixed.
- There is absence of comparability because of these limitations.
- There is always the possibility that someone else may have written it, or at least heavily influenced what was or was not written.
- It can be very difficult for people to convey complexity in writing on a questionnaire: it tends to be much easier in an interview situation.

A further problem relates to the nature of the data recorded following the question-specific invitations for free-text comments. The space provided was only small and the answers were predominantly only one sentence long, with a small number extending to two sentences and only a handful reaching three. Although the specific question provides some context for the response, it is not advisable to read too much into such short extracts. Care has been taken not to over-analyse the free-text responses, and to stick closely to their exact words and content throughout the analyses. Although the shortcomings of this method are acknowledged, it was felt that the comments did

provide useful supplemental information to the HOPEFUL study aims.

### Data input

All data obtained from the clinical forms from centres and questionnaires direct from patients were input and collated in a central anonymised project database created in Microsoft ACCESS held at the coordinating centre of the study in Oxford. Input validation was carried out for one in five questionnaires and one in five clinical data forms. Data validation for each variable was also carried out prior to analysis to ensure data accuracy. This data validation involved comparing outliers or unusual values against the raw data, or by referring back to hospital notes (e.g. a weight of 180 kg was confirmed as correct); logical checks on pairs of related variables (e.g. comparing weight and height to make sure there were no unusual combinations) and date validity (e.g. date of admission  $\leq$  date of procedure  $\leq$  date of discharge). Any unusual values that could not be verified in this way were set as missing.

Of the total 1122 patients who consented to participate or who were deceased, there were data on 1108. This comprises 930 patients for whom there was both clinical and patient questionnaire data (Hyst  $n = 397$ , UAE  $n = 533$ ), 122 with clinical forms only (Hyst  $n = 62$ , UAE  $n = 60$ ) and 56 with questionnaire only (all UAE).

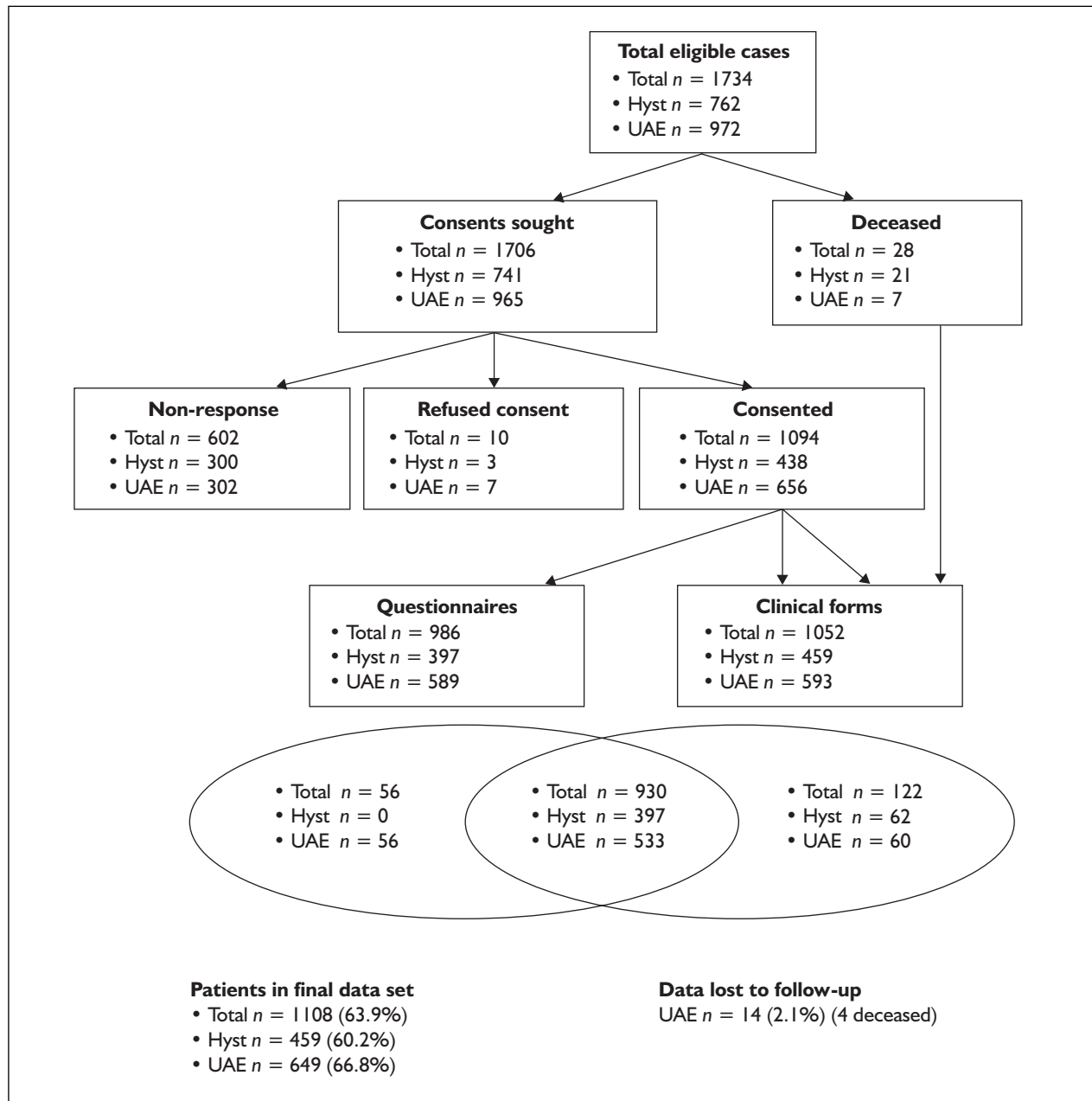
### Flow of patient numbers

*Figure 8* summarises the flow of patient numbers from eligibility to data input.

### Confounding variables

The project team discussed possible confounding factors a priori and compiled a list of variables to be considered. Collection of data on these was incorporated in both the questionnaires and the clinical forms with some variables duplicated across both to increase the chance of gathering information as indicated in *Figure 9*.

The *a priori* confounders considered were age, ethnicity, parity, smoking, educational level, (obesity defined as BMI  $\geq 30$ ), blood pressure (BP) (high BP defined as diastolic  $\leq 90$  mmHg or systolic  $\geq 140$  mmHg), reported menopausal status, age at menarche, gynaecological co-morbidity, medical co-morbidity, prior pelvic surgery, prophylactic antibiotic use and fibroid



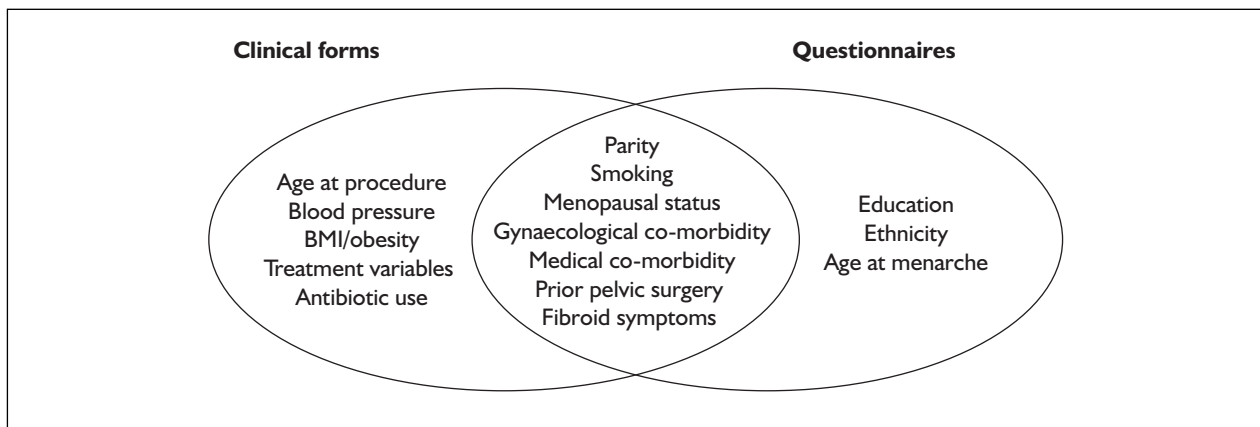
**FIGURE 8** Flow of patient numbers

symptoms at the time of the procedure. Fibroid symptoms from clinical forms and patient questionnaires are both used as they can vary considerably. Symptoms taken from the patient questionnaires reflect the patient’s recollection of her symptoms retrospectively and those recorded in the clinical forms reflect those the patient and/or the clinician thought were important at the time of treatment.

Details of fibroid characteristics were also considered, but due to the amount of missing data it was not possible to assess these as confounders.

The available data are presented in *Tables 12 and 13* (baseline characteristics) (pp. 48–9). Most of the reported fibroids were intramural in nature.

Where these possible confounding variables required a *a priori* categorisation, this was agreed by the project team. Clinical advice was provided by the clinical advisors on the HOPEFUL Project Team. For example, patients with one or more medical conditions that may influence outcome were categorised globally as having a medical comorbidity. Patients with no mention of any of the *a priori* medical conditions were categorised as not



**FIGURE 9** Source of data on a priori confounding variables

**TABLE 7** Medical co-morbidity – numbers of conditions not patients (percentage in cohort)

Medical condition	Hyst (n = 459)	UAE (n = 649)	Total (n = 1108)
Cardiovascular	36 (7.8%)	25 (3.9%)	61 (5.5%)
Respiratory	33 (7.2%)	32 (4.9%)	65 (5.9%)
Thyroid	14 (3.1%)	14 (2.2%)	28 (2.5%)
Diabetes	6 (1.3%)	9 (1.4%)	15 (1.4%)
Psychiatric	14 (3.1%)	15 (2.3%)	29 (2.6%)
DVT	11 (2.4%)	10 (1.5%)	21 (1.9%)
Anaemia	51 (11.1%)	41 (6.3%)	92 (8.3%)
Other	2 (0.4%)	0 (0.0%)	2 (0.2%)
<i>Total</i>	<i>167 (36.4%)</i>	<i>146 (22.5%)</i>	<i>313 (28.2%)</i>

**TABLE 8** Gynaecological co-morbidity – numbers of conditions not patients (percentage in cohort)

Gynaecological condition	Hyst (n = 459)	UAE (n = 649)	Total (n = 1108)
Pelvic inflammatory disease	16 (3.5%)	18 (2.8%)	34 (3.1%)
Urinary tract Infections (recent or recurrent)	10 (2.2%)	9 (1.4%)	19 (1.7%)
Adenomyosis	7 (1.5%)	4 (0.6%)	11 (1.0%)
Endometriosis	24 (5.2%)	44 (6.8%)	68 (6.1%)
Other	2 (0.4%)	8 (1.2%)	10 (0.9%)
<i>Total</i>	<i>59 (12.9%)</i>	<i>83 (12.8%)</i>	<i>142 (12.8%)</i>

having medical co-morbidity. The gynaecological co-morbidity and the prior pelvic surgery variables were categorised in the same way.

Tables 7–9 show a breakdown of the conditions used to categorise the global confounders: medical co-morbidity, gynaecological co-morbidity and prior pelvic surgery, respectively.

There were 263 (23.7%) patients [Hyst  $n = 137$  (29.8%), UAE  $n = 126$  (19.4%)] with 313 medical conditions at the time of their treatment indicated on both the questionnaires and the clinical forms; 218 had one condition only, 41 had two, three had three and one had four conditions at the time of

treatment. These 263 patients are classified as having a medical co-morbidity for the purposes of the primary outcome analysis.

There were 130 (11.7%) patients [Hyst  $n = 55$  (12.0%), UAE  $n = 75$  (11.6%)] with 142 gynaecological conditions at the time of their treatment indicated on the questionnaires and the clinical forms; 118 had one condition only and 12 had two conditions. These 130 patients are classified as having a gynaecological co-morbidity for the purposes of the primary outcome analysis.

There were 228 (20.6%) patients [Hyst  $n = 65$  (13.9%), UAE  $n = 169$  (25.3%)] with 253 different

**TABLE 9** Prior pelvic surgery – numbers of surgeries not patients (percentage in cohort)

Prior pelvic surgery	Hyst (n = 459)	UAE (n = 649)	Total (n = 1108)
Myomectomy	4 (0.9%)	74 (11.4%)	78 (7.0%)
Caesarean	37 (8.1%)	59 (9.1%)	96 (8.7%)
Ovarian/fallopian procedure	22 (4.8%)	25 (3.9%)	47 (4.2%)
Bowel/bladder surgery	5 (1.1%)	10 (1.5%)	15 (1.3%)
Other	3 (0.7%)	14 (2.1%)	17 (1.5%)
<i>Total</i>	71 (15.5%)	182 (28.0%)	253 (22.8%)

categories of prior pelvic surgeries between them; 205 had only one, 21 had two and two had three prior pelvic surgery types each. These 228 patients are classified with prior pelvic surgery for the purposes of the primary outcome analysis.

The distribution of patients with medical or gynaecological co-morbidity or prior pelvic surgery at baseline is shown in *Figure 10*.

These dichotomous global confounders (medical co-morbidity, gynaecological co-morbidity and prior pelvic surgery) were then used in the analysis of the primary outcomes. Individual conditions could not be looked at in detail due to the lack of numbers of patients having the conditions and the problems of multiple testing.

## Outcome measures

The primary outcome is the relative safety between the two treatments, that is, a comparison of complication rates.

The secondary outcome is efficacy of treatment. There is an overlap between these outcomes, with four possible scenarios, as shown in *Figure 11*:

- No complications and resolution of symptoms.
- No complications but symptoms were unresolved or recurred later.
- Complications with resolution of symptoms.
- Complications with symptoms unresolved or recurring later.

Note: although unresolved symptoms are possible after hysterectomy, this scenario is considered unlikely and this path is therefore not included in the health economic analysis detailed in Chapter 8.

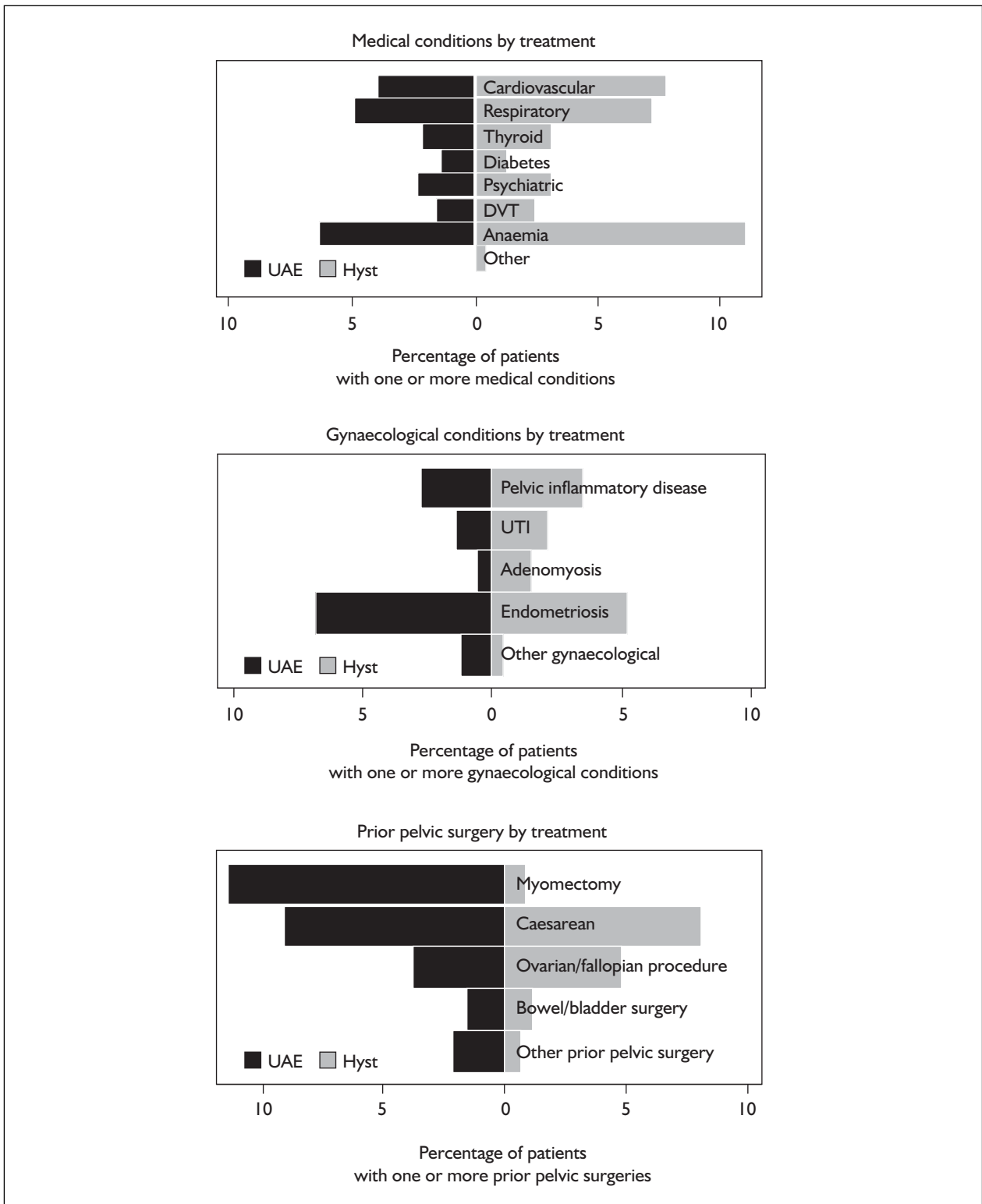
The outcomes shaded refer to safety of treatment, that is, complications, whereas the outcomes unshaded refer to the efficacy of treatment, that is, resolution of symptoms.

## Primary outcome measures Comparative safety/complication rates (UAE versus Hyst)

The primary outcome measure addresses comparative safety, that is, negative events resulting from treatment measured as complication rates. The project team agreed *a priori* on the definitions in *Box 1* regarding the categorisation of complication severity. The clinicians were sent a blinded list of all the complications reported in both clinical forms and questionnaires in order to categorise the complications into the types in *Box 1*. A project team meeting followed this independent assessment, where agreement was reached on the final categorisation of complications. The numbers of individual complications are reported in *Table 16* (p. 53). Recorded complications were then grouped by severity of complication – severe, major and minor.

Some examples of these complications are as follows:

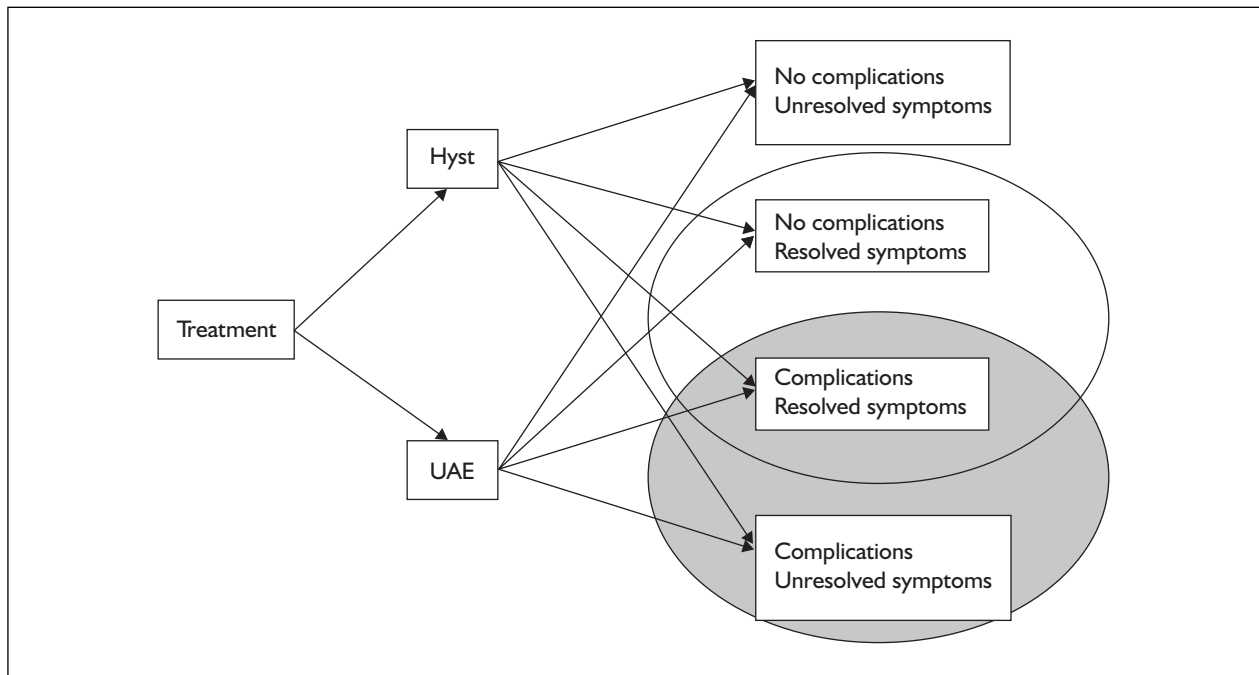
- *Severe complication* Patient A: renal failure, treated on intensive therapy unit – categorised as ‘organ failure’.
- *Major complications* Patient A: bronchopneumonia – return to intensive therapy unit – ‘major infection’. Patient B: blood transfusion after stitches burst and blood loss – categorised as ‘haemorrhage requiring transfusion’. Patient C: bladder perforated during operation, repaired in theatre – categorised as ‘structural damage caused by treatment’. Patient D: embolisation of ovarian artery leading to ovarian failure – classified as ‘structural damage caused by treatment – non-target embolisation’. Patient E: urgent hysterectomy for sepsis of fibroids 4<sup>3</sup>/<sub>4</sub> months post-UAE – categorised as ‘major infection’. Patient F: returned to theatre for resuture of wound – ‘other major complication’.
- *Minor complications* Minor infections included urinary tract infection, *E. coli*, wound infection, methicillin-resistant *Staphylococcus aureus* and haemolytic *Streptococcus*; haematoma included



**FIGURE 10** Distribution of medical conditions, gynaecological conditions and prior pelvic surgery by treatment

wound (mostly hysterectomy) and groin (mostly UAE); fibroid extraction (not requiring myomectomy or hysterectomy), usually resection of the fibroid by hysteroscope or forceps delivery of half-expelled fibroid; other minor

complications include granulated tissue to vault requiring silver nitrate cauterisation, haemorrhage not requiring transfusion, bradycardia and severe pain requiring readmission.



**FIGURE 11** Safety and efficacy of treatment

**BOX 1** Primary outcome measures: complications<sup>a</sup>

*Severe complications within 30 days/life-threatening\**

- death
- pulmonary embolus
- myocardial infarction
- cerebrovascular accident (stroke)
- organ failure
- other severe (life-threatening complications)

*Major complications – not life-threatening but require treatment and have possible long-term implications*

- permanent amenorrhoea (premature menopause under 40 years not due to removal of ovaries)
- radiation burn<sup>U</sup>
- haemorrhage requiring transfusion<sup>H</sup>
- structural damage caused by treatment:  
 damage to bladder, ureter, bowel<sup>H</sup>  
 non-target embolisation<sup>U</sup>  
 injury to uterine arteries requiring further embolisation<sup>U</sup>
- major infection  
 non-target embolisation causing tissue necrosis<sup>U</sup>  
 fibroid removal<sup>U</sup> by myomectomy or hysterectomy within 6 months  
 infection causing septicemia\*  
 emergency hysterectomy due to infection<sup>U</sup>
- DVT\*
- other major complications leading to long-term problems

*Minor complications – possibly requiring treatment – no long-term implications*

- Various minor infections\* – treatable with simple antibiotics (<30 days)
- Haematoma\* (possibly delaying discharge)
- Adverse drug reaction\*/contrast reaction<sup>U</sup>
- Permanent amenorrhoea if over 40 years<sup>U</sup>
- Temporary inability to pass urine – requiring a catheter\*
- Fibroid extraction<sup>U</sup>, requiring assistance
- Other minor complications requiring treatment <30 days\*

<sup>a</sup> The following annotations are used: \* Both cohorts; <sup>H</sup> Hyst only; <sup>U</sup> UAE only.



Each patient with one or more complications was then categorised according to the most severe of their complications; for example, patient A above experienced both severe and major complications and was categorised as severe, and a patient with a major and a minor complication was categorised as major.

Complication data were principally drawn from the clinical forms, although there were 77 complications identified from 55 patients in the readmission section of the patient questionnaires. Twenty-four of these were duplicates from complications already identified from the clinical forms, but a further 31 patients reported one or more complications in their patient questionnaire that had not previously been identified (2.8% of the patients). The majority of these additional complications were identified among the UAE cohort, including requiring assistance with extraction of fibroids, infections, and severe pain causing readmission to hospital. *Figure 12* shows the sources of the data on complications.

There were 234 (21.1%) patients [Hyst  $n = 120$  (26.1%), UAE  $n = 114$  (17.6%)] with a total of 341 complications following their index treatment. A total of 165 of these patients had only one complication, 49 had two complications and 20 had more than two complications. These 234 patients were categorised by their most severe complication as described for the purposes of the primary outcome analysis (*Figure 13*).

These categorisations were then used to create the two dichotomous primary outcome variables: Primary outcome [1] – complication versus no complication; and primary outcome [2]

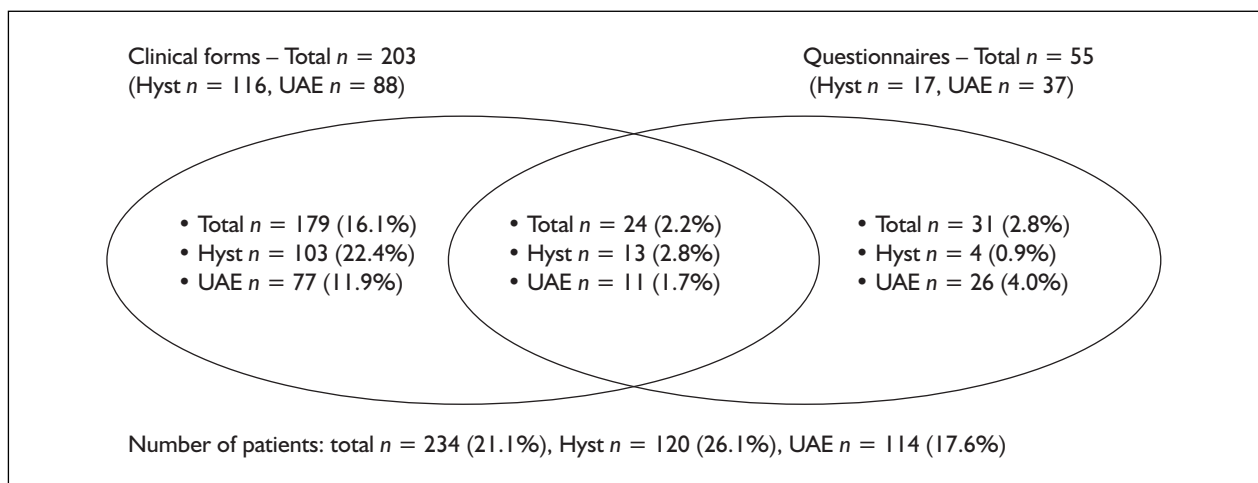
severe/major complication versus minor/no complication.

Individual complications could not be tested in detail due to the lack of sufficient patients with each complication, the fact that some patients had more than one complication, the non-comparability of the individual complications between the two cohorts and the problems that would arise with multiple testing. Although there is an ordered nature to the gradation of severity of complications, there were very few severe complications, so carrying out an ordered analysis using all four categories was not considered possible. Combining the severe and major complications into a single category was considered, but the nature of the severe (life-threatening) complication group was considered too different from the major complication group to combine. Carrying out two separate analyses on the dichotomous primary outcome variables as described above is similar to carrying out an ordered analysis, but is easier to comprehend.

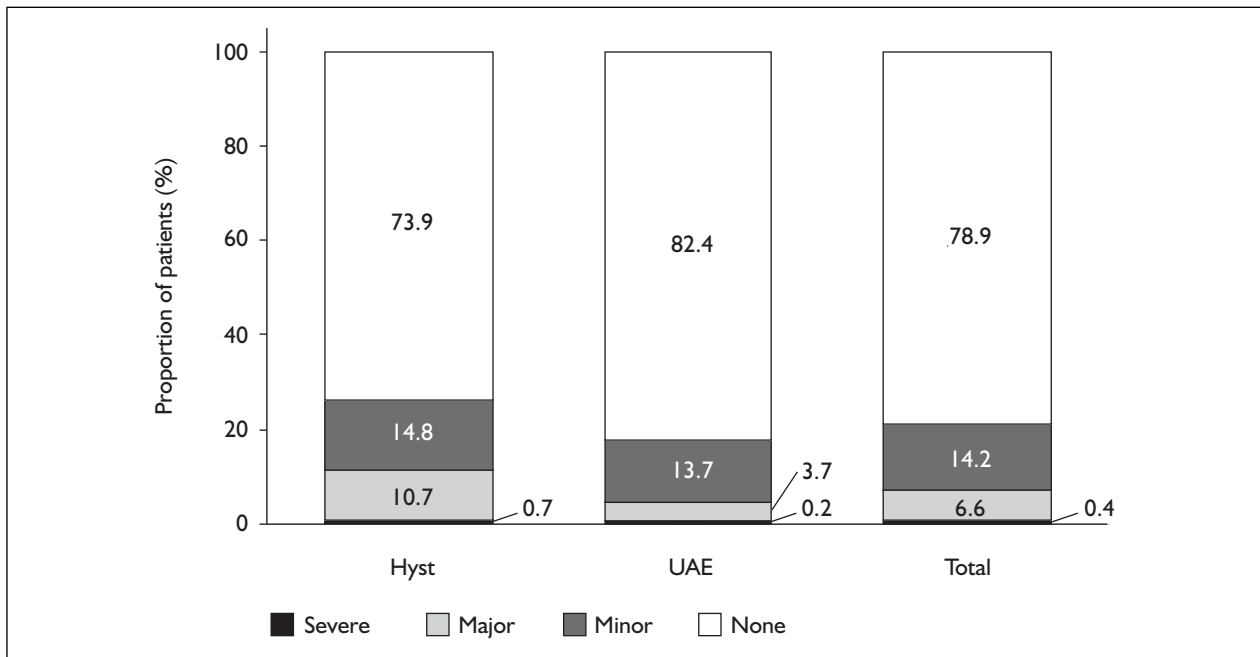
#### **UAE-only: general side-effects of treatment**

Some UAE patients also suffer from GSEs of the treatment. These include post-embolisation syndrome (fever, pain, nausea lasting from a few hours to a few days), vaginal discharge caused by the disintegrating fibroids, natural expulsion of the whole or bits of the fibroid (not requiring assistance) and temporary amenorrhoea.

Post-embolisation syndrome is well known and well recognised by physicians who perform embolotherapy.<sup>52-54</sup> It occurs in relation to embolisation of the liver, kidneys, spleen and other solid organs and is part of the immune response.<sup>55-57</sup> It is easily treated with



**FIGURE 12** Source of complication data per patient coded with a complication



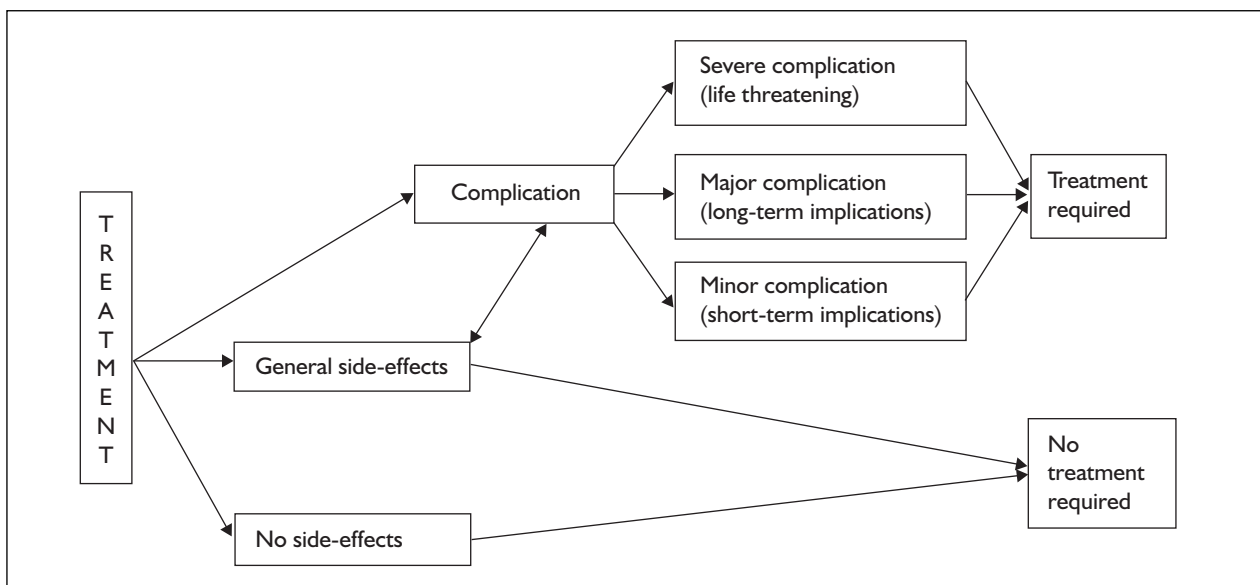
**FIGURE 13** Severity of complications (total n = 1108, Hyst n = 459, UAE n = 649)

anti-inflammatory and antipyretic drugs. Indeed, it is increasingly recognised as part of the post-procedural effects of aortic and thoracic stent grafting secondary to the metallic stent. The discomfort associated with embolisation is easily controlled with a simple analgesia regimen. GPs would normally refer a patient back to hospital if they required more than this.

to necrotise and possibly disintegrate. If expulsion of fibroids required assistance it was classified as a complication, otherwise it was classified as a general side-effect of UAE. Temporary amenorrhoea sometimes occurred for a few months, with normal periods being resumed. If this became permanent, especially for the younger women, again it was classed as a complication.

Vaginal discharge is also a natural consequence of the embolisation procedure caused by stopping the blood flow to the fibroids, thus causing them

It was decided *a priori* by the project team on the advice of the clinicians not to include GSEs as complications. However, because other studies



**FIGURE 14** Flow chart defining effects of treatment

**TABLE 10** General side-effects of UAE treatment

GSE	No. of patients with GSE (denominator = 649)
Natural fibroid expulsion – no treatment required	49 (7.6%)
Chronic discharge	82 (12.6%)
Post-embolisation syndrome – pain, nausea, vomiting and fever (not involving hospitalisation)	115 (17.7%)
Temporary amenorrhoea	21 (3.2%)
<i>Total with one or more GSEs</i>	<i>212 (32.7%)</i>

have considered them as complications, GSEs were also investigated and presented in this monograph to provide the complete picture of all outcomes from both treatments. Please note that when one of these GSEs led onto a complication the patient was categorised as having the complication.

An example of this is where a chronic vaginal discharge may have led to a requirement for intervention to extract a disintegrating fibroid or treatment with antibiotics for a minor infection. Another example is where the pain was so severe that a patient had to be readmitted to hospital. Sometimes a patient may experience both a complication and a GSE and these would also be categorised as having the complication. *Figure 14* shows how complications and GSEs may relate to each other.

Women in the UAE cohort may have experienced one or more GSEs. *Table 10* gives the number of

GSEs reported amongst the 649 women in the UAE cohort. There were 212 (32.7%) patients who reported a total of 267 GSEs following their index treatment. One patient (0.15%) experienced all four of these GSEs, six (0.92%) experienced three GSEs, 40 (6.2%) experienced two GSEs and 165 (25.4%) experienced only one. For the purposes of analysis, a woman experiencing one or more GSEs was categorised as having a GSE versus not having a GSE.

### Secondary outcome measures Comparative efficacy (UAE versus Hyst)

The secondary outcomes of this study relate to comparative efficacy information gathered retrospectively by patient questionnaire on change in reported general health, items related to resolution of fibroid symptoms and satisfaction with treatment. These items use responses to specific questions on the patient questionnaire completed by both groups as outlined below.

### General health and change in general health: Q22 and Q23

- 22.** In general, would you say your health is:  
 1 excellent  2 very good  3 good  4 fair  5 poor
- 23.** How would you rate your health since receiving your fibroid treatment compared with before?  
 1 much better  2 better  3 about the same  4 worse  5 much worse

### Resolution of fibroid/urinary symptoms: Q19 and Q25

- 19.** We would like to know what the principle symptoms of your fibroids were like prior to your index treatment and whether your treatment changed these symptoms.
- (a) (i) Before your treatment were you troubled by heavy menstrual bleeding (with or without anaemia)? 1 yes  2 no  3 not sure
- (ii) If yes, since your treatment has this: 1 improved  2 stayed the same  3 worsened
- (b) (i) Before your treatment were you troubled by painful periods? 1 yes  2 no  3 not sure
- (ii) If yes, since your treatment has this: 1 improved  2 stayed the same  3 worsened
- (c) (i) Before your treatment were you troubled by bulk-related symptoms, for example abdominal mass causing pain, pressure on the bladder or bowel, or other? 1 yes  2 no  3 not sure
- (ii) If yes, since your treatment has this: 1 improved  2 stayed the same  3 worsened

25. We would like to know what your bladder function is like now compared with **before** your **index** treatment.
- (a) (i) Before your treatment were you troubled by a frequent need to urinate during the day?  
 1 yes  2 no  3 not sure
- (ii) Since your treatment has this: 1 improved  2 stayed the same  3 worsened
- (b) (i) Before your treatment were you troubled by a frequent need to urinate during the night?  
 1 yes  2 no  3 not sure
- (ii) Since your treatment has this: 1 improved  2 stayed the same  3 worsened
- (c) (i) Before your treatment did you lose urine unexpectedly (e.g. when sneezing)?  
 1 yes  2 no  3 not sure
- (ii) Since your treatment has this: 1 improved  2 stayed the same  3 worsened

**Satisfaction with treatment and feelings about treatment: Q24**

Parts (a) and (f) provide an opportunity to obtain free-text data

24. It is a few years since your treatment for fibroids, and we would like to know what your feelings are now about your treatment. *(Please tick)*
- (a) My expectations about my treatment have now been fulfilled 1 yes  2 no
- If no, please tell us why: a2 .....
- .....
- .....
- (b) The treatment has relieved my symptoms 1 yes  2 no
- (c) I feel much better since I had the treatment 1 yes  2 no
- (d) If I needed to have treatment for fibroids I would undergo the same treatment  
 1 yes  2 no
- (e) I would recommend this treatment to a friend 1 yes  2 no
- (f) I have suffered from problems caused by the treatment 1 yes  2 no
- If yes, please give details about the problems:
- f2 .....
- .....
- .....
- .....

**UAE-only efficacy**

Efficacy of treatment in relation to fibroid/uterine size shrinkage, changes in menstrual symptoms pre- to post-treatment and whether any further treatments were required for fibroid symptoms are applicable only to the UAE cohort.

**Reduction in fibroid/uterine size**

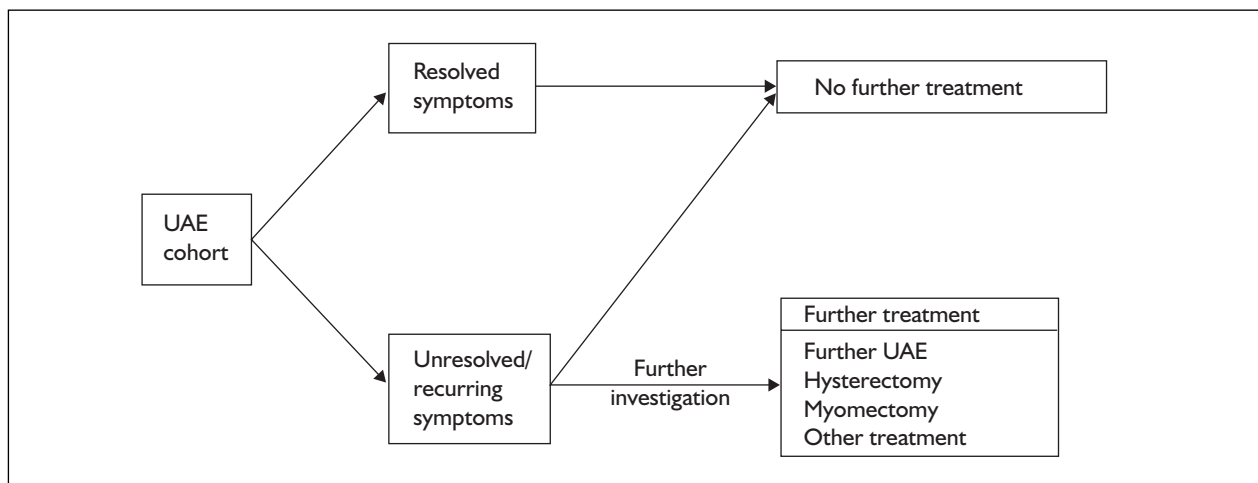
Data was collected on the size of the indicator fibroid and uterus when images were taken both pre- and post-UAE. For some patients US imaging was used, but for the majority MRI was

undertaken. Data collected was sparse, but where available fibroid/uterine volume reduction was examined from the pre-UAE size to approximately 6 months post-UAE. Volumes were determined by multiplying the product of the maximum diameters in three planes of the fibroid/uterus by 0.5233 (ellipsoid formula). In addition, shrinkage in maximum diameter was also examined for both indicator fibroid and uterus, in order to include those measurements where only one or two diameters of the fibroid/uterus were available.

**Resolution of menstrual symptoms: Q34**

Retrospective data was obtained from the patient questionnaire Q34 completed by the UAE group only

- 34.** We would like to know what your periods were like **after treatment**, compared with **before** your **first** UAE treatment.
- (a) Compared with before your first UAE treatment, how often did your periods come after your first UAE treatment?  
 1 have no periods  2 less often  3 about the same as before  4 more often
- If you have no periods go straight on to Section 4, question 35*
- (b) Compared with before your first UAE treatment, for how long did your menstrual bleeding last after your first UAE treatment?  
 1 far fewer days  2 fewer days  3 about the same  4 more days  5 many more days
- (c) Compared with before your first UAE treatment, how heavy were your periods after your first UAE treatment?  
 1 very much lighter  2 lighter  3 unchanged  4 heavier  5 very much heavier
- (d) Before your first UAE treatment did you suffer from period pains?  
 1 no pains  2 mild pains  3 moderate pains  4 severe pains
- (e) Compared with before your UAE treatment, what was your experience of period pains after your first UAE treatment? 1 better  2 about the same  3 worse



**FIGURE 15** Efficacy of treatment: further treatment for unresolved fibroid symptoms

### Requirement for any further treatments for fibroid symptoms

Further treatments for unresolved fibroid symptoms (includes cases where symptoms initially resolved but then recurred) were investigated using information from both the clinical data forms and the questionnaire. *Figure 15* indicates possible pathways following treatment. Both the type/s of further treatment and their timing after the index treatment are considered.

### UAE-specific topics

Several topics of specific importance to UAE treatment were investigated. These considered issues of factors influencing choice of UAE, factors influencing outcome of treatment and fertility issues.

### Factors influencing choice of UAE (Q21)

Q21 asked patients about the factors that influenced their choice of UAE, providing several

**21** (a) Were you offered a choice of treatment for your fibroids at your hospital consultation?  
 1 yes  2 no  3 not sure  *If no or not sure, please go to question 22.*  
*If yes, please complete the following.*

(b) What treatments were you offered?  
 1 hysterectomy  2 myomectomy  3 uterine artery embolisation (UAE)   
 4 Other  (4b specify .....)

(c) Which treatment did you choose?  
 1 hysterectomy  2 myomectomy  3 uterine artery embolisation (UAE)   
 4 Other  (4b specify .....)

(d) Please could you tell us about what major factors influenced your choice of treatment?  
 (1) .....  
 (2) .....  
 (3) .....  
 (4) .....  
 (5) .....  
 (6) .....  
 (7) .....  
 (8) .....

lines for free-text comments without further prompting. The responses were categorised using the patients' own words, and then these were grouped into themes.

**Outcome predictor variables**

Factors which might predict variation in outcome measures including complications, GSEs and any need for further treatment for fibroids were investigated.

**Operator experience**

HOPEFUL collected data on all embolisations performed in each centre from their first until the end of 2002 (or until September 1998 in one case and March 2000 in another). This enabled us to consider the effect of operator experience on outcomes. All the collaborating radiologists were experienced in interventional procedures in many organ systems including the pelvis (post-partum haemorrhage and gynaecological bleeding from other causes). In keeping with Royal College of Radiologists (RCR) recommendations concerning training for carotid artery stenting (CAS), AN considered that 10 UAE procedures would provide the learning curve for this specific technique.

Operator experience effect was examined in two ways. All centres were included in the analyses.

The first analysis used the initial 10 cases considered sufficient to train an already experienced (in other embolisation techniques) radiologist in the UAE technique. The first 10 women in each centre were thus grouped and compared against the rest. The second analysis looked at trends over time using the most powerful test available, the cases in each centre are split into tertiles and the tertiles are compared. The first tertile generally included the first 10 cases.

**Location of indicator fibroid**

Data on fibroid location were collected in the pretreatment imaging section of the clinical data form or from post-UAE imaging where the location of the indicator fibroid was not indicated in pre-imaging.

**Post-UAE fertility**

Data on post-UAE pregnancies and their outcomes were investigated utilising information obtained from clinical forms and patient questionnaires. Fertility was examined in relation to baseline characteristics of the women together with their stated fertility aspirations.

Additional data arising from free-text comments on fertility issues are discussed in Chapter 9.

# Chapter 3

## Analysis

### Statistical analysis

All statistical analyses were carried out in STATA.<sup>58</sup>

#### General issues

##### Sample size (power)

Primary outcome [1] of the study was the difference in complication rates between the two cohorts. VALUE<sup>12</sup> reported complication rates of 3.5% for operative complications and a further 9% for postoperative complications, but this was found to be under-reported during the ascertainment and validation exercise. In addition, the complication rate was found to be 1.5 times higher for patients with fibroids compared with women with DUB.<sup>12</sup> Hence to cover this possible under-reporting it is assumed for the purpose of this calculation that the rate of complications for hysterectomy is 20%. In order to detect a halving of the OR [an equivalent to a complication rate of 11.11% in the UAE cohort (RR of 1.8)] with a power of 90% at the 5% significance level, 370 patients would be required to be recruited in each cohort, a total of 740 patients. To detect an OR of 0.6 [equivalent to 13.0% complication rate in UAE (RR of 1.5)] with a 90% power, 626 patients would need to be recruited in each cohort, 1252 patients in total.

HOPEFUL also planned to look at the difference in serious complication rates between the two cohorts (primary outcome [2]). In VALUE<sup>12,50</sup> the postoperative serious complication rate for hysterectomy in women with symptomatic fibroids was 4.4% (95% CI 3.9 to 4.9). A halving of the OR (equivalent to a serious complication rate of 2.2%) with a power of 70% at the 5% significance level would require 902 patients in each cohort, 1804 patients in total.

It was expected that approximately 1000 patients would be eligible in each cohort. In this case the power of detecting a halving of the OR for primary outcome [1] is 99.9% and for primary outcome [2] it is 74.9%.

The actual numbers of complications and patients recruited into the HOPEFUL study led to a *post-hoc* power of 90% to detect a significant difference at the 5% level for primary outcome [1].

#### Missing values

Missing values were expected to occur in some of the variables due to retrospectively collecting data from different sources and different centres. These missing values were assumed to be missing at random<sup>59</sup> as the information required was the type of data routinely collected during hospital admission and not unusual data. This assumption assumes that the probability that a data value is missing depends on values of variables that were actually measured and not on values of variables that were not collected. There were no missing values in the primary outcome variables because if a complication was not reported on either the clinical form or the questionnaire, it was assumed that no complication occurred.

These missing values were examined in order to compare whether there was any differential loss of complications in the two treatment cohorts. If only those patients with complete data were included in the analysis (complete participant analysis) there would be a significant loss of information. Multiple imputation methods were therefore implemented in order to utilise all the available data.

The MICE (Multiple Imputation by Chained Equations) method of multiple imputation by chained equations using 'regression switching' was used to impute the missing values.<sup>60,61</sup> The basic idea of this multiple imputation method is to create a small number of copies of the data, each of which has the missing values suitably imputed, and to analyse each complete dataset independently. Estimates of the parameters are then averaged across copies to give a single estimate with standard errors computed according to 'Rubin's rules'<sup>59,62</sup> devised to allow for between- and within-imputation components of variation in the parameter estimates. This method initially uses the 'closest predictor' option, where each variable with a missing value is given the estimate of value from the closest complete case (using all the variables) as its imputed value. Then each variable is imputed in turn, conditional on all the other variables (observed and imputed combined) until all the incomplete variables have been imputed. A second pass through the data is then carried out using the imputed values created in the first pass. This

process is continued until the imputations are stable, which usually occurs after between 10 and 20 iterations.<sup>62</sup>

This process is repeated five times to create five complete sets of data, all of which contain the original non-missing values and also a separate set of imputed values. As the missing values are created using a random model, these data sets are not the same but can give an estimate of the variability in the predicted missing values that can be taken into account in the analysis. The gain in efficiency achieved by having more than one imputation rapidly diminishes and therefore three to five imputations are usually considered sufficient to give reasonable efficiency provided that the amount of missing data is not too large. Choosing five imputations gives a greater than 95% efficiency for the HOPEFUL data set.<sup>61</sup>

To create the imputed datasets the 'ice' program within STATA<sup>63,64</sup> was utilised using the following complete variables: centre, treatment, outcome, age at procedure, medical co-morbidity, gynaecological co-morbidity, prior pelvic surgery and menopausal status. The following incomplete variables were estimated using linear regression: age at questionnaire, parity, height, weight at procedure, weight at completion of questionnaire, ethnicity, education, diastolic BP, systolic BP and age at menarche. Logistic regression was used for smoking and prophylactic antibiotic use, and multiple logistic regression was used for year of questionnaire and fibroid symptoms from both clinical forms and questionnaires.

The confounding variables to be used in the analysis were then created for all five imputed datasets:

- parity grouped into nulliparous and multiparous
- BMI calculated at time of procedure and then grouped into obese and not obese
- ethnicity grouped into white, black or mixed black and other
- education grouped into primary, secondary and tertiary education
- high BP calculated from systolic and diastolic BP.

The resulting five imputed data sets were then analysed separately using logistic regression and combined to create the adjusted ORs of the effects of treatment on outcome when all the confounding variables are included, using the 'micombine' command in STATA.<sup>63-65</sup>

### **Clustering by centre**

Standard statistical methods assume that the outcome for each individual is independent of the outcome for other individuals. This assumption may be violated when different individuals in the same group are sampled because, on average, the outcome or exposures for an individual in the group may be more similar to individuals in the group than to individuals in the rest of the population. These groups are described as clusters.

Patients from different centres may be more dissimilar than patients in the same centre due to known geographic variation in socio-demographic factors which may affect their risk of an adverse outcome. Adjustment for clustering by centre will therefore be carried out in the primary outcome analysis.<sup>66</sup> Failure to take this potential clustering into account would lead to standard errors that are too small, leading to *p*-values that are too small and CIs that are too narrow. Adjusting for clustering by centre does not affect the size of the ORs and is therefore only carried out on the final model at the end of the analysis.

### **Baseline comparability**

Baseline characteristics are presented as means and SDs separately for the two treatment cohorts and tested for statistical significance using *t*-tests for the continuous variables such as age and BMI. Numbers and percentages are presented for the categorical variables such as education, ethnicity and parity and these are compared using  $\chi^2$  tests on the appropriate degrees of freedom for the non-missing values of each variable. The denominators for calculation of the percentages are from the overall cohort (total *n* = 1108, Hyst *n* = 459 and UAE *n* = 649). Numbers and percentages of missing values are also given where appropriate.

### **Confounders**

In general, confounding occurs when a confounding variable is associated with the treatment cohort and also influences the outcome. Failure to control for confounding variables would bias any interpretation of the comparison between the two treatment cohorts. Randomisation of patients to treatment cohorts in RCTs minimises the risk of confounding. However, in this retrospective observational study, confounding variables must be considered before comparing treatment cohorts.

All *a priori* possible confounders considered were first studied for differences between the treatment



cohorts (see the section ‘Baseline characteristics’, p. 47). In addition, they were studied for associations with the primary outcome variable using univariate logistic regression. A simple logistic regression was carried out to estimate the crude OR. Then logistic regression was carried out for each *a priori* possible confounder and any change in the OR for the treatment cohort effect compared with the crude OR was studied after adjusting for the confounder in order to investigate if confounding was present. The variables where confounding appeared to be present and/or where there was a difference between treatment cohorts were then included in the full model for the primary outcome analysis.

### Primary outcome measures

#### Comparative safety/complication rates (UAE versus Hyst)

##### Primary outcome [1] complications versus no complications

Primary outcome [1] analysis utilised logistic regression, with the main outcome variable being complications versus no complications and the main exposure of interest being the treatment cohort adjusting for confounding variables.

Several models are presented with and without clustering by centre:

- The crude unadjusted analysis – no missing value imputation required.
- A fully adjusted analysis (full model) – including all the identified confounding factors. Multiple imputation methods used to estimate missing values in order to utilise all the data available – five imputation data sets were analysed and combined to provide ORs.
- A significant confounder analysis (minimum model) where only those confounders that were statistically significant (10% level) were kept in the model. Backward elimination from the full model was carried out dropping the least significant ( $p \geq 0.10$ ) confounder in turn. All the dropped variables are included singly in a further logistic regression in addition to the minimum model in order to check that no significant effects have been obscured by their associations with other variables.

##### Primary outcome [2], severe/major complications versus minor/no complications

The above method was repeated for primary outcome [2]: severe/major complication versus minor/no complication.

### UAE-only cohort GSEs

#### GSEs and complications

GSEs of the UAE treatment, including chronic discharge, natural fibroid expulsion without assistance, post-embolisation syndrome, not requiring readmission and temporary amenorrhoea, have not been classified as complications in this study. However, these side-effects are of concern to patients considering undergoing UAE and it is important to be able to provide information to women on the likelihood of experiencing such effects. We therefore undertook to examine GSEs and their association with any complications experienced by the women, for example a chronic discharge may have led to fibroid extraction or be treated as a minor infection, both of which have been classified as complications in this study.

#### GSEs and confounders

The relationship between GSEs and the *a priori* potential confounders were investigated using descriptive statistics and  $\chi^2$  tests.

### Secondary outcomes measures

#### Comparative efficacy (UAE versus Hyst)

Comparative secondary outcomes are presented as numbers and percentages of responses and tested using  $\chi^2$  significance tests.

#### UAE-only efficacy

- Reductions in fibroid/uterine size are presented as numbers and mean reduction from pre-UAE measurements to approximately 6-month post-UAE measurements.
- Resolution of menstrual symptoms are presented as numbers and percentages of responses.
- Requirements for further treatment, in particular myomectomy, hysterectomy or further UAE treatment are presented as a Venn diagram due to some of the women requiring more than one further treatment. The timing of the further treatment is also investigated together with the reasons for any further treatment needed within 1 year of the index treatment. Time to first event analysis is presented using cumulative percentages and Kaplan–Meier survival curves.

### UAE-specific topics

#### Factors influencing choice

The factors influencing choice are analysed by grouping together themes and presenting the results.

#### Outcome predictor variables

Operator experience and fibroid location are investigated in relation to primary outcome [1],

GSEs and further treatment in order to examine whether these were predictive of success of treatment.

### **Post-UAE fertility**

Details of post-UAE pregnancies and their outcomes were recorded and are described.

## **Free-text analysis**

The reliability and validity of the free-text comments may have been affected by the passage of time between the index treatment and the date of the survey. Two main aspects of this possibility are discussed briefly below.

### 1. *Selective recall, recall bias*

As the study asks about events and reactions to events that happened up to 10 years previously, it is possible that the responses may be affected by recall bias. It is generally advised that questions asking about events more than six months ago should be avoided;<sup>67</sup> however, an exception is made for 'topics of high saliency to respondents (e.g. death, childbirth), where memory is better'. This study asks about an event that is likely to have had high salience for the respondents, and asks more about experiences of events than about the dates or details. Regarding the general issue of recall bias, the free-text comments are therefore not likely to be any more affected by 'inaccuracies' than are the tick box responses.

### 2. *Narrative inquiry*

A different kind of influence may, however, be present in the free-text comments in relation to the passage of time between the index treatment and the present. The free-text space allows for a certain level of narrative about respondents' experiences. There is little space so the narratives are very short. Because of the significant nature of the index event in relation to pain, symptom severity and fertility, respondents are likely to have either talked about them or have thought through them in depth. Over the years they will have developed their own narrative of why they had treatment, what the treatment was like and what effect it had. It is possible, therefore, that what is being written in the free-text sections relates more to the respondent's developed narrative than to their actual experience at the time. Acting against this is the magnitude of the index event, and the likelihood of big initial stories that had no need of embellishment or refinement. Also, a modified story relates to

how individuals are feeling now, so in its own right is representative of the after-effects of the index event.

The process of analysis of the free-text comments was as follows:

1. The free-text comments were all typed out verbatim.
2. Comments were printed out in table form with three columns for:
  - (a) the respondent ID code
  - (b) the respondent's recorded comment and
  - (c) a column for the researchers to start the analysis process by jotting down suggested categories that the comments appear to fall into.
3. Two researchers read through the comments and independently developed a list of categories using the constant comparison method,<sup>68</sup> which could be used to sort the data for further analysis.
4. The researchers came together to discuss the similarities and differences between their coding and to agree an initial list of categories. Examples of categories at this stage were 'Emotional repercussions', 'Expected a different result' and 'Weight gain'.
5. Data files were constructed for each agreed category, then each individual comment was cut and pasted into the appropriate data file.
6. Each data file was then reviewed to check its suitability as a free-standing category, or whether its data might better be shared between several other categories or given a new category heading.
7. Once the categories were stable, the free-text data from each one were reviewed. The researchers were looking for:
  - (a) pure description
  - (b) interpretations
  - (c) crossed or misunderstandings
  - (d) rationale behind comment
  - (e) guidance to underpin improvements in practice.
8. A descriptive account of the raw data under each of the data files was prepared.

Care has been taken not to infer any statistical implications from the free-text data, or to over-analyse data that are inherently limited by its method of collection.

In total, 742 of 986 (75.3%) women who returned questionnaires included free-text comments at Q35 or additional comments on other parts of the questionnaire. On average respondents wrote 69

words. The response rate in the UAE group was significantly higher [UAE  $n = 468/589$  (79.5%) versus Hyst  $n = 274/397$  (69.0%) – (1)  $\chi^2$ ,  $p < 0.001$ ). In addition, the UAE cohort tended to write longer responses in their free-text responses on average than the hysterectomy cohort (74 versus 59 words). This may reflect the higher education level of the UAE group and a tendency to be more proactive in accessing their treatment. We can only speculate as to the reasons why some respondents did not write comments. We cannot assume that an issue raised by one respondent is not important to others who did not raise it. Findings from such free-text comments cannot therefore be used to estimate the prevalence in the population of particular problems mentioned in the comments.

As described, free-text comments were used to supplement and expand on the quantitative data on secondary efficacy outcomes relating to satisfaction with treatment and feelings about treatment (Q24) in Chapter 6.

Emergent themes not related to specific questions addressed on the questionnaire are reported in Chapter 9.

## Health economics methods

The rationale and methodology used in the health economic evaluation are described fully in Chapter 8.



## Chapter 4

# Results: recruitment, baseline characteristics, confounders and missing values

### Recruitment

Of the eligible women identified for the HOPEFUL study, 63.1% (1094/1734) consented to participate [Hyst  $n = 438$  (57.4%), UAE  $n = 656$  (67.4%)]. In addition to the consenting women there were 28 (1.6%) patients who had died since their index fibroid treatment and for whom we had ethical approval to obtain clinical data [Hyst  $n = 21$  (2.8%), UAE  $n = 7$  (0.7%)]. This provided a maximum total of 1122 (64.7%) patients in the study. However, 14 patients were completely lost to recruitment (unable to obtain either questionnaires or clinical data forms), including four of the deceased UAE patients. Causes of death are further detailed in *Table 4* (p. 23) and Appendix 7. There were consequently 1108 (63.9% of the total eligible) patients recorded in HOPEFUL [Hyst  $n = 459$  (60.2%), UAE  $n = 649$  (66.8%)] (*Figure 8*, p. 30).

For these 1108 patients, 88.8% of the clinical forms were completed by the research nurses with a further 6.1% completed from the VALUE database, providing 94.9% of clinical data collected (Hyst 100%, UAE 89.4%). Similarly, 88.8% of the patient questionnaires were completed [Hyst  $n = 396$  (86.2%), UAE  $n = 588$  (90.6%)].

The average length of follow-up since index treatment (recorded to either time of questionnaire completion or last clinical follow-up

date, whichever is latest) was 8.6 years (SD = 3.4, range 0–11.2 years) for the hysterectomy cohort and 4.6 years (SD = 2.0, range 0–9.2 years) for the UAE cohort (*Table 11*). In summary, 8.5% of the UAE cohort had less than 2 years of follow-up, 45.0% had 2–5 years and 46.5% had more than 5 years. In the hysterectomy cohort, 12.9% had less than 2 years of follow-up, 0.4% had 2–5 years and 86.7% had more than 5 years.

Some of the patients who consented to take part did not complete the questionnaire. These patients therefore only had details from their hospital records, from which limited short-term follow-up was available. In addition, hospital notes were not available for some patients as they had been destroyed in line with NHS policy. For these hysterectomy patients only clinical data for up to 6 weeks from the VALUE database were available for use in addition to questionnaire response.

### Baseline characteristics

*Tables 12* and *13* show the baseline characteristics for the two cohorts at time of treatment. The denominators for calculation of the percentages are from the overall cohort (total  $n = 1108$ , Hyst  $n = 459$  and UAE  $n = 649$ ). Numbers and percentages of missing values are also given where appropriate.

The distributions of baseline characteristics age at procedure, education level, ethnicity and parity all differ significantly ( $p < 0.0001$ ) between the two cohorts and are shown in *Figure 16*. Although the difference in mean age at procedure between the two cohorts is statistically significant [the hysterectomy cohort being 2.7 years older than the UAE cohort (95% CI 1.9 to 5.5)], this was not considered to be clinically significant. There was an excess of women over the age of 60 years in the hysterectomy cohort [Hyst  $n = 45$  (9.8%), UAE  $n = 20$  (3.1%)]. This reflects the greater number of postmenopausal women in the hysterectomy cohort. This is adjusted in the primary outcome analysis by treating age at procedure and postmenopausal status as confounders. The UAE

**TABLE 11** Follow up since index treatment

Follow-up (years)	Hyst (n = 459)	UAE (n = 649)
≤1	59 (12.9%)	32 (4.9%)
1–2		23 (3.5%)
2–3	2 (0.4%)	97 (14.9%)
3–4		115 (17.7%)
4–5		80 (12.3%)
5–6	1 (0.2%)	122 (18.8%)
6–7		111 (17.1%)
7–8		59 (9.1%)
8–9		9 (1.4%)
9–10	234 (51.0%)	1 (0.2%)
10–11	162 (35.3%)	
>11	1 (0.2%)	

**TABLE 12** Baseline characteristics between treatment cohorts – demographics and medical related<sup>a</sup>

		Hyst (n = 459)	UAE (n = 649)	Total (n = 1108)	Significance (p) <sup>b</sup>
<b>Demographic variables</b>					
Age at procedure (years)	Mean (n) SD	46.5 (459) 6.8	43.8 (649) 6.5	44.9 (1108) 6.8	<0.0001
Age groups at procedure (years)	<35	19 (4.1%)	64 (9.9%)	83 (7.5%)	<0.0001
	35–39	46 (10.0%)	116 (17.9%)	162 (14.6%)	
	40–44	115 (25.1%)	169 (26.0%)	284 (25.6%)	
	45–49	165 (35.9%)	187 (28.8%)	352 (31.8%)	
	50–54	87 (19.0%)	94 (14.5%)	181 (16.3%)	
≥55	27 (5.9%)	19 (2.9%)	46 (4.2%)		
Highest level of education	Primary	150 (32.7%)	64 (9.9%)	214 (19.3%)	<0.0001
	Secondary	138 (30.1%)	195 (30.0%)	333 (30.1%)	
	Tertiary	98 (21.3%)	320 (49.3%)	419 (37.8%)	
	Missing	73 (15.9)	70 (10.8%)	142 (12.8%)	
Ethnicity	White	382 (83.2%)	480 (74.0%)	862 (77.8%)	<0.0001
	Black	6 (1.3%)	97 (14.9%)	103 (9.3%)	
	Other	9 (2.0%)	10 (1.5%)	19 (1.7%)	
	Missing	62 (13.5%)	62 (9.6%)	124 (11.2%)	
Parity	Nulliparous	65 (14.2%)	296 (45.6%)	361 (32.6%)	<0.0001
	Multiparous	391 (85.2%)	328 (50.5%)	719 (64.9%)	
	Missing	3 (0.6%)	25 (3.9%)	28 (2.5%)	
Menopausal status	Post-menopausal	39 (8.5%)	35 (5.4%)	74 (6.7%)	0.41
	Not post-menopausal	420 (91.5%)	614 (94.6%)	1034 (93.3%)	
Age at menarche (years)	Mean (n) SD	12.4 (392) 1.6	12.5 (573) 1.5	12.5 (965) 1.5	0.27
<b>Medical-related variables</b>					
Smoking	Never	235 (51.2%)	376 (57.9%)	611 (55.1%)	0.006
	Current/ex	210 (45.7%)	238 (36.7%)	448 (40.4%)	
	Missing	14 (3.1%)	35 (5.4%)	49 (4.4%)	
BMI	Mean (n) SD	26.7 (321) 4.9	26.5 (311) 5.5	26.6 (632) 5.2	0.67
Obesity (obese: BMI ≥30)	Not obese	257 (56.0%)	248 (38.2%)	505 (45.6%)	0.92
	Obese	64 (13.9%)	63 (9.7%)	127 (11.5%)	
	Missing	138 (30.1%)	338 (52.1%)	476 (43.0%)	
BP (high BP: diastolic ≥90 mmHg and/or systolic ≥140 mmHg)	Normal	242 (52.7%)	272 (41.9%)	514 (46.4%)	<0.0001
	High BP	213 (46.4%)	114 (17.6%)	327 (29.5%)	
	Missing	4 (0.9%)	263 (40.5%)	267 (24.1%)	
Gynaecological co-morbidity	No	404 (88.0%)	574 (88.4%)	978 (88.3%)	0.83
	Yes	55 (12.0%)	75 (11.6%)	130 (11.7%)	
Medical co-morbidity	No	322 (70.2%)	523 (80.6%)	845 (76.3%)	<0.0001
	Yes	137 (29.8%)	126 (19.4%)	263 (23.7%)	
Prior pelvic surgery	No	394 (85.8%)	480 (74.0%)	874 (78.9%)	<0.0001
	Yes	65 (14.2%)	169 (26.0%)	234 (21.1%)	

<sup>a</sup> Data given as numbers (percentages) unless stated otherwise.

<sup>b</sup> Significance level t-test for continuous variables and  $\chi^2$  for non-missing categorical variables.

cohort were more highly educated, more ethnically diverse and more likely to be nulliparous than the hysterectomy cohort. Nulliparity may be a factor in choosing to avoid hysterectomy.

There were no statistically significant differences between the two cohorts in age at menarche, BMI

or obesity. There were statistically significant differences between the two treatment cohorts for several medical-related variables: high BP ( $p < 0.0001$ ), medical co-morbidity ( $p < 0.0001$ ) and prior pelvic surgery ( $p < 0.0001$ ) (Figure 17). High BP was more common among the women in the hysterectomy cohort. However, only 60% of

**TABLE 13** Baseline characteristics between treatment cohorts: treatment, symptom and fibroid related<sup>a</sup>

		Hyst (n = 459)	UAE (n = 649)	Total (n = 1108)	Significance (p) <sup>b</sup>
<b>Treatment-related variables</b>					
Type of hysterectomy	Total abdominal	398 (86.7%)			
	Sub-total abdominal	23 (5.0%)			
	Vaginal	24 (5.2%)			
	Laparoscopically assisted vaginal	12 (2.6%)			
	Other	1 (0.2%)			
	Missing	1 (0.2%)			
Arteries embolised	Single uterine artery		27 (4.2%)		
	Both uterine arteries		543 (83.7%)		
	Both uterine & left ovarian		1 (0.2%)		
	Left ovarian only		1 (0.2%)		
	Missing		77 (11.9%)		
Embolitic material used	PVA particles only		282 (43.5%)		
	PVA + gelfoam		102 (15.7%)		
	PVA + coils		132 (20.3%)		
	PVA +gelfoam+coils		5 (0.8%)		
	Gelfoam/coils/both		31 (4.8%)		
	Missing		97 (14.9%)		
Prophylactic antibiotics	No	53 (11.5%)	169 (26.0%)	222 (20.0%)	<0.0001
	Yes	406 (88.5%)	422 (65.0%)	828 (74.7%)	
	Missing	0	58 (8.9%)	58 (5.2%)	
<b>Symptom-related variables</b>					
Fibroid symptoms – questionnaire	Menstrual only	173 (37.7%)	133 (20.5%)	306 (27.6%)	<0.0001
	Both	165 (35.9%)	384 (59.2%)	549 (49.5%)	
	Bulk only	59 (12.9%)	72 (11.1%)	131 (11.8%)	
	Missing	62 (13.5%)	60 (9.2%)	122 (11.0%)	
Fibroid symptoms – clinical forms	Menstrual only	222 (48.4%)	221 (34.1%)	443 (40.0%)	<0.0001
	Both	68 (14.8%)	261 (40.2%)	329 (29.7%)	
	Bulk only	98 (21.3%)	78 (12.0%)	176 (15.9%)	
	Missing	71 (15.5%)	89 (13.7%)	160 (14.4%)	
<b>Fibroid characteristics – indicator fibroid</b>					
Location	Submucosal	10 (2.2%)	44 (6.8%)		
	Intramural	44 (9.6%)	130 (20.0%)		
	Subserosal	12 (2.6%)	26 (4.0%)		
	Pedunculated	12 (2.6%)	6 (0.9%)		
	Missing	381 (83.0%)	443 (68.3%)		
Volume: 0.5236d <sub>1</sub> d <sub>2</sub> d <sub>3</sub> (cm <sup>3</sup> )	Mean (n) SD	289.0 (45) 400.6	330.1 (276) 379.2		
Maximum diameter (cm)	Mean (n) SD	6.5 (166) 3.9	8.5 (345) 3.5		
Number of fibroids	1	65 (14.2%)	96 (14.8%)		
	2	20 (4.4%)	48 (7.4%)		
	3	9 (2.0%)	11 (1.7%)		
	>3	50 (10.9%)	97 (14.9%)		
	Missing	315 (68.6%)	397 (61.2%)		
Other variables of interest Fertility aspirations	Did not want children	315 (68.6%)	319 (49.2%)	634 (57.2%)	<0.0001
	Hoped to have children	26 (5.7%)	187 (28.8%)	213 (19.2%)	
	Not sure/other	25 (5.4%)	76 (11.7%)	101 (9.1%)	
	Missing	93 (20.3%)	67 (10.3%)	160 (14.4%)	

<sup>a</sup> Data given as numbers (percentages) unless stated otherwise.  
<sup>b</sup> Significance level t-test for continuous variables and  $\chi^2$  for non-missing categorical variables.

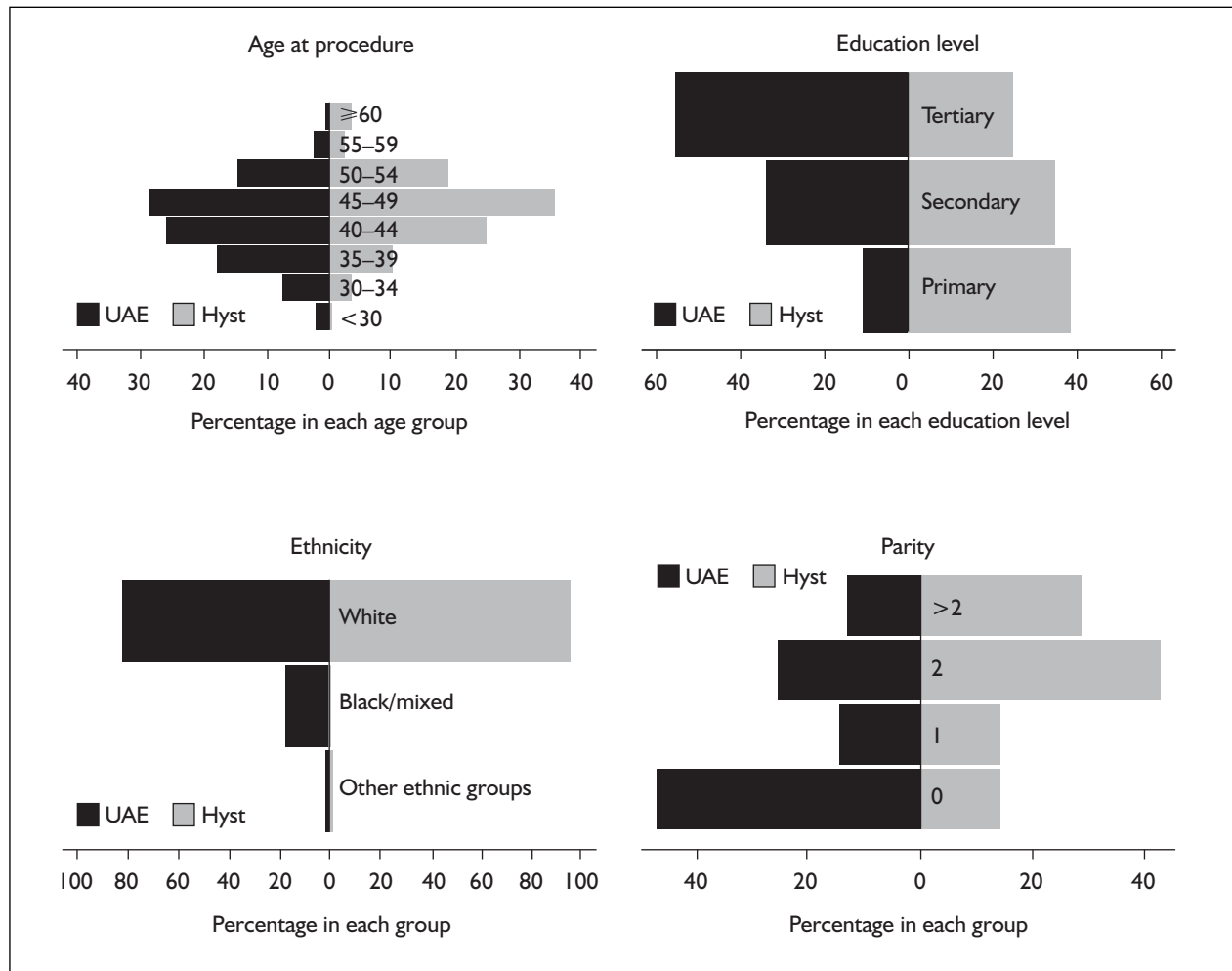


FIGURE 16 Significantly different baseline demographic characteristics of the treatment cohorts

the UAE cohort had their blood pressure reported compared with 99% of the hysterectomy cohort.

The hysterectomy cohort had more concomitant medical conditions than the UAE cohort. Prior pelvic surgery, on the other hand, was more common in the UAE cohort. There were more never-smokers in the UAE cohort ( $p = 0.006$ ) than the hysterectomy cohort. There was no statistical difference between the cohorts for gynaecological co-morbidity ( $p = 0.83$ ).

Figure 17 also shows reported fibroid symptoms prior to treatment for the two treatment cohorts. There were statistically significant differences between the different fibroid symptom categories, both as reported by questionnaire ( $p < 0.0001$ ) and by clinical form ( $p < 0.0001$ ).

Prophylactic antibiotic use differed significantly between treatment groups; 88.4% of the hysterectomy cohort and only 65.0% of the UAE

cohort received them ( $p < 0.0001$ ). Antibiotics were not routinely given to patients undergoing UAE, particularly in the early part of the HOPEFUL study period. Some centres changed their policy mid-way through the study period due to a perceived high number of patients presenting with post-embolisation syndrome. Antibiotic use may be correlated with time of procedure and centre. Adjustment will be carried out for these in the primary outcome analysis.

## Confounders

Any association between the various *a priori* confounding variables and both treatment cohort and primary outcome were investigated. Changes in the ORs of the treatment effect when each variable is included in a univariate analysis were also assessed. All the variables were considered to be confounding variables with the possible exception of gynaecological co-morbidity, which



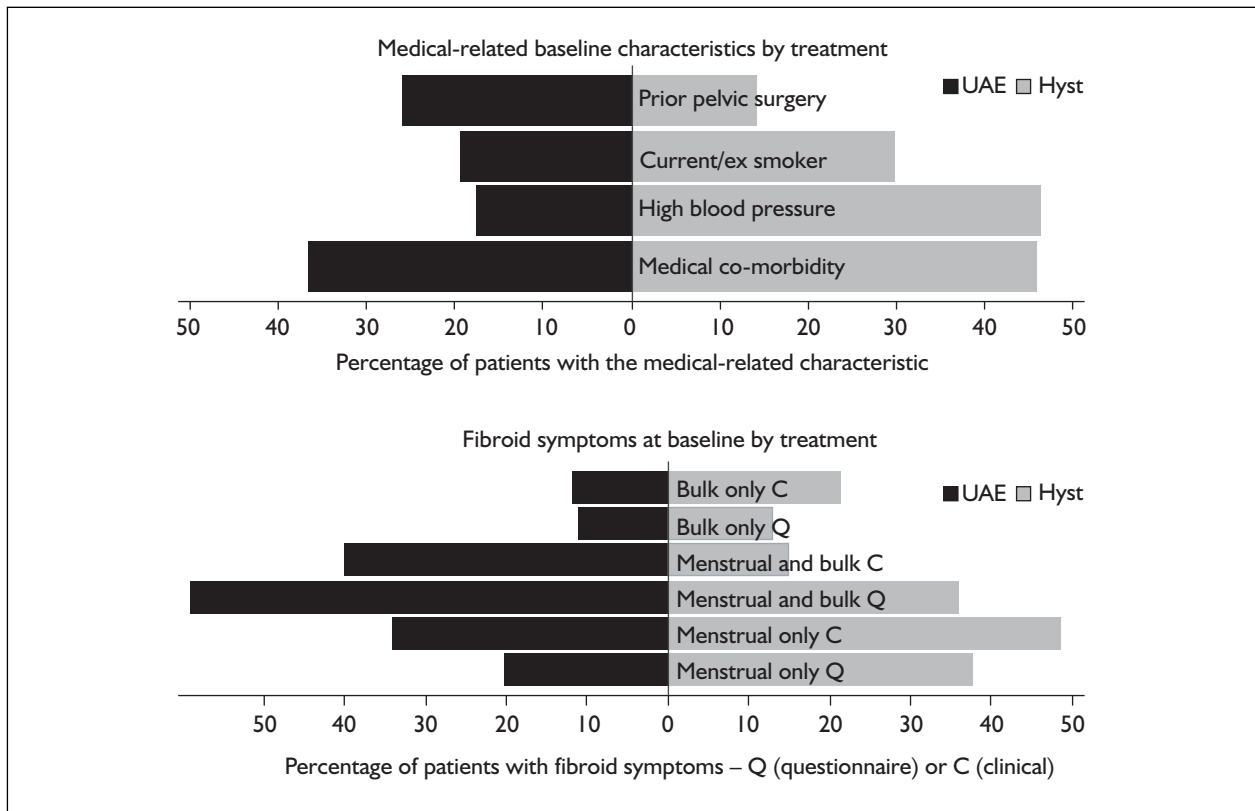


FIGURE 17 Baseline medical-related and symptom-related characteristics of the treatment cohorts. C, clinical; Q, questionnaire.

TABLE 14 Are the confounding variables associated with treatment, primary outcome [1] and are they confounders?

Confounding variable	Treatment ( $\chi^2$ )	Primary outcome [1] ( $\chi^2$ )	Odds ratio (outcome)	Confounder
Age at procedure	$p < 0.0001$	$p = 0.608$		Yes
Educational group	$p < 0.0001$	$p = 0.861$		Yes
Ethnic group	$p < 0.0001$	$p < 0.0001$	Black vs white -0.9 Other vs white -5.2	Yes
Parity group	$p < 0.0001$	$p = 0.541$		Yes
Reported menopausal status	$p < 0.0001$	$p = 0.010$	Postmenopausal vs not 2.0	Yes
Age at menarche	$p = 0.275$	$p = 0.048$		Yes
Smoking group	$p = 0.006$	$p = 0.601$		Yes
Obesity	$p = 0.820$	$p = 0.043$	Obese vs not obese 1.5	Yes
High BP	$p < 0.0001$	$p = 0.220$		Yes
Gynaecological co-morbidity	$p = 0.828$	$p = 0.724$		No
Medical co-morbidity	$p < 0.0001$	$p < 0.0001$	Medical co-morbidity vs none 1.9	Yes
Prior pelvic surgery	$p < 0.0001$	$p = 0.023$	Prior pelvic surgery vs none 1.5	Yes
Prophylactic antibiotics	$p < 0.0001$	$p < 0.0001$	Antibiotics vs none 0.5	Yes
Fibroid symptoms (clinical)	$p < 0.0001$	$p = 0.844$		Yes
Fibroid symptoms (questionnaire)	$p < 0.0001$	$p = 0.934$		Yes

appeared to have no association with treatment, outcome or to act as a confounder. Age at procedure was investigated both as a grouped (categorical) variable (age bands of 5 years) and as a linear variable. There was no benefit to using age as a categorical variable so the continuous variable was used in the full model. Table 14 details the association between the variables.

In summary, the following confounding variables were included in the full model: age at procedure, educational level, ethnic group, parity group, reported menopausal status, age at menarche, smoking group, obesity, high BP, gynaecological co-morbidity, medical co-morbidity, prior pelvic surgery, prophylactic antibiotics and fibroid symptoms.

TABLE 15 Missing data

Complication type	Hyst <sup>a</sup>	UAE <sup>b</sup>
Severe	1/3 (33.3%)	1/1 (0%)
Major	14/49 (28.6%)	15/24 (62.5%)
Minor	21/68 (30.9%)	50/89 (56.2%)
No complications	125/339 (36.9%)	362/535 (67.7%)
Total	161/459 (35.1%)	427/649 (65.8%)

<sup>a</sup> Number of patients with missing data/total number of patients (%).

## Missing values and primary outcome analysis

Some 53.1% (588/1108) of the women had missing data items in one or more of the confounding variables used in the primary outcome analysis. Table 15 presents the number of patients with missing data by severity of complication.

There is a differential proportion of patients with missing data items between the two cohorts, the hysterectomy cohort missing some data in 35.1% of cases and the UAE cohort in 65.8% of the patients. In addition to this overall difference, there are also differences between the different complication categories. If a complete participant analysis was carried out there would be a 30.0% loss of patients with complications and a 36.9% loss of patients without complications in the hysterectomy cohort, and a 57.9% loss of patients with complications and a 67.7% loss of patients without complications in the UAE cohort. This differential loss means that any complete participant analysis would be biased. Therefore, a complete participant analysis was not carried out and multiple imputation methods for dealing with the missing values were used in order to enable all the available information to be fully utilised, without biasing the results. The overall percentage of data items missing from all the confounding variables was 9.5% (1575/16,620, missing/total possible), a small percentage suitable for applying multiple imputation methods for estimating the missing values.

## Key findings – baseline characteristics

Of the 1734 eligible patients, data were collected on 1108 (63.9%) consenting (or deceased) patients

[Hyst  $n = 459$  (60.2%), UAE  $n = 649$  (66.8%)]. The average length of follow-up was 8.6 years (SD 3.4) for the hysterectomy cohort and 4.6 years (SD 2.0) for the UAE cohort. A minimum of 2 years of follow-up was attained for 91.5% of the UAE cohort and 87.1% of the hysterectomy cohort.

As expected, the two cohorts presented a different baseline profile for many of the *a priori* confounders. These included educational level (UAE higher), ethnicity (UAE more ethnically diverse, but still with only a small number of non-white in the cohort), parity (UAE more likely to be nulliparous), menopausal status (more post-menopausal women in the hysterectomy cohort) and smoking (less common in the UAE cohort). Medical co-morbidity was higher in the hysterectomy cohort, whereas the incidence of prior pelvic surgery was higher in the UAE cohort. Prophylactic antibiotics were more likely to be given to patients in the hysterectomy cohort.

In spite of all attempts to collect complete data, there were missing data items in one or more of the *a priori* confounding variables for 53.1% of the women, although there were less than 10% missing items in total. In order to utilise all the available data, missing values were estimated using well-tested multiple imputation methods. These methods provide the most unbiased estimate of the main comparison available, since to exclude women with any missing data affects the precision enormously while also omitting subjects, which could bias the estimates.

# Chapter 5

## Results: primary outcome measures

### Comparative safety (UAE versus Hyst)

All complications were categorised according to the *a priori* defined complication types (Box 1, p. 34). The number of patients with each complication is given in Table 16. These numbers may include patients in more than one category. There were 234 (21.1%) patients [Hyst  $n = 120$  (26.1%), UAE  $n = 114$  (17.6%)] with a total of 341 complications following their index treatment. A total of 165 of these patients had only one complication, 49 had two complications and 20 had more than two complications.

Patients were then categorised according to their most severe complication (Table 17).

These were then used to create the two primary outcome measures:

- primary outcome [1]: severe/major/minor complication versus no complication
- primary outcome [2]: severe/major complication versus minor/no complication.

### Primary outcome [1]: complications versus no complications

All patients with one or more complication are categorised as having a complication and all those patients with no reported complications are categorised as not having a complication. This is then used as the primary outcome variable for the logistic regression. Table 18 gives the summary for this outcome variable by treatment cohort.

TABLE 16 All recorded complications

Severity of complication	Type of complication	Hyst $n = 459$	UAE $n = 649$	Total $n = 1108$
<b>Severe</b>	a. Death	0	0	0
	b. Pulmonary embolus	3 (0.7%)	0	3 (0.3%)
	c. Myocardial infarction	0	0	0
	d. Cerebrovascular accident (stroke)	0	0	0
	e. Organ failure	1 (0.2%)	0	1 (0.1%)
	f. Other severe	1 (0.2%)	1 (0.2%)	2 (0.2%)
	<i>Total severe</i>	<i>5 (1.1%)</i>	<i>1 (0.2%)</i>	<i>6 (0.5%)</i>
<b>Major</b>	a. Permanent amenorrhoea (<40 years)	0	1 (0.2%)	1 (0.1%)
	b. Radiation burn	0	0	0
	c. Blood transfusion required	34 (7.4%)	4 (0.6%)	38 (3.4%)
	d. Structural damage caused by treatment	16 (3.5%)	5 (0.8%)	21 (1.9%)
	e. Septicaemia, emergency myomectomy/hysterectomy	2 (0.4%)	17 (2.6%)	19 (1.7%)
	f. Thrombosis	2 (0.4%)	0	2 (0.2%)
	g. Other major	9 (2.0%)	1 (0.2%)	10 (0.9%)
	<i>Total major</i>	<i>63 (13.7%)</i>	<i>28 (4.3%)</i>	<i>91 (8.2%)</i>
<b>Minor</b>	a. Minor infections (<30 days)	62 (13.5%)	38 (5.9%)	100 (9.0%)
	b. Haematoma requiring treatment	6 (1.3%)	4 (0.6%)	10 (0.9%)
	c. Adverse drug reaction	3 (0.7%)	8 (1.2%)	11 (1.0%)
	d. Permanent amenorrhoea ( $\geq 40$ years)	1 (0.2%)	9 (1.4%)	10 (0.9%)
	e. Retention of urine requiring catheterisation	10 (2.2%)	9 (1.4%)	19 (1.7%)
	f. Fibroid extraction requiring assistance	0	41 (6.3%)	41 (3.7%)
	g. Other minor (<30 days)	26 (5.7%)	27 (4.2%)	53 (4.8%)
	<i>Total minor</i>	<i>108 (23.5%)</i>	<i>136 (21.0%)</i>	<i>244 (22.0%)</i>
<i>Total complications</i>	<i>176 (38.3%)</i>	<i>165 (25.4%)</i>	<i>341 (30.8%)</i>	

**TABLE 17** Complications (categorised as most severe complication per patient)

Complication severity	Hyst (n = 459)	UAE (n = 649)	Total (n = 1108)
Severe	3 (0.7%)	1 (0.2%)	4 (0.4%)
Major	49 (10.7%)	24 (3.7%)	73 (6.6%)
Minor	68 (14.8%)	89 (13.7%)	157 (14.2%)
No complication	339 (73.9%)	535 (82.4%)	874 (78.9%)

**TABLE 18** Primary outcome [1] – complications versus no complications

Primary outcome [1]	Hyst (n = 459)	UAE (n = 649)	Total (n = 1108)	Significance $\chi^2_{(1)}$
No complications	339 (61.7%)	535 (82.4%)	874 (78.9%)	$p = 0.001$
Complications	120 (26.1%)	114 (17.6%)	234 (21.1%)	
Total	459 (100%)	649 (100%)	1108 (100%)	

**TABLE 19** Primary outcome [1] – complications versus no complications

Model	OR for treatment UAE vs Hyst	95% CI	95% CI (adjusted for centre clustering)
Crude unadjusted	0.602	0.450 to 0.805	0.316 to 1.148
Minimum model <sup>a,c</sup>	0.483	0.346 to 0.676	0.262 to 0.892
Full model <sup>b,c</sup>	0.419	0.282 to 0.620	0.225 to 0.778

<sup>a</sup> Minimum model: medical co-morbidity, prior pelvic surgery, high BP, obesity, ethnic group, antibiotics, and age at menarche.

<sup>b</sup> Full model: Age at operation, medical co-morbidity, gynaecological co-morbidity, prior pelvic surgery, high BP, obesity, parity group, smoking group, education group, ethnic group, antibiotics, fibroid symptoms from questionnaires, fibroid symptoms from clinical forms, menopausal status and age at menarche.

<sup>c</sup> All models carried out using multiple imputations on missing data values and then combining the results of 5 imputation datasets. Each dataset contains the original dataset plus a set of imputed missing values.

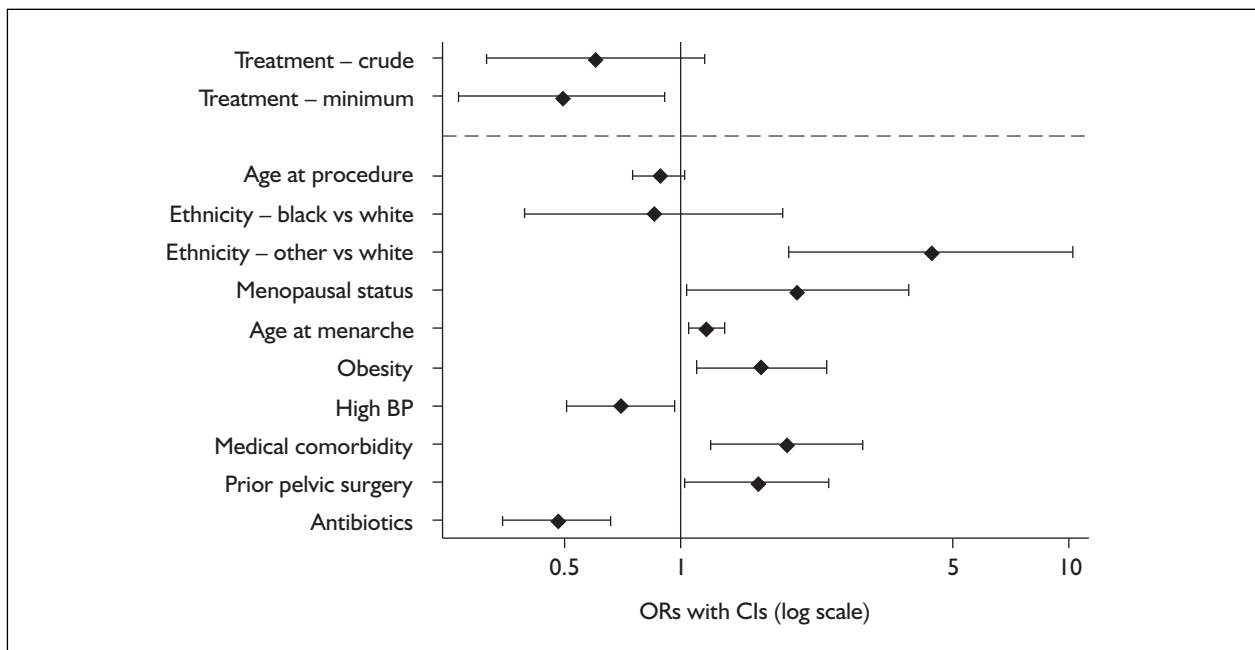
The ORs derived from logistic regression for the effect of treatment on the primary outcome, after using multiple imputation methods for estimating missing values, are presented in *Table 19* together with 95% CIs both with and without adjusting for clustering by centre for the three main models: crude (treatment only), full (all confounding variables) and minimum [all significant confounding variables (10% level)].

The crude OR of 0.60 (95% CI 0.32 to 1.15) is not significantly different from 1.0 (treatment cohorts have the same probability of a complication) after adjusting for clustering by centre. However, it has been shown that the confounding variables vary between cohorts. Including all the confounding variables in the model reduces the OR to 0.42 (95% CI 0.23 to 0.78), which reaches significance, even after adjusting for clustering by centre. The OR for the minimum model which incorporates

only those confounding variables which are statistically significant lies between the two at 0.48 (95% CI 0.26 to 0.89). The reason for the non-significance is that they may be associated with the other confounding variables and once these other variables are in the model, they no longer explain any further differences between the treatment cohorts.

*Figure 18* shows the ORs (on a logarithmic scale) for all the confounding variables in the minimum model, together with their 95% CIs after adjusting for clustering by centre. Both the crude and adjusted treatment ORs are also presented (above the dashed line). The coefficients and ORs for the logistic regression models together with their CIs can be found in Appendix 14.

*Figure 18* demonstrates the difference it makes to the treatment effect by including all the significant



**FIGURE 18** Primary outcome [1] – complications versus no complications: ORs (UAE/Hyst) for all variables in minimum model together with the crude treatment effect. Minimum model adjusted for clustering by centre, 1108 patients using imputation.

**TABLE 20** Primary outcome: severe/major complications versus minor/no complications

Primary outcome [2]	Hyst (n = 459)	UAE (n = 649)	Total (n = 1108)	Significance $\chi_{(1)}^2$
Minor/no complications	407 (88.7%)	624 (96.1%)	1031 (93.1%)	$p < 0.0001$
Severe/major complications	52 (11.3%)	25 (3.9%)	77 (6.9%)	
Total	459 (100%)	649 (100%)	1108 (100%)	

(at the 10% level) confounding variables, the adjusted treatment OR being shifted to the left. In addition, it indicates the variables which are important in determining whether a patient may have a complication or not. Being obese, having a later onset of menarche, an existing medical comorbidity or having already undergone prior pelvic surgery all raise the odds of experiencing a complication, whereas using prophylactic antibiotics at the time of the procedure reduces the odds of experiencing a complication. High BP also appears to be slightly protective, although this is unexpected and would need further investigation. The increased risk for the ‘other’ ethnic group may be due to the small number of patients present in the HOPEFUL study and would need to be investigated by further studies.

**Primary outcome [2]: severe/major complications versus minor/no complications**

Primary outcome [2] is created by categorising all patients who had severe and/or major

complications as yes, and all patients with minor or no complications as no. A summary of the numbers of patients in each of these categories is given in *Table 20* by treatment cohort. There is a significant difference in the complication rates for the two treatments.

The ORs derived from logistic regression for the effect of treatment on primary outcome [2], after using multiple imputation methods for estimating missing values, are presented in *Table 21*, together with 95% CIs, both with and without adjusting for clustering by centre for the three main models: crude (treatment only), full [all confounding variables) and minimum [all significant confounding variables (10% level)]. (Note: the minimum model is different for the primary outcome [2] analysis.)

The crude OR for UAE versus hysterectomy for severe/major complications is 0.31 (95% CI 0.15 to 0.66) after adjusting for clustering by centre. Including all the confounding variables in the

**TABLE 21** Primary outcome [2]: severe/major complications versus minor/no complications

Model	OR for treatment UAE vs Hyst	95% CI	95% CI (adjusted for clustering) centre
Crude unadjusted	0.313	0.191 to 0.513	0.148 to 0.663
Minimum model <sup>a,c</sup>	0.250	0.146 to 0.427	0.130 to 0.479
Full model <sup>b,c</sup>	0.207	0.107 to 0.404	0.100 to 0.432

<sup>a</sup> Minimum model: medical co-morbidity, high BP, obesity, antibiotics and age at menarche.  
<sup>b</sup> Full model: Age at operation, medical co-morbidity, gynaecological co-morbidity, prior pelvic surgery, high BP, obesity, parity group, smoking group, education group, ethnic group, antibiotics, fibroid symptoms from questionnaires, fibroid symptoms from clinical forms, menopausal status and age at menarche.  
<sup>c</sup> All models carried out using multiple imputations on missing data values and then combining the results of 5 imputation datasets. Each dataset contains the original dataset plus a set of imputed missing values.

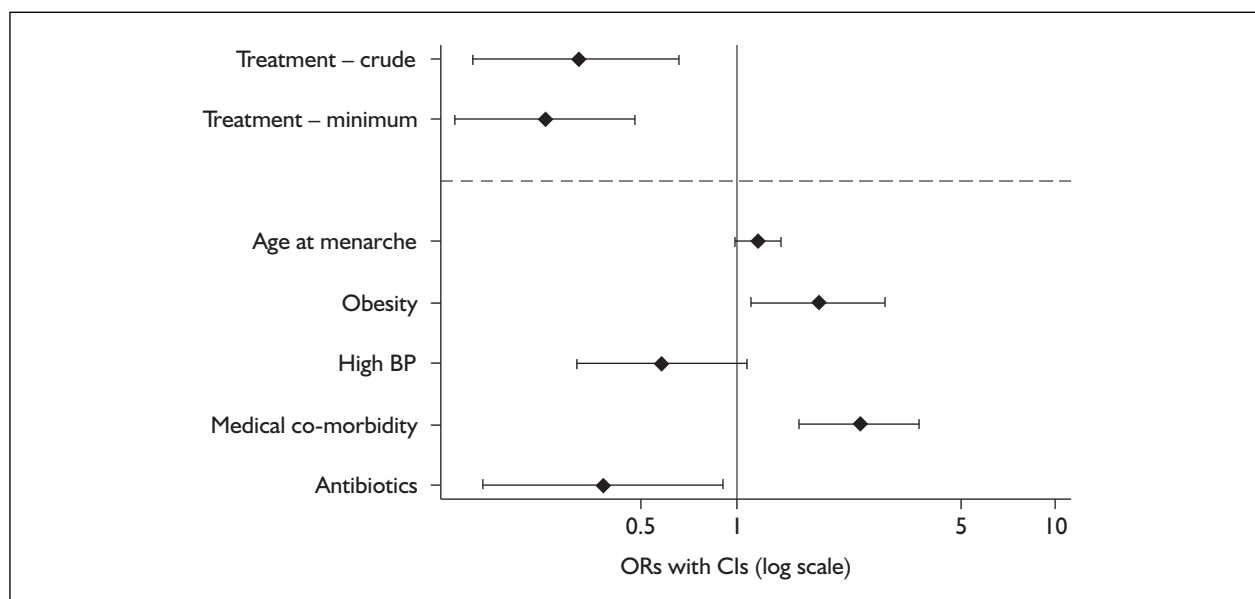
model reduces the odds ratio to 0.21 (95% CI 0.10 to 0.43). The OR for the minimum model which incorporates only those confounding variables which are statistically significant is 0.25 (95% CI 0.13 to 0.48).

The OR for the treatment effect is smaller than for primary outcome [1] analysis, indicating that the extra risk associated with undergoing a hysterectomy is primarily associated with severe and/or major complications. Patients undergoing UAE may still experience complications, but they are more likely to be minor.

Figure 19 shows the ORs for all the confounding variables in the minimum model for primary outcome [2] (severe/major versus minor/none), together with their 95% CIs after adjusting for

clustering by centre (on a logarithmic scale). Both the crude and adjusted treatment ORs are also presented (above the dashed line). The coefficients and ORs for the logistic regression models together with their CIs can be found in Appendix 14.

Figure 19 shows there is some reduction in the treatment effect by including the significant (at 10%) confounding variables, but it is not as great as for the primary outcome [1]. Being obese or having an existing medical co-morbidity raises the odds of experiencing a severe/major complication, whereas using prophylactic antibiotics at the time of the procedure reduces the odds of experiencing a severe/major complication, although this is not as strong as for primary outcome [1]. The increased risk for the ‘other’ ethnic group has all



**FIGURE 19** Primary outcome [2] – severe/major versus minor/no complications: ORs (UAE/Hyst) for all variables in minimum model together with the crude treatment effect. Minimum model adjusted for clustering by centre, 1108 patients using imputation.

but disappeared, possibly due to the smaller numbers of patients in this ethnic group who had complications.

## UAE-only: general side-effects

### General side-effects and complications

Patients in the UAE cohort may have experienced one or more GSEs, including natural fibroid expulsions ( $n = 49$ , 7.6%), chronic discharge ( $n = 82$ , 12.6%), post-embolisation syndrome ( $n = 115$ , 17.7%) or temporary amenorrhoea ( $n = 21$ , 3.2%). Patients were categorised as having either one or more GSEs or no GSEs.

GSEs may follow or precede complications; for example, a chronic discharge may require a fibroid extraction or an infection may precede chronic discharge. Therefore, there is some overlap between complications and GSEs. Of the 114 (17.6%) women who experienced complications in the UAE cohort, 58 (8.9%) also experienced GSEs; 26 (4.0%) of these women had GSEs which were related to their complications and 32 (4.9%) did not. The majority of the related GSE and complications were chronic discharge caused by pelvic infection, chronic discharge leading to fibroid extraction, or both. An additional 154 (23.7%) women experienced GSEs only. In total 268 (41.3%) patients who underwent UAE experienced some adverse effects of the treatment.

Frequency of GSEs, complications and their overlap is shown in *Figure 20*.

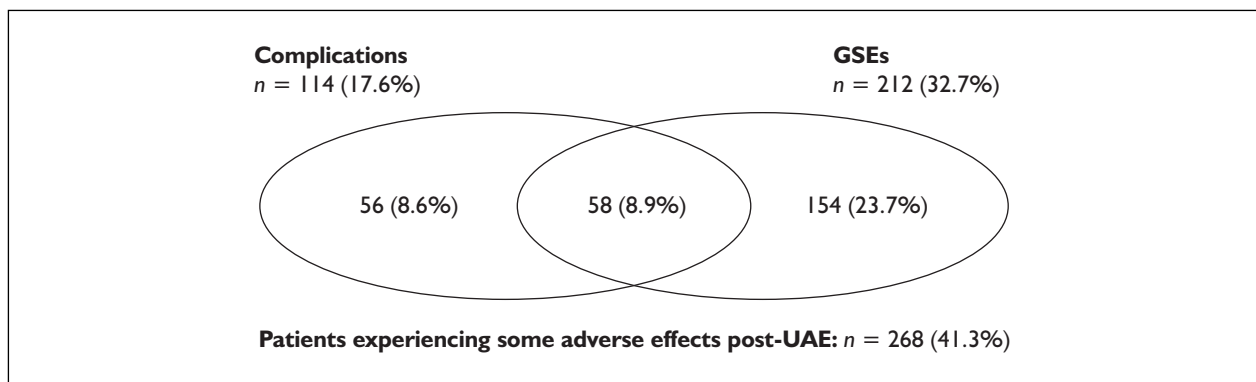
The relationship between GSEs and severity of complication is investigated in *Table 22*. The majority of the GSE/complication overlap appears to be between minor complications and GSEs.

There may have been bias in recording of complications and GSEs between centres with centres which were carrying out their own research into outcomes of UAE recording these more often compared with standard practice. This was investigated by examining complications and GSEs and their overlap by centre (*Table 23*). The centres did vary considerably, implying that reporting of complications and GSEs is not consistent between centres.

### GSEs and confounders

Confounding factors were found to affect complication rates. These were therefore investigated to examine whether they were also confounding factors for GSEs. The confounding variables that were found to be associated with GSEs ( $\chi^2$ ) were complication severity ( $p < 0.0001$ ), medical co-morbidity ( $p = 0.22$ ), ethnicity ( $p = 0.061$ ), parity ( $p = 0.044$ ) and prophylactic antibiotic use ( $p < 0.0001$ ).

In order to investigate the relationship between confounders and GSEs, regardless of whether



**FIGURE 20** Primary outcome – UAE only: summary of complications and GSEs ( $n = 649$ )

**TABLE 22** GSEs and complications

GSEs	Complications					Significance $\chi_{(1)}^2$
	Severe	Major	Minor	None	Total	
GSE	1 (0.5%)	9 (4.2%)	48 (22.6%)	154 (72.6%)	212 (100%)	$p < 0.0001$
No GSE	0 (0%)	15 (3.4%)	41 (9.4%)	381 (87.2%)	437 (100%)	
Total	1 (0.2%)	24 (3.7%)	89 (13.7%)	535 (82.4%)	649 (100%)	

**TABLE 23** Complications and GSEs by centre

Complication/GSE	Number women (%)	Range by centre (%) <sup>a</sup>	Test for heterogeneity ( $\chi^2$ )
All complications	114 (17.6%)	4.6–61.5	$p < 0.0001$
Complications/no GSEs	56 (8.6%)	1.5–46.2	$p < 0.0001$
Complications and GSEs	58 (8.9%)	0, 1.4–20.4	$p < 0.0001$
GSEs/no complications	154 (23.7%)	0, 2.3–57.1	$p < 0.0001$
All GSEs	212 (32.7%)	0, 4.6–76.2	$p < 0.0001$
All adverse events	268 (41.3%)	10.1–79.4	$p < 0.0001$

<sup>a</sup> 10 centres – 1 centre only had 5 patients and 1 complication hence the 0% is for this centre and the range is then given from the next lowest %.

**TABLE 24** GSEs and complications with respect to other confounding variables

Model	OR (95% CI) <sup>d</sup>	
	Minor complication vs no complications	Major complications vs no complications
Crude unadjusted	2.896 (1.442 to 5.816)	1.484 (0.805 to 2.737)
Minimum model <sup>a,c</sup>	2.850 (1.458 to 5.572)	0.997 (0.459 to 2.165)
Full model <sup>b,c</sup>	2.994 (1.536 to 5.834)	0.979 (0.403 to 2.382)

<sup>a</sup> Minimum model: complication severity, ethnicity, parity and prophylactic antibiotics use.  
<sup>b</sup> Full model: age at operation, medical co-morbidity, gynaecological co-morbidity, prior pelvic surgery, high BP, obesity, parity group, smoking group, education group, ethnic group, antibiotics, fibroid symptoms from questionnaires, fibroid symptoms from clinical forms, menopausal status and age at menarche.  
<sup>c</sup> All models carried out using multiple imputations on missing data values and then combining the results of 5 imputation datasets. Each dataset contains the original dataset plus a set of imputed missing values.  
<sup>d</sup> 95% CI adjusted for clustering by centre.

complications occurred, a logistic regression analysis was carried out using the GSE variable described above as the outcome variable and incorporating the severity of complication and the other confounders as covariates. A crude model of GSEs versus no GSEs, a full model and a minimum model as described for the primary outcome analysis were carried out (Table 24). Because severity of complications is a three-category variable (there was only one severe complication so no comparisons can be carried out for severe complications), the logistic regression quotes two ORs comparing separately major complications and minor complications with no complications.

The minor complications more than double the OR of women experiencing GSEs, possibly due to GSEs that are associated with the later onset minor complications such as infections and fibroid extraction. There appears to be no increase in the ORs for those experiencing major complication, probably due to the timing of these major complications, which occur within 6 weeks of the initial UAE procedure.

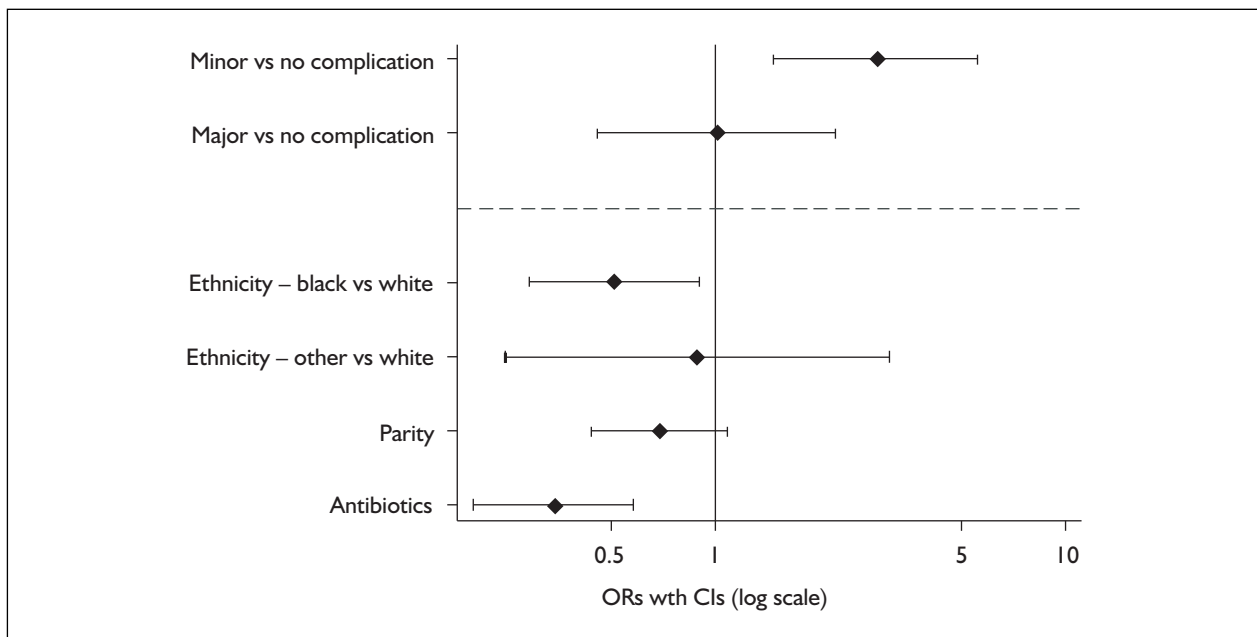
Figure 21 shows the ORs for the confounders in the minimum model.

Figure 21 demonstrates that having a minor complication raises the risk of having a GSE. Being nulliparous or of black/mixed ethnic origins appears to reduce the risk of experiencing a GSE. Prophylactic antibiotics also appear to be protective against GSEs even after taking the complications into account. This is in addition to being protective against complications as previously reported.

## Key findings – primary outcomes (safety)

The crude incidence of *a priori* defined complications (severe, major or minor) was higher for the hysterectomy cohort (26.1 versus 17.6%). The crude incidence of severe/major complications was also higher for the hysterectomy cohort (11.3 versus 3.9%). The OR for all complications for UAE versus hysterectomy was 0.48 (95% CI 0.26 to 0.89) after using multiple logistic regression and





**FIGURE 21** GSEs – GSE versus none: ORs for variables in minimum model, including complication severity. 649 UAE-only cohort using imputation. Minimum model, after adjusting for clustering by centre.

adjusting for significant confounders (at the 10% level), clustering by centre and missing values (by multiple imputation). This was importantly less than the crude OR. The odds for severe or major complications against minor or none was 0.25 (95% CI 0.13 to 0.48), again importantly reduced by adjustment for confounding. The extra risk of complications associated with hysterectomy is primarily associated with severe and/or major complications. Analysis of the actual complications shows that the excess in the hysterectomy group was mainly attributable to an increased incidence of the need for blood transfusion (7.4 versus 0.4%) and structural damage (3.5 versus 0.8%).

Multiple logistic modelling indicated that obesity and medical co-morbidity predisposed to complications in both groups whereas the use of prophylactic antibiotics was protective, especially when analysing all complications. Patients undergoing UAE are more likely to experience minor complications if any.

Expected GSEs of UAE, including chronic although self-limiting discharge, spontaneous

fibroid expulsions and post-embolisation syndrome, were reported by 32.7% of the women, with 8.9% of these also experiencing complications. The majority of the women with complications and related GSEs (4.0% of the total) suffered chronic discharge caused by disintegrating fibroids/infection, chronic discharge leading to assisted fibroid expulsion, or both. In total, 41.3% of the UAE cohort experienced some adverse effects (complications and/or GSEs) of their treatment although most were GSEs that the patients were informed about prior to the procedure. The duration of these adverse effects varied from a matter of a few hours to persisting for several months. Multiple logistic modelling of GSEs for the UAE cohort, adjusting for complications and confounders, found that prophylactic antibiotics were also protective against GSEs, in addition to being protective for both cohorts against complications. GSE reporting varied widely between centres, probably due to some centres undertaking their own research and directly asking women specific questions about GSEs whereas others did not.



## Chapter 6

### Results: secondary outcome measures

#### Comparative efficacy (UAE versus Hyst)

##### General health and change in health: Q22/Q23

The patient questionnaire asked about the woman's general health at the time of her treatment and any change in health since the treatment. It must be noted that the patients in the hysterectomy cohort were slightly older than the UAE group (on average 2.7 years) at the time of their index treatment and with the differential follow-up time this age difference was 7.3 years (95% CI 6.48 to 8.12) at the time of completing their questionnaires. A total of 986 questionnaires were returned in total (Hyst  $n = 397$ , UAE  $n = 589$ ) and these are used as the denominators for percentages in the tables in this chapter.

In the hysterectomy cohort, 87.4% of women reported that their general health was good, very good or excellent at baseline, with only 11.1% reporting fair or poor general health. Similarly in the UAE cohort, 89.0% reported good, very good or excellent general health and only 10.2% reported fair or poor general health. There was no

statistically significant difference between the general health of the two cohorts ( $\chi^2$ ,  $p < 0.625$ ) (Table 25).

At the time of completing the questionnaire, 75.3% of women in the hysterectomy group reported that their health had improved, 15.4% that it had stayed the same and 5.3% that it had worsened since their index treatment. In the UAE cohort, only 65.5% of women reported an improvement in their health, 29.0% reported that their health was unchanged and 3.9% that their health had worsened after their index treatment. Hence although fewer of the UAE cohort reported worsening health, more of them reported no change after the index treatment. This was statistically significant ( $p < 0.0001$ ) (Table 26).

##### Resolution of fibroid and urinary symptoms: Q19/Q25

Symptoms caused by fibroids are categorised into HMB, painful periods and bulk-related symptoms (including urinary symptoms). It would be expected that HMB and painful periods would be eliminated by hysterectomy and bulk-related symptoms would be reduced. However, 11 (2.8%)

TABLE 25 General health at time of index treatment

General health	Hyst ( $n = 397$ )	UAE ( $n = 589$ )	Total ( $n = 986$ )	Significance $\chi_{(4)}^2$
Excellent	47 (11.8%)	110 (18.7%)	157 (15.9%)	$p = 0.625$
Very good	160 (40.3%)	246 (41.8%)	406 (41.2%)	
Good	140 (35.3%)	168 (28.5%)	308 (31.2%)	
Fair	33 (8.3%)	50 (8.5%)	83 (8.4%)	
Poor	11 (2.8%)	10 (1.7%)	21 (2.1%)	
Missing	6 (1.5%)	5 (0.8%)	11 (1.1%)	

TABLE 26 Change in health after index treatment

Change in health	Hyst ( $n = 397$ )	UAE ( $n = 589$ )	Total ( $n = 986$ )	Significance $\chi_{(4)}^2$
Much better	180 (45.3%)	222 (37.7%)	402 (40.8%)	$p < 0.0001$
Better	119 (30.0%)	164 (27.8%)	283 (28.7%)	
About the same	61 (15.4%)	171 (29.0%)	232 (23.5%)	
Worse	16 (4.0%)	14 (2.4%)	30 (3.0%)	
Much worse	5 (1.3%)	9 (1.5%)	14 (1.4%)	
Missing	16 (4.0%)	9 (1.5%)	25 (2.5%)	

of women who received hysterectomy reported their HMB was the same or worse, 10 (2.5%) reported that their painful periods were the same or worse and 14 (3.5%) women reported that their bulk-related symptoms were the same or worse. In the UAE cohort, the equivalent numbers were 67 (11.4%) reporting their HMB was the same or worse, 95 (16.1%) reporting their painful periods were the same or worse and 73 (12.4%) reporting that their bulk-related symptoms were the same or worse. This lack of improvement in fibroid symptoms was significantly worse in the UAE group ( $p < 0.001$ ) and is further considered in the UAE-only cohort analysis of resolution of symptoms and need for further treatment (p. 71) and also in Chapter 9.

Patients were asked about existing urinary symptoms and their improvement or otherwise after treatment. For the hysterectomy cohort, 63 (15.9%) of the women reported worsened diurnal urinary frequency, 69 (17.4%) reported worsened nocturia and 97 (24.4%) reported worsened urinary incontinence. For the UAE cohort, 27 (4.6%) reported worsened diurnal urinary frequency, 26 (4.4%) reported worsened nocturia and 36 (6.1%) reported worsened urinary incontinence. Some women reported worsening urinary symptoms for more than one of these. Overall 123 (26.8%) women in the hysterectomy

cohort and 52 (8.0%) women in the UAE cohort reported one or more worsening urinary symptoms. This deterioration in urinary function was significantly worse in the hysterectomy group ( $p < 0.0001$ ).

### Satisfaction with treatment: Q24

Women were asked several questions relating to their satisfaction with their treatment. It was expected that the hysterectomy cohort would have their symptoms relieved by their treatment; however, only 88.7% reported that their symptoms were better, 80.6% reported that they felt better since their treatment, 86.4% reported that their expectations were fulfilled, 70.3% would have a hysterectomy in the same situation and 70.0% would recommend hysterectomy to a friend. In comparison, in the UAE cohort, 70.8% of the women had their expectations fulfilled (significantly less than in the Hyst cohort,  $p < 0.0001$ ), 80.1% had their symptoms relieved (significantly less than in the Hyst cohort,  $p < 0.0001$ ), 73.7% felt better since their treatment (significantly less than in the Hyst cohort,  $p < 0.0001$ ), 80.3% would have a repeat UAE (not significantly different from the Hyst cohort,  $p = 0.52$ ) and 86.6% would recommend the treatment to a friend (significantly more than for the Hyst cohort,  $p = 0.007$ ); 55.7% of the hysterectomy cohort and 65.9% of the UAE cohort reported experiencing no problems caused

**TABLE 27** Satisfaction with index treatment from questionnaire (Q24)

Satisfaction with index treatment		Hyst (n = 397)	UAE (n = 589)	Total (n = 986)	Significance $\chi_{(1)}^2$ test
Symptoms relieved	Yes	352 (88.7%)	472 (80.1%)	824 (83.6%)	$p < 0.0001$
	No	3 (0.8%)	82 (13.9%)	85 (8.6%)	
	Missing	42 (10.6%)	35 (5.9%)	77 (7.8%)	
Felt better since treatment	Yes	320 (80.6%)	434 (73.7%)	754 (76.5%)	$p < 0.0001$
	No	14 (3.5%)	84 (14.3%)	98 (9.9%)	
	Missing	63 (15.9%)	71 (12.1%)	134 (13.6%)	
Would have repeat treatment for fibroids	Yes	279 (70.3%)	473 (80.3%)	752 (76.3%)	$p = 0.52$
	No	49 (12.3%)	73 (12.4%)	122 (12.4%)	
	Missing	69 (17.4%)	43 (7.3%)	112 (11.4%)	
Recommend to a friend	Yes	278 (70.0%)	510 (86.6%)	788 (79.9%)	$p = 0.007$
	No	47 (11.8%)	48 (8.1%)	95 (9.6%)	
	Missing	72 (18.1%)	31 (5.3%)	103 (10.4%)	
Expectations fulfilled	Yes	343 (86.4%)	417 (70.8%)	760 (77.1%)	$p < 0.0001$
	No	24 (6.0%)	150 (25.5%)	174 (17.6%)	
	Missing	30 (7.6%)	22 (3.7%)	52 (5.3%)	
Reported problems caused by treatment	No	221 (55.7%)	388 (65.9%)	609 (61.8%)	$p = 0.18$
	Yes	72 (18.1%)	100 (17.0%)	172 (17.4%)	
	Missing	104 (26.2%)	101 (17.1%)	205 (20.8%)	

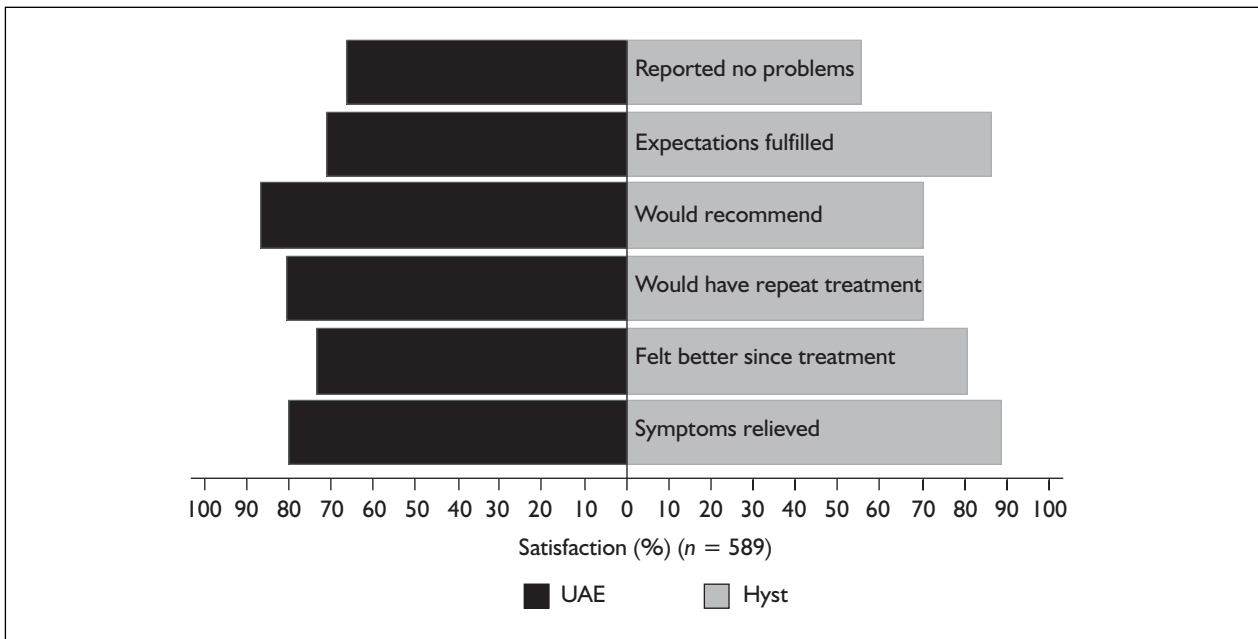


FIGURE 22 Satisfaction with treatment

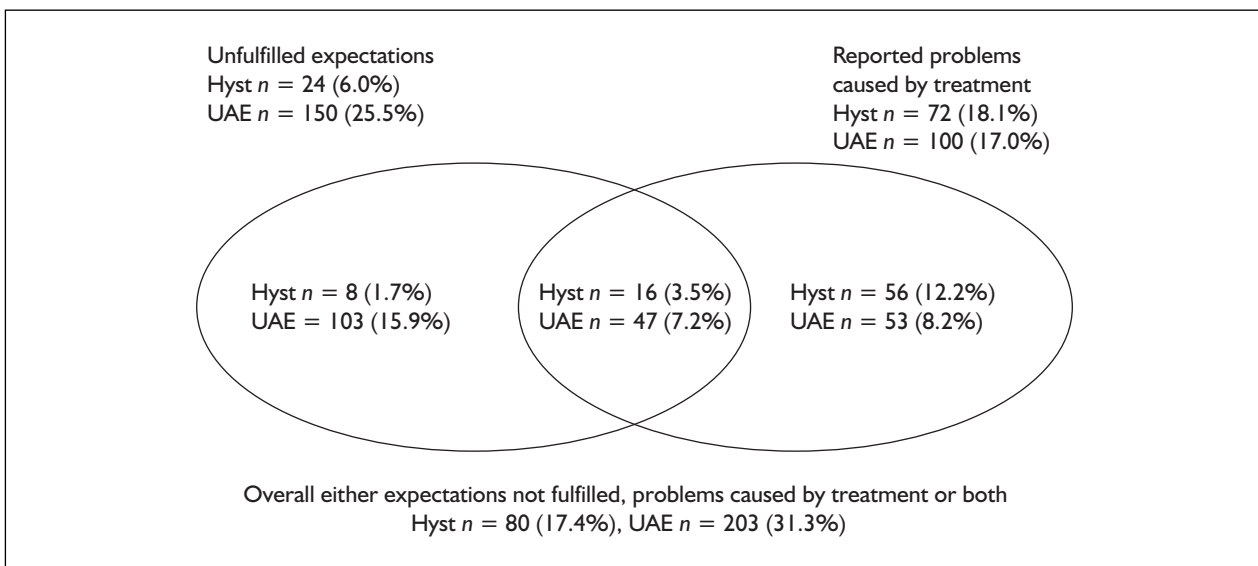


FIGURE 23 Unfulfilled expectations, reported problems caused by treatment and their overlap

by their treatment (not statistically different,  $p = 0.18$ ) (Table 27 and Figure 22).

Some of the women who reported that their expectations were not fulfilled also reported problems caused by their treatment (Figure 23). Some of these problems were due to complications arising from the treatment procedures. For the 283 (25.5%) women [Hyst  $n = 80$  (17.4%), UAE  $n = 203$  (31.3%)] who reported their expectations were not fulfilled and/or they experienced problems caused by their treatment, 76 (6.9%)

[Hyst  $n = 32$  (7.0%), UAE  $n = 44$  (6.8%)] also experienced complications which may have led to their response to this question.

The information presented in Table 27 suggests that respondents' feelings regarding their treatment decisions and their outcomes have several dimensions across which different positive and negative considerations are weighed up, and somehow come together to guide decision-making and to underpin evaluation. It seems contradictory that, whereas 86.6% of UAE but only 70.0% of

hysterectomy respondents ( $p = 0.007$ ) would recommend the treatment to a friend, significantly smaller numbers of UAE than hysterectomy respondents recorded that:

- their symptoms were relieved ( $p < 0.0001$ )
- they had felt better since their treatment ( $p < 0.0001$ ) or that
- their expectations had been fulfilled ( $p < 0.0001$ ).

The free-text responses to Q24(a) and (f), regarding why their expectations had not been fulfilled, and what further problems had been caused by the treatment, were analysed to try to gain some insight into the evaluation processes that respondents had been using.

The free-text responses were analysed as described in Chapter 3. Patient ID numbers have been removed to protect identities when responses of direct quotes are presented. The women's ages at the time of questionnaire completion and the type of treatment they received, hysterectomy (H) or UAE (U) are included after each quotation.

Use of numbers of responses to report this data would be misleading, and there are significant limitations in the free-text dataset because of the lack of specific prompting of responses. However, the strength of this format is that concerns mentioned spontaneously and independently by several people justify analytical attention. A total of 168 respondents wrote a comment in response to Q24(a) and wrote 1915 words in total, which indicates an average of 11 words per respondent; 171 respondents wrote comments in response to Q24(f) and wrote 2812 words in total, which indicates an average of 16 words per respondent.

**Q24(a). My expectations about my treatment have now been fulfilled: yes/no. If no, please tell us why**

There was space for only a short response, and there was no prompting about the kind of response to make. This means that we cannot assume that, because someone has said, for example, "I have since had a hysterectomy" and therefore falls into the 'further treatment needed' category, they might not also, if prompted, have given a long list of continuing symptoms, and fallen as well under the heading 'continue to get the same problems'. Despite this limitation, several clear patterns are evident. A full list of comments is provided in Appendix 16, grouped according to the boxes in this chapter. From the precoded responses we know that a much higher

proportion of the women having a hysterectomy said they had had their expectations fulfilled (86.4%) than did those who had a UAE (70.8%). There were therefore very few free-text comments in response to Q24(a) from the hysterectomy cohort.

Seven responses from the hysterectomy cohort referred specifically to prior expectations. The responses were varied, with no particular pattern. They are therefore listed here in full (*Box 2*).

Responses from the UAE cohort were more numerous and fell into two main groups: the largest being 'specific expectations about the fibroids' and the other main group being 'expectations about symptom relief'. Examples of these two main groups are given in *Boxes 3* and *Box 4*. Some women had very high expectations (*Box 5*). In all cases more examples of similar responses are included in Appendix 16.

**BOX 2 Hysterectomy – expectations prior to procedure**

"Did not expect to still have numbness of the stomach" (H, 43 years)  
 "Not entirely – expected to have flatter abdomen, it remained much the same – also inclined to put on weight" (H, 64 years)  
 "No follow-up treatment offered and did not take HRT – suffer from head hair loss and other male symptoms" (H, 63 years)  
 "Treatment stopped the bleeding, but didn't feel the NEW WOMAN a hysterectomy and HRT was reputed to make me" (H, 64 years)  
 "Did not expect to have hot flushes" (H, 57 years)  
 "I did not have any expectations" (H, 39 years)  
 "I did not expect a prolapse. I did not expect to lose ovaries and Fallopian tubes" (H, 60 years)

**BOX 3 UAE – expectations about fibroids**

"The fibroid only shrank less than 50%" (U, 52 years)  
 "Generally satisfied, but I had hoped the fibroid would shrink more than the 40% it did" (U, 49 years)  
 "My intermural fibroid shrunk only by 23%. Expected as much as 60%" (U, 39 years)

**BOX 4 UAE – expectations about symptom relief**

"Although there has been improvement my uterus is still very bulky" (U, 53 years)  
 "I was hoping my periods would stop all together" (U, 46 years)  
 "Lost less fibroid mass than I had hoped and no effect on bladder, although I admit I was not promised more" (U, 49 years)

**BOX 5** UAE – high levels of expectations

“Would have liked total disappearance, not just shrinkage” (U, 52 years)  
 “I anticipated fibroids shrinking and being absorbed back into body, as explained prior to treatment, This was not the case” (U, 38 years)  
 “Wanted to be completely free of fibroids with fully functioning uterus” (U, 42 years)

**BOX 6** UAE – continue to get the same symptoms

“My periods are still the same, sometimes pain is worse. I wish I had opted for a hysterectomy” (U, 46 years)  
 “I don't think the treatment worked for me. I still have fibroids and the symptoms associated with them” (U, 44 years)  
 “Periods remain heavy and other symptoms unresolved” (U, 48 years)

**BOX 7** UAE – symptoms return after initial improvement

“A year after treatment I had heavier periods. I was alright for 1 year” (U, 56 years)  
 “The fibroids took much longer to shrink than I expected and returned within 18 months of the operation” (U, 39 years)  
 “Fibroids recurred 9–12 months later – until this I was better” (U, 50 years)

Expectations about the likely effectiveness of treatments are formed from a range of source information, both reliable and unreliable. The expectations formed then influence individual decision-making about treatment choices, and attitudes towards coping with treatment and outcome. They influence hope and disappointment.

It is important to reiterate that due to the nature of questions 24(a) and (f), which ask about unfulfilled expectations and problems caused by treatment, mostly negative responses will be elicited. The responses here show a lot of disappointment. Access to and management of expectations in relation to UAE in particular seem to be an area where more attention is needed to ensure that treatment choices are well founded and patients are well informed about realistic possible outcomes.

There was one comment from the hysterectomy cohort regarding continuing to get ‘urine infections and stomach pain and thrush’. Otherwise the comments about continuing with

**BOX 8** Effect of treatment on fertility

“I might have liked to be able to have another child maybe!” (H, 47 years)  
 “Would have liked to have more children” (H, 50 years)  
 “Feel the fibroids still there. Uterus still big and never had any children” (U, 50 years)  
 “I am still childless and have gone through the menopause early” (U, 45 years)  
 “The fibroids did not shrink enough to allow conception” (U, 46 years)  
 “Had undertaken treatment to improve fertility prospects with no success” (U, 47 years)  
 “It created more scar tissue internally than I expected, it reduced my chances of pregnancy more than expected” (U, 46 years)

**BOX 9** UAE – further treatment required, or not worked

“In my case I was unlucky – they grew back and I had to have a hysterectomy” (U, 43 years)  
 “I think I was unlucky. I had it done twice and it didn't work for me” (U, 30 years)  
 “The treatment was successful for approximately 2 years. The symptoms returned and I had a hysterectomy” (U, 40 years)  
 “Fibroids became necrotic, had years of bad infections. Then had to have a hysterectomy” (U, 48 years)  
 “It was unsuccessful for me” (U, 45 years)  
 “I did not experience any benefits” (U, 50 years)  
 “Treatment did not work for me” (U, 55 years)

the same symptoms are all from the UAE cohort (*Box 6*).

Particularly noticeable was the number of people who spontaneously and independently volunteered the information that at first, sometimes for a long while, things seemed to have gone well, until the symptoms started to return. These were all in the UAE group (*Box 7*).

Several people commented on the effect of the treatment on their fertility. Two of these were from the hysterectomy cohort, reflecting continued disappointed feelings many years after the event and the others were from the UAE cohort (see *Box 8* for examples).

A common reason for expectations not being fulfilled was when those having UAE at first ended up having to have further treatment or simply stated that it had not worked (*Box 9*).

The main messages from this analysis of reasons why people felt their expectations had not been fulfilled are:

- Sometimes UAE simply does not work and the same symptoms continue.
- Where UAE does appear to have worked at first, symptoms can come back after months or a year or two and require further treatment.
- People having UAE may end up having a hysterectomy within a year or two.
- People can go into the treatment with very high expectations about the nature of the outcome.
- Expectations about outcome can be expressed in great detail in relation to fibroid size.
- People opting to have UAE may still be very keen to have children.

Several factors act together to make UAE a very different option to hysterectomy. In addition to the basic differences between invasive and non-invasive treatment, and a definite end to reproductive potential and continued potential, there are other differences that may affect patient decision-making. A description of the technical procedure of UAE will include the method by which it works, the predicted effect on the fibroids and the details of expected fibroid shrinkage. This image of steady shrinkage, to which a specific percentage reduction in fibroid size may be added, has a logic and simplicity, creating a neat picture of a procedure offering twin benefits on two enormous issues for women: maintenance of fertility and freedom from menstrual problems, while appearing to work in a progressive and logical manner. The detailed comments about the expected degree of shrinkage present a powerful image that can draw in people's hopes and promote strong and specific expectations about outcomes.

**Question 24(f). I have suffered from problems caused by the treatment: yes/no. If yes, please give details about the problems**

This prompt was followed by three lines on which the women could write about their problems. The full list of comments in response to this question is given in Appendix 16. There was much more of a balance in number of comments from the hysterectomy and the UAE group, reflecting the equal (Hyst 18.1%, UAE 17.0%) proportion of respondents reporting problems in the precoded response.

The descriptions of problems from Q24(f) fell under some of the same headings as the responses to Q24(a), such as expectations. Several UAE respondents mentioned that they expected a shorter and easier recovery period (*Box 10*).

Due to the different natures of the procedures, there are different risks, but women who had

**BOX 10 Longer recovery than expected**

"I was much more ill in the week after treatment than I expected" (U, 48 years)  
 "The protracted period of painful suffering I endured for 2 years after being told that it would last a few weeks" (U, 44 years)  
 "The recovery period was much longer than expected – about 10 weeks" (U, 51 years)

**BOX 11 Damage related to procedure**

"They damaged my kidney during surgery" (H, 44 years)  
 "Emergency return to theatre for suture as artery damaged during procedure, suffered to a certain extent due to the trauma of the operation, although symptoms relieved" (H, 47 years)  
 "Hysterectomy led to 3 further operations in following 5 weeks (one which led to stomach being cut open at right-angles to initial incision for approx. 6 inches and left open for about 2.5 weeks!). I could probably write a book about this" (H, 43 years)  
 "I had problems after my hysterectomy and had further treatment ... to repair my bladder which turned out to be far worse than original surgery" (H, 47 years)  
 "The doctor perforated my bowel. Lungs collapsed, kidneys failed and I went on dialysis. I was in hospital for 3 months" (H, 45 years)  
 "Only initially as I got an infection within a couple of days and had to be re-admitted as blood suddenly started pouring down my legs when I was walking outside" (H, 49 years)  
 "A hernia on operation site. Operated on a year after my hysterectomy, but in last few years has come back again" (H, 51 years)

hysterectomy or UAE both reported damage related to the procedure (*Box 11*). Some women who had hysterectomies experienced accidental damage to other organs during surgery or had complications due to infections, bleeding or hernias at the incision sites some of which required additional hospital treatment (*Box 11*).

Damage to women who had UAE is of a different nature than women who had hysterectomy. Due to the breaking down of the fibroid tissue, continued bleeding, discharge and (at times) infections after UAE treatment are common but vary in severity and need for treatment. In the examples below women report these problems occurring any time from the week following the procedure to 2 years after (*Box 12*).

Women who had UAE also reported problems with pain relief during the procedure, immediately after or ongoing after the procedure. Some thought the pain relief during or immediately



**BOX 12 Discharge and infections post-treatment**

“Initially had pelvic infection which extended recovery period. Probably up to 3 months following treatment before back to good health” (U, 46 years)

“My womb went septic 2 weeks after the UAE. I had to have an emergency hysterectomy done on ... – was on life-support, then intensive care for ...” (U, 39 years)

“Heavy discharge and infection almost continuously for 2 years following treatment (treated by GP only)” (U, 45 years)

“I was bleeding heavily after 1 month of treatment, admitted to hospital. I got infections and I became very anaemic. I had to be given 2 pints of blood” (U, 49 years)

“7 months after treatment fragments of the fibroid became infected. I spent time in hospital having antibiotic treatment” (U, 39 years)

“Big fibroid was killed and became a big problem at home. After operation had problems with stomach, first 12 days didn't function at all, then sent home, 2 days later ended up in emergency where given proper antibiotic” (U, 40 years)

“Septicaemia following procedure, which necessitated 6 nights in hospital for i.v. antibiotics and other treatment” (U, 53 years)

after the procedure was insufficient; while others thought too much morphine was used, causing constipation and extending the recovery period. Others mentioned ongoing pain after the procedure which was thought to be due to the dying fibroids or to nerve damage at the catheter insertion site (*Box 13*).

Since Q24(f) asked about problems caused by the treatment, most responses indicate that new unpleasant symptoms have come. Within this category, many subcategories were created to include comments related to problems with abdomen, adhesions, anaemia, artery, back, bleeding (post-hysterectomy), bloating, cancer, discharge/fibroid changes after UAE, lack of energy, food intolerances, groin/legs, hair growth problems, hernia, infections, menstrual period (post-UAE), mental health/emotions, migraines, mobility/movement, muscle problems, osteoarthritis, ovaries, pain, pelvic, respiratory problems, scar tissue/skin-related, sleep problems, stomach/nausea, uterus/womb, vagina and veins on legs. A complete list of responses about new unpleasant symptoms in these subcategories can be found in Appendix 16. Categories relating to some of the most commonly reported problem areas and symptoms, including bowel, fertility, menopause, sex, urinary and weight gain, are given below.

**BOX 13 Pain relief post-treatment**

“The pain from the embolisation went on for several months ...” (U, 43 years)

“Leg pain high in right leg, a trapped nerve feeling (groin)” (U, 46 years)

“Only issue was during procedure – lots of pain, sedation seemed to wear off during procedure. Very constipated after treatment, caused bad cramps relieved with strong painkillers (morphine), longer in hospital because of this” (U, 32 years)

“Complications after surgery – severe pain with large clots, readmitted to hospital and told by consultant that fibroid was very hot, which was causing pain, could only wait for fibroids to cool and reduce, took months before I could return to work” (U, 49 years)

“No problems caused by treatment but aftercare in hospital was not a good experience – the nurses were neglectful as pain relief did not work” (U, 47 years)

“I lost the use of my left leg for 2 months and suffered unimaginable pain and no one cared” (U, 49 years)

**BOX 14 Bowel problems post-treatment**

“Prolapse of bowel – moves down if constipation have to push back then OK” (H, 37 years)

“IBS causing excessive diarrhoea for 9 years. I was taking HRT. I am now troubled with the opposite way with very occasional diarrhoea but regular constipation and pain” (H, 52 years)

“After op my bowel was twisted and then righted itself, since then I have had bowel problems which I believe MAY be associated with this. I have not sought medical advice about these problems” (H, 48 years)

**BOX 15 Fertility issues**

“Not being able to have more children.” (H, 38 years)

“I have struggled for many years to come to terms with not being able to have children. This has severely affected my mental health at times” (H, 35 years)

“I was unable to conceive and after 2 years suffered degeneration of the ‘dead’ fibroids, leading to a hysterectomy, which revealed advanced endometriosis which had not been previously diagnosed (this could have caused the infertility not the fibroids)” (U, 43 years)

Several comments referred to bowel problems, including prolapse, irritable bowel syndrome (IBS), diarrhoea, constipation, pain, urgency, twisted bowel, bloating and piles (*Box 14*).

Several women made comments citing their fertility problems or their inability to have more children as a major problem caused by the treatment (*Box 15*).

**BOX 16 Early menopause**

“Early menopause – I am now suffering aching joints, premature sexual feelings diminished from onset and ongoing 10 years after treatment” (H, 46 years)  
 “Instant menopause and ‘its’ problems” (H, 47 years)  
 “I became menopausal 2 weeks after surgery” (H, 44 years)  
 “Had accident, major trauma and went into menopause. Medical ... ‘beads’ used in UAE moved, cutting off ovaries – menopause but not immediately” (U, 38 years)  
 “Early menopause?? Periods very light only 4–5 periods in last 3 years” (U, 40 years)

**BOX 17 Menopausal symptoms**

“... hot flushes for 10 years in various cycles and intensity. None during the night” (H, 53 years)  
 “Hot flushes sometimes difficult to cope with especially in summer – still persistent after surgical menopause” (H, 50 years)  
 “Hot sweats all the time” (H, 45 years)  
 “Frequent hot flushes, excessive sweating. Unable to sleep because of the heat my body is generating” (U, 50 years)

Both women who had hysterectomies and women who had UAEs cite an early menopause as a problem caused by their treatment. Their comments seem to indicate that they are troubled by a sudden, early onset of menopausal symptoms following their treatment and the length of time they have to endure these symptoms (*Box 16*).

Many women have difficulty coping with the menopausal symptoms of hot flushes and excessive sweating and report that they are problematic in their daily lives (*Box 17*).

While it is intended to help them cope with difficult menopausal symptoms, some women have difficulty finding the right kind of hormone replacement therapy (HRT) or do not like using it in place of having a natural menopause (*Box 18*).

Prolapse or organs falling out of place, whether vaginal, cervical, bowel or bladder, were reported by women as a problem caused by their treatment (*Box 19*).

Sexual problems, such as vaginal dryness, bleeding, pain, a loss of sensation and decrease in sexual desire or libido, were reported by both groups, women who had hysterectomies and women who had UAE. Some women also reported emotional upset after their procedures regarding

**BOX 18 HRT**

“... HRT helped but never found right one” (H, 34 years)  
 “Finding suitable HRT. Had implant at time of op – that worked well. Patches not very good, tablets better, but I was not really sure they were the right strength – I probably erred on side of caution” (H, 42 years)  
 “Sudden earlier menopause requiring HRT instead of gradual natural one” (H, 46 years)

**BOX 19 Prolapse**

“Recently found that I have a weakness in the vagina (partial prolapse). Pelvic floor exercises have been recommended by consultant” (H, 39 years)  
 “Prolapse on to bladder and bowel” (H, 50 years)  
 “Fibroid not reduced enough. Due to cervical prolapse and difficult position of fibroid – safest option was to have a hysterectomy – sadly” (U, 36 years)

**BOX 20 Sexual problems**

“Problem with sex – not easy, very dry and painful at times” (H, 50 years)  
 “loss of libido, dryness, emotional loss of feeling feminine ...” (H, 43 years)  
 “I have suffered very bad. This has had an effect on my sex life. I am very stressed by this and my body has changed very badly. I was not told about the side effects of the treatment ...” (H, 39 years)  
 “... several episodes of light bleeding on intercourse” (H, 44 years)  
 “Very little muscle control – painful sex (due to infections)” (H, 45 years)  
 “The treatment caused my genitals and vagina to shrink and lose a lot of feeling. This made me feel angry and depressed” (U, 47 years)  
 “Loss of sexual appetite (could be my age of course! – but it was quite noticeable)” (U, 44 years)  
 “Some pain on intercourse, whereas never had any before the UAE” (U, 46 years)

changes to their body image and their feelings of femininity (*Box 20*).

Urinary or bladder problems, such as pain or discomfort, bladder weakness (or stress incontinence), prolapse (or cystocele) and infections (or cystitis) are often cited as a result of the treatment (*Box 21*).

Weight gain was mentioned as a problem caused by treatment 14 times (*Box 22*). Twelve out of 14 of those comments were reported by women who had hysterectomies who have a higher age on average than the UAE cohort. It may be important to note that age may be a contributing factor to this reported weight gain as well.

**BOX 21** *Urinary problems*

“Weakness of bladder, leaking when sneezing, etc. ...” (H, 48 years)  
 “Weaker bladder. Diagnosed with cystocele ...” (U, 33 years)  
 “I have had a few bladder problems since my treatment for fibroids – more prone to cystitis and stress incontinence” (U, 49 years)  
 “Been left with fibroid, giving pain and causing problems to bladder/bowel: no solution has been offered medically” (U, 52 years)

**BOX 22** *Weight gain*

“I have further health problems including weight gain ... eating disorder since 1985 and vitamin deficiency” (H, 51 years)  
 “I still have trouble with my tummy – I don’t have any bleeding, but I do have very bad pains – bloatedness and cannot lose weight easily” (H, 28 years)  
 “I have fibromyalgia and IBS – weight gain (but I can’t say if it’s from the fibroid). Bloating” (H, 44 years)  
 “in the 2 days I was in hospital, my weight increased (and stayed) by 0.5 stone – mainly the top of my legs” (U, 48 years)  
 “I have piles, weight gain and sluggish metabolism” (U, 35 years)

**BOX 23** *Further treatment required*

“At least two minor ops to relieve adhesions ...” (H, 39 years)  
 “Since menopause, continued bleeding and discharge caused by disintegration of fibroids resulting in hysteroscopy in ...” (U, 46 years)  
 “... laparotomy couldn’t remove, embolisation, then myomectomy – stomach lining falling apart, had hernia op, but still have problems now” (U, 29 years)  
 “Fibroids became necrotic, suffered years of infections and subsequently had a hysterectomy. Still suffering recurrent infections ...” (U, 43 years)  
 “... in 2001 developed persistent cough and a nasty vaginal discharge, which antibiotics did not relieve ... identified rotting fibroid, but failed to remove successfully. Developed septicaemia and admitted for 4 days. Fibroid eventually moved out of uterus and was removed by forceps ...” (U, 54 years)  
 “I started bleeding continuously (slightly) and my gynae suggested I have something done as my cells were leaking. Had small op and fine now” (U, 53 years)

Many women, especially those who had UAEs, reported further symptoms, side-effects and the need for further treatment as a major problem for them. The various problems mentioned include adhesions, pain or discomfort, coughing, stomach problems, infections, bleeding, discharge, lack of

**BOX 24** *Post-treatment beliefs and speculations*

“Irregular lower right abdominal pain, at times severe, possible scar tissue, eventually requiring emergency surgery for strangulated inguinal hernia – September 2000 – possible connection?” (H, 56 years)  
 “Not sure if the treatment was the cause of discomfort when bladder was full, and sometimes still get this discomfort – investigated” (H, 54 years)  
 “Unexplained weight gain. Skin irritation, migraines, irritable” (H, 46 years)  
 “Not sure” (U, 44 years)  
 “I feel it was the 2nd angiogram to check my fibroid being fed again by other vessels that caused a little tenderness when lifting ...” (U, 56 years)  
 “It could be a coincidence but I have repeated attacks of vaginal thrush which I never had before the operation” (U, 38 years)  
 “Tired ache in right thigh which radiates into groin after walking. This may or may not be related” (U, 41 years)  
 “I now have non-Hodgkin’s lymphoma as a result of the treatment” (U, 53 years)  
 “Periods have completely stopped – not sure if this is related to UAE” (U, 39 years)  
 “Heavy period and pain on the lower abdomen for no apparent reason (U, 47 years)  
 “I was unwell prior to the treatment and after the treatment I was diagnosed with coeliac disease – I’m not sure whether the total intolerance of gluten was triggered by the treatment” (U, 48 years)  
 “Not sure but may have caused intolerance symptoms to wheat and dairy. Symptoms were discharge after eating (sometimes heavy flow)” (U, 30 years)

fibroid shrinkage and infertility. Women mentioned various treatments for these problems including follow-up consultations, antibiotics, assisted fibroid removal, and (surgical) procedures including laparoscopies, hysteroscopies, myomectomies and hysterectomies (*Box 23*).

Some women are not as certain that the treatment caused the problems they are now having, but they are still trying to resolve some problems or find their causes. Some examples of their post-treatment beliefs and speculations are given in *Box 24*.

As unlikely as it is for women to include positive emotions or comments when they were asked to list problems caused by treatment, it is interesting to note that many women included some sense of positive feeling in their comments in addition to including the negatives of their treatment (*Box 25*).

Q24(a) and (f) asked questions regarding unfulfilled expectations and problems caused by

**BOX 25** *Positive emotions and comments*

“Emotional – but only for a few weeks” (H, 53 years)  
 “Urine problems, not serious” (H, 40 years)  
 “Contracted hospital infection after treatment, now fully recovered” (U, 52 years)  
 “... I did not need a second embolisation as it shrunk within next 2 years as predicted” (U, 56 years)  
 “... I was given the best treatment by staff” (U, 36 years)  
 “Still get pain – but much better. Would still choose over hysterectomy” (U, 36 years)  
 “All short-term and now resolved ...” (U, 44 years)  
 “Caught an infection after treatment – painful, rest at home and prescribed tablets. Better after a few days” (U, 46 years)  
 “I had pain for a number of months after the treatment but I was able to carry on with everyday life” (U, 44 years)  
 “Initially satisfied after UAE in 1995 ... Recovered well” (U, 54 years)  
 “Food intolerances which has now largely resolved itself” (U, 42 years)

treatment, which naturally elicited mostly negative responses. These women may often feel angry and want to place the blame for the problems they have experienced before, during or after their treatment. Some may be more confused and still pondering what went wrong and wanting more information. Many women seem to still be trying to address some of their expectations before and after the procedure and their symptoms years after treatment.

It may be helpful for clinicians to discover if these expectations and beliefs about problems after procedures are due to specific and preventable reasons such as a lack of information, misinformation, preventable bad outcomes of the procedure and unrealistically high expectations. Clinicians may be able to approach patients with more information, correct information, corrections or improvements to the procedures or corrections to patients’ unrealistic expectations as needed.

Some women who had hysterectomies seem to be uninformed about the nature of the procedure and its outcomes at times. There is a tendency for older generations not to question doctors, and this group does have a higher average age than the UAE cohort. Older generations may not easily find information about their procedures because they do not access the Internet as often as younger generations. Alternatively, information on the Internet may not always be accurate or interpreted correctly by those reading it. Women who had UAE may have researched the procedure more, but perhaps formed very specific expectations

based on possible misinterpretations or incorrect information from their sources.

It is also important to consider the differences of patients’ values when addressing expectations. Some women may be glad to have hysterectomies and completely satisfied with not having periods or hormones as before, whereas others will be surprised and disappointed by some of the side-effects of the treatment, such as menopausal symptoms. Others may have emotional difficulty with the loss of their ability to have children or feelings of femininity. Many UAE women want to keep their uterus in the hope of getting pregnant, which may not be a realistic expectation depending on various factors contributing to their fertility. The results of their UAE may vary from the information they have received due to their own individual factors. Therefore, they may be more disappointed than women who have hysterectomy due to the many possible outcomes of the procedure.

Important issues to address with UAE women include pain relief during and after the procedure, expectations about the recovery period, fibroid shrinkage, time-length of symptom relief and effects on fertility. Although patients are informed of the risks of potential damage prior to any surgical procedure, women having UAE may need to be better informed about expecting a discharge and GSEs (such as elevated temperature). They may need more information about the signs of serious infection and when to seek further treatment following their procedure.

It is also a matter of patients’ individual choice regarding how long they will tolerate GSEs and other symptoms before seeking further treatment. Perhaps clinician-created or clinician-approved, printed information about commonly reported problems or symptoms may be helpful for both clinicians and patients. If information is available about the likelihood of these problems being linked to treatment, it could prevent misinformation. Problems or symptoms frequently reported by patients as resulting from their treatments include bowel problems, menopausal symptoms, urinary/bladder problems, sexual problems and weight gain.

## UAE-only efficacy

### Reduction in fibroid and uterine size

There were 593 (91.4%) completed clinical forms in the UAE cohort. Of the 649 women in the UAE cohort, 526 (81.0%) women had at least one

**TABLE 28** Reduction in fibroid and uterine size

Variable	Mean (n) SD	Range
Fibroid volume reduction	47.3% (162) 36.2%	-157.4 to 100
Fibroid maximum diameter reduction	27.5% (189) 26.1%	-29.6 to 100
Uterine volume reduction	42.6% (178) 41.2%	-368.8 to 94.9
Uterine maximum diameter reduction	18.7% (161) 16.0%	-29.4 to 63.7

reported image, 469 (72.2%) had pre-UAE recorded imaging and 377 (58.1%) had recorded imaging at approximately 6 months post-UAE. The number of images per woman varied between none and seven. The majority of the pre-UAE imaging used MRI scanning ( $n = 299$ , 46.1%), with most of the remainder ( $n = 164$ , 25.3%) using US. For the patients with US images, all three fibroid or uterine dimensions were not always recorded. For this reason, in addition to considering fibroid/uterine volume, the maximum dimension of the fibroid/uterus was also considered.

The pre-UAE image was taken on average 3.8 months prior to the procedure, and the 6-month follow-up was on average 5.6 months post-UAE.

On average a 47.3% reduction in fibroid volume and 42.6% reduction in uterine volume were demonstrated at 6 months post-UAE (Table 28). Note that 100% reduction is when the fibroid has been expelled either naturally or with help. Ten of the fibroids increased in volume, including one patient with a leiomyosarcoma, and there was increase in the uterine volume in nine of the women, indicating a growth in fibroid/uterine size.

### Resolution of menstrual symptoms: Q34

Of the 589 UAE women who completed their questionnaires, 582 (98.8%) completed the UAE-specific section of the questionnaire. Responses to Q34 asking about menstrual symptoms after UAE are shown in Figures 24 and 25.

#### Frequency of periods

Fifty-eight women (9.8%) reported that they had no periods at the time of completion of the questionnaire, 133 (22.6%) reported less frequent periods, 346 (58.7%) reported that frequency was unchanged and 26 (4.4%) reported that their periods were more often (4.4% of data were missing).

#### Duration of periods

A total of 283 (48.0%) women reported that their periods lasted for fewer or far fewer days, 176

(29.9%) reported that duration was unchanged and 47 (8.0%) reported that periods now lasted for more or many more days. (14.1% of data were missing).

#### Heaviness of period

A total of 377 (64.0%) of women reported that their periods were lighter or very much lighter, 104 (17.7%) reported that they were unchanged and 27 (4.6%) reported that they were heavier or very much heavier (13.7% of data were missing).

#### Period pain

A total of 279 women (47.4%) reported that their period pains were better after treatment, 191 (32.4%) reported that they were unchanged and 22 (3.7%) reported that the pains were worse after treatment (16.5% of data were missing).

#### Period pain changes

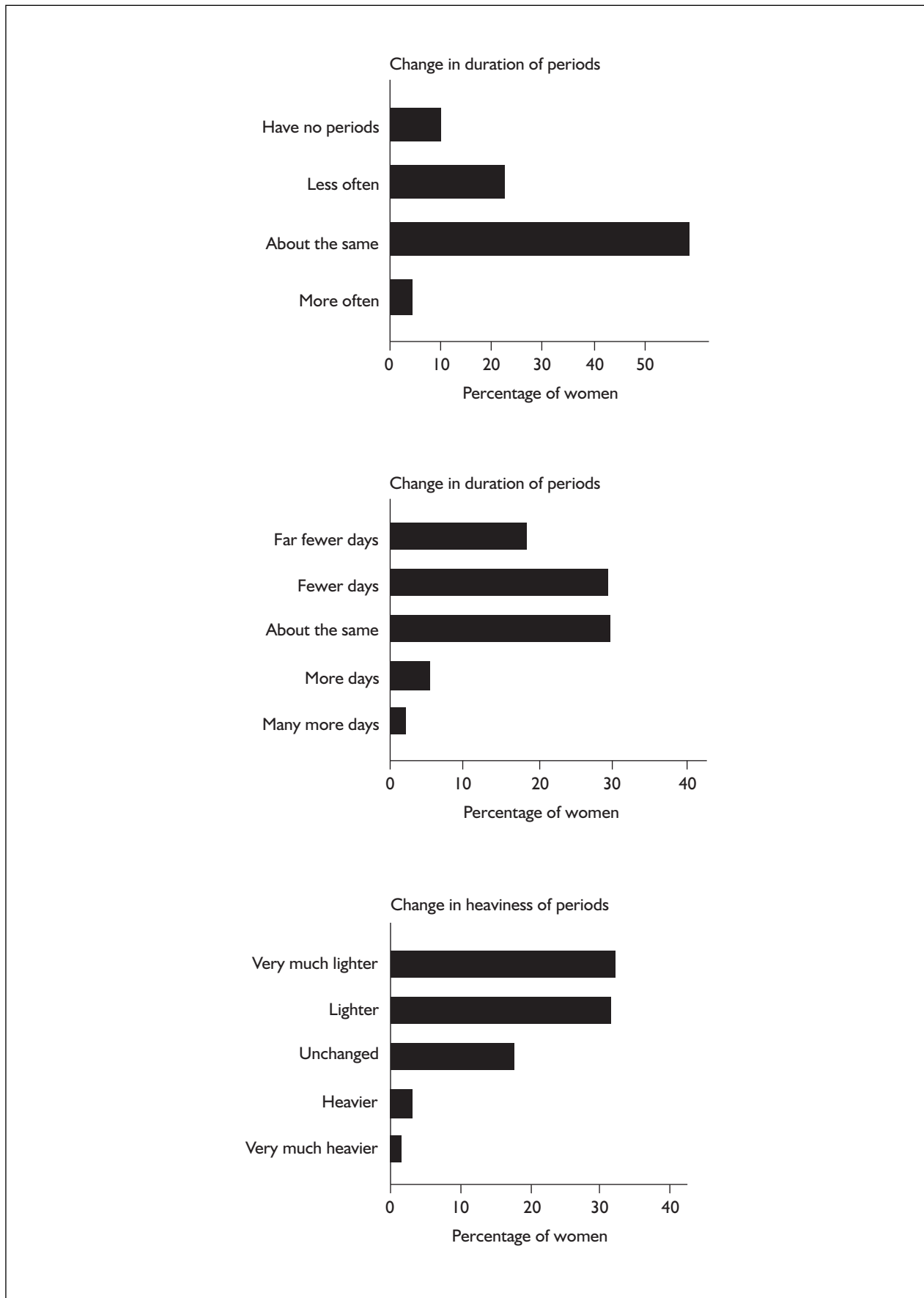
These are relative to experiences before treatment; for those who experienced severe pains before treatment ( $n = 170$ ), 136 (80.0%) reported an improvement, 27 (15.9%) reported no change and six (3.5%) reported they were worse after treatment (0.6% of data was missing).

### Post-UAE further fibroid treatment required

Invasive further fibroid treatment was investigated. Details of the further treatment and the time after the index UAE are presented in Table 29. Reasons given for undergoing further treatment are shown in Table 30.

It was not possible to differentiate between further treatment for unresolved symptoms or re-growth of fibroids due to the retrospective nature of the questionnaires. However, treatment within the first year is likely to be for complications or for unresolved symptoms. Treatment after the first year is more likely to be for recurrence or even new fibroids.

A total of 119 (18.3%) women underwent further treatment for fibroids, 73 (11.2%) underwent a hysterectomy, 32 (4.9%) underwent a myomectomy



**FIGURE 24** Changes in periods since index UAE treatment (n = 589) – UAE cohort only

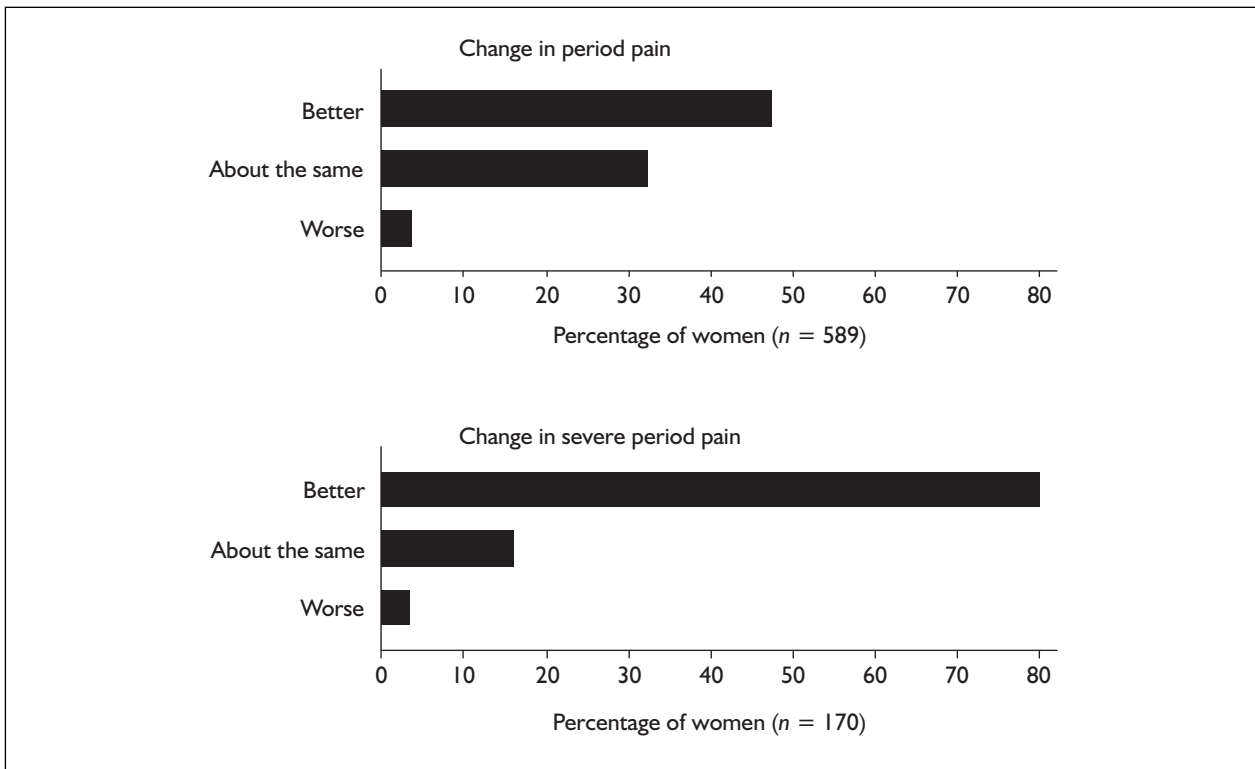


FIGURE 25 Changes in painful periods

TABLE 29 Further fibroid treatment for the UAE cohort by time of treatment

Time of further treatment (years)	Further UAE	Myomectomy	Hysterectomy	Total further treatment	First event <sup>a</sup> (No. of women)
<1	16 (2.5%)	13 (2.0%)	25 (3.9%)	54 (8.3%)	48 (7.4%)
1-2	6 (0.9%)	7 (1.1%)	17 (2.6%)	30 (4.6%)	27 (4.2%)
2-3	3 (0.5%)	2 (0.3%)	17 (2.6%)	22 (3.4%)	19 (2.9%)
3-4	2 (0.3%)	4 (0.6%)	6 (0.9%)	12 (1.8%)	11 (1.7%)
4-5	0	4 (0.6%)	7 (1.1%)	11 (1.7%)	9 (1.4%)
5-6	1 (0.2%)	2 (0.3%)	1 (0.2%)	4 (0.6%)	4 (0.6%)
6-7	1 (0.2%)	0	0	1 (0.2%)	1 (0.2%)
Total	29 (4.5%)	32 (4.9%)	73 (11.2%)	134 (20.6%)	119 (18.3%)

<sup>a</sup> First event = first further treatment required – denominator for percentages = 649.

and 29 (4.5%) a further UAE. Some of these patients received more than one type of further treatment for fibroids (Figure 26). Figure 27 shows the cumulative percentages of the number of women who underwent each of the three main further treatments by time.

In addition, some of the UAE cohort had other types of treatment to deal with continued fibroid symptoms; 16 (2.5%) had further medical treatment including hormonal treatment and iron supplements for anaemia, six (0.9%) underwent a D&C to remove the remnants of disintegrating fibroids, five (0.8%) underwent a transcervical

resection of the endometrium (TCRE) and a further 32 (4.9%) underwent further investigation, mostly hysteroscopy. Note that this may be under-reported.

In order to take into account the differential follow-up of the women in the UAE cohort, a survival analysis was carried out using the date of the first further treatment event as a failure and the date of questionnaire or last clinical follow-up (whichever is latest) as the date for censoring. The probability of needing further treatment was then calculated using life table methods for yearly intervals (Table 31) and a Kaplan–Meier survival curve was produced (Figure 28) The survival curve

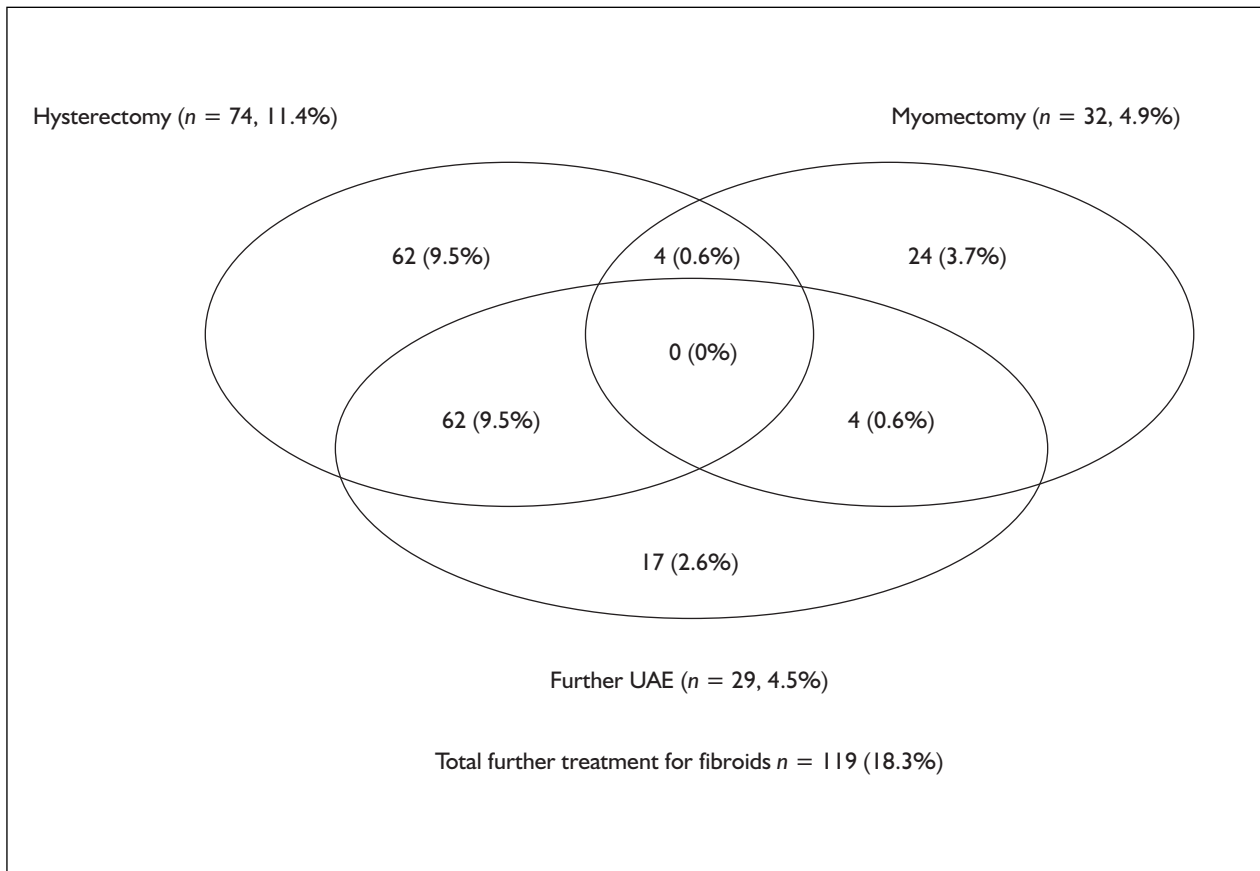


FIGURE 26 Venn diagram to show multiple further treatments post-UAE

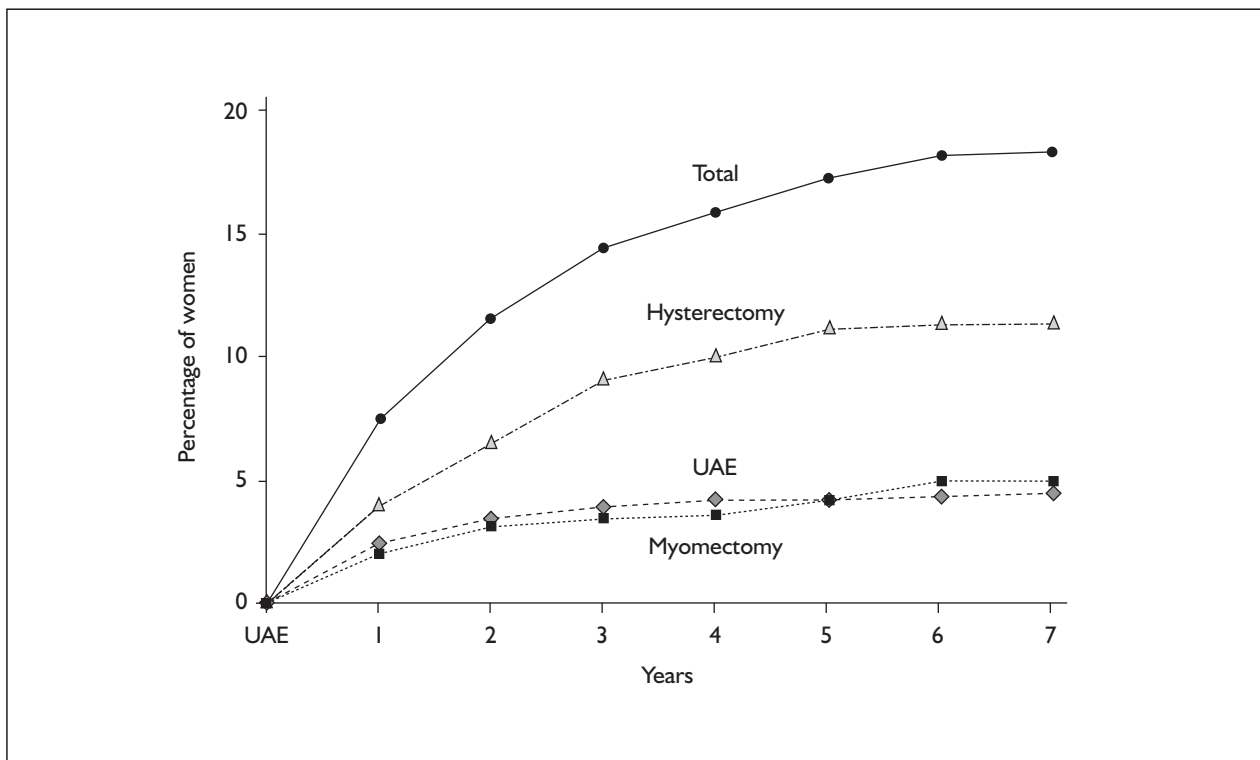


FIGURE 27 Further treatment for fibroids after index UAE: cumulative percentage of women to first further treatment



**TABLE 30** Further fibroid treatment – reasons by time<sup>a</sup>

Time of further treatment (years)	Reason	UAE	Myomectomy	Hysterectomy	Total
< 1	Planned	1 (0.2%)	1 (0.2%)	1 (0.2%)	3 (0.5%)
	Complications	0	6 (0.9%)	7 (1.1%)	13 (2.0%)
	Unresolved/re-growth	13 (2.0%)	3 (0.5%)	17 (2.6%)	33 (5.1%)
	Other/unknown	2 (0.3%)	3 (0.5%)	0	5 (0.8%)
	Total	16 (2.5%)	13 (2.0%)	25 (3.9%)	54 (8.3%)
≥ 1	Planned	0	0	0	0
	Complications	0	2 (0.3%)	0	2 (0.3%)
	Unresolved/re-growth	12 (1.8%)	11 (1.7%)	43 (6.6%)	66 (10.2%)
	Other/unknown	1 (0.2%)	6 (0.9%)	5 (0.8%)	12 (1.8%)
	Total	13 (2.0%)	19 (2.9%)	48 (7.4%)	80 (12.3%)
All	Planned	1 (0.2%)	1 (0.2%)	1 (0.2%)	3 (0.5%)
	Complications	0	8 (1.2%)	7 (1.1%)	15 (2.3%)
	Unresolved/re-growth	25 (3.9%)	14 (2.2%)	60 (9.2%)	99 (15.3%)
	Other/unknown	3 (0.5%)	9 (1.4%)	5 (0.8%)	17 (2.6%)
	Total	29 (4.5%)	32 (4.9%)	73 (11.2%)	134 (20.6%)

<sup>a</sup> Denominator for percentages = 649.

**TABLE 31** Time to first event (further treatment for fibroids – further UAE, myomectomy or hysterectomy)

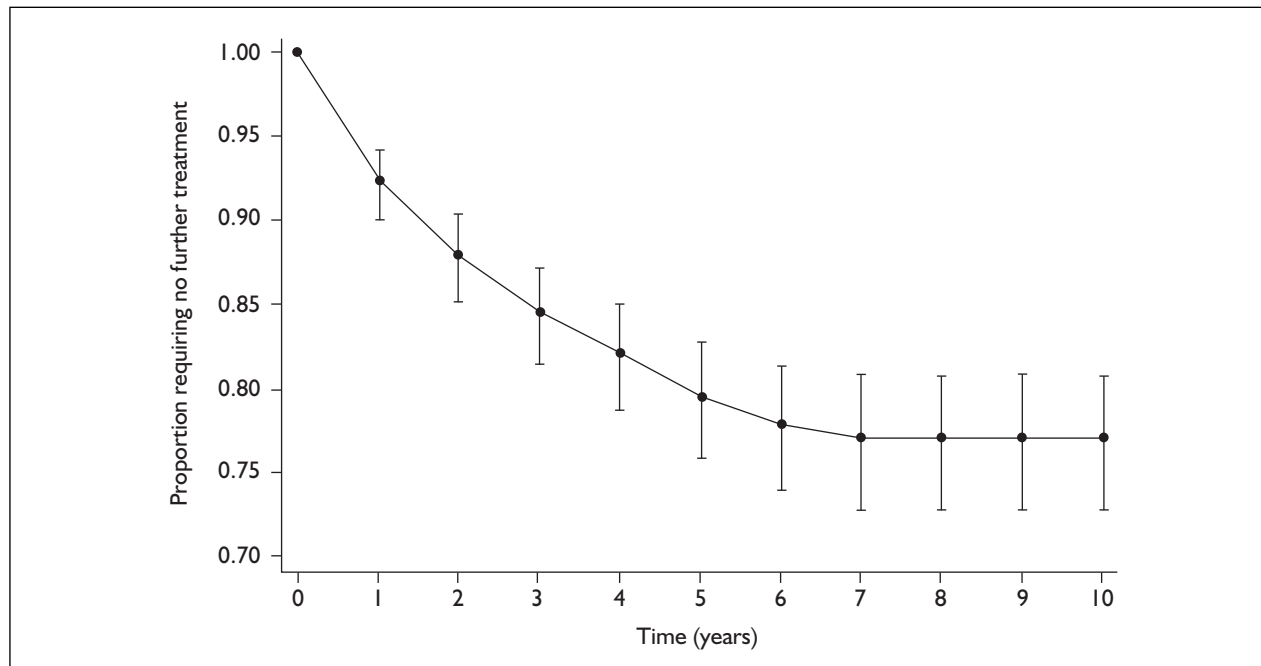
Interval (years)	Total (women at start of interval)	Women requiring further treatment	Women lost to follow-up (censored)	Probability of not needing further treatment (survival)	Error	95% CI
0–1	649	48	27	0.9245	0.0105	0.9010,0.9425
1–2	574	27	18	0.8803	0.0130	0.8522,0.9033
2–3	529	19	82	0.8460	0.0147	0.8147,0.8724
3–4	428	11	96	0.8215	0.0160	0.7877,0.8505
4–5	321	9	66	0.7959	0.0176	0.7587,0.8280
5–6	246	4	100	0.7796	0.0191	0.7395,0.8143
6–7	142	1	84	0.7718	0.0204	0.7288,0.8089
7–8	57	0	47	0.7718	0.0204	0.7288,0.8089
8–9	10	0	9	0.7718	0.0204	0.7288,0.8089
9–10	1	0	1	0.7718	0.0204	0.7288,0.8089

is essentially the inverse of the cumulative percentage to first event (labelled total), but taking into account the numbers of women at each follow-up point. The probability of not needing further treatment within 10 years is 0.772, i.e. the probability of requiring further treatment within 10 years is 0.228.

### Key findings – secondary outcomes (efficacy)

Secondary outcomes concerning efficacy were available retrospectively from patient

questionnaires. The general health of both cohorts was similar at baseline. Of those women completing questionnaires, 75% of the hysterectomy cohort reported improved health status (average 9 years post-surgery) compared with 65% of the UAE cohort (average 5 years) ( $p < 0.0001$ ). Relief of fibroid symptoms (89 versus 80%,  $p < 0.0001$ ) and feeling better since their index treatment (81 versus 74%,  $p < 0.0001$ ) was also significantly higher for the hysterectomy cohort than the UAE cohort. However, only 70% of the hysterectomy cohort would recommend their treatment to a friend compared with 86% of the UAE cohort ( $p = 0.007$ ).



**FIGURE 28** Survival graph for probability of no further treatment required

The expectations of the UAE cohort were less likely to be fulfilled (71 versus 86%,  $p < 0.0001$ ), possibly due to the high expectations of women in the UAE cohort. There was no difference between the cohorts for reported problems (17% Hyst versus 18% UAE,  $p = 0.18$ ). From the free-text analysis of expectations not fulfilled, it is apparent that the management of expectations is particularly important for the UAE cohort. Many of the women are self-referred and have high, maybe unrealistic, expectations, some choosing UAE in the hopes of achieving pregnancy.

Hysterectomy removes the uterus, thus completely solving the fibroid-related symptoms. UAE may either technically fail, completely or partially resolve the symptoms, or may only resolve them initially, with a possible recurrence of symptoms. Of the UAE cohort, 18.3% underwent one or more further fibroid treatments [defined here as further UAE (4.5%), myomectomy (4.9%) and hysterectomy (11.2%)]. After adjusting for differential time of follow-up using survival analysis of first further treatment, the UAE women had a 23% (95% CI 19 to 27%) chance of requiring further treatment for fibroids.

# Chapter 7

## Results: UAE-specific topics

### Factors influencing choice of treatment (Q21)

During 1994–5 when the hysterectomy group were treated, women were not often offered a choice because UAE was not available. Thus only patients in the UAE cohort answered Q21 about factors influencing their choice of treatment. There were 529 responses from the 589 questionnaires (89.8% response rate). These responses were in free text and have been categorised using the free-text data analysis method described in Chapter 3. The main themes were no response/no choice, a wish to avoid hysterectomy, a shorter recovery time/time in hospital, fertility issues, researching for alternative treatments to hysterectomy and then requesting UAE, and other unrelated issues. The factors most frequently mentioned by women influencing their choice of UAE to treat fibroid

symptoms were shorter recovery time/less time in hospital, not wanting a hysterectomy, not wanting major surgery, wishing for a less invasive treatment, wishing for a chance to have children and wanting to keep their womb/other organs (*Figure 29*).

### Predictors of outcome

Possible predictors of treatment outcomes were investigated with regard to complications, GSEs of treatment and requirement for further treatment.

### Operator experience

Operator experience and its effect on outcome were investigated by (1) comparing the first 10 cases in each centre with the rest and (2) by splitting the patients in each centre into equal

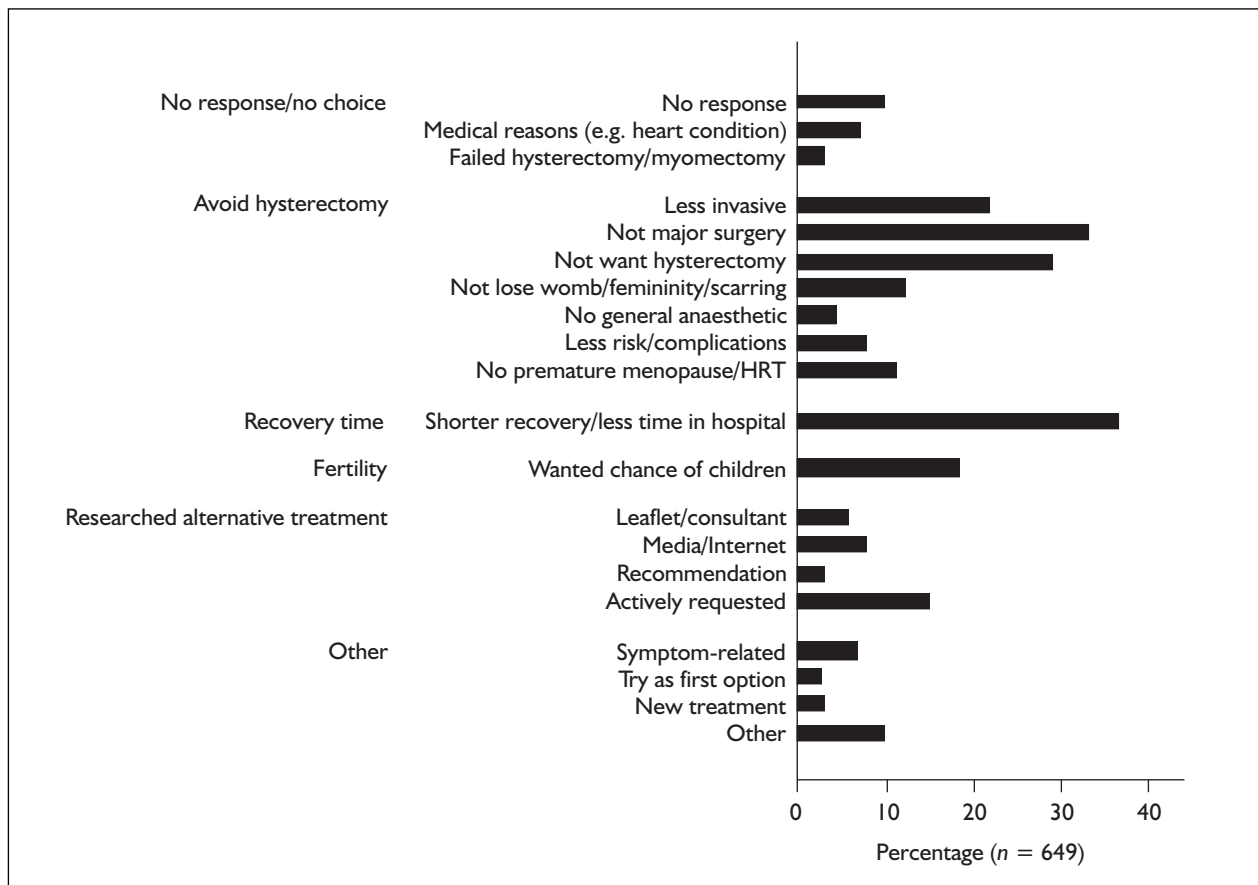


FIGURE 29 Factors influencing choice of UAE treatment (free-text categorised)

**TABLE 32** Effect of operator experience on outcome – early (first 10) versus late

Outcome		Early (≤10 in each centre) (n = 95)	Late (>10 in each centre) (n = 554)	Significance $\chi_{(1)}^2$	OR (late/early) (95% CI)
Primary outcome [1]	Complications	19 (20.0%)	95 (17.1%)	$p = 0.500$	0.828 (0.478 to 1.435)
	No complications	76 (80.0%)	459 (82.9%)		
GSEs with/without complications	GSE	36 (37.9%)	176 (31.8%)	$p = 0.240$	0.763 (0.485 to 1.199)
	No GSE	59 (62.1%)	378 (68.2%)		
Further treatment	Further treatment	24 (25.3%)	95 (17.1%)	$p = 0.059$	0.612 (0.366 to 1.024)
	No further treatment	71 (74.7%)	459 (82.9%)		

**TABLE 33** Effect of operator experience on outcome – tertiles

Outcome		1st tertile (n = 214)	2nd tertile (n = 216)	3rd tertile (n = 219)	Significance (all same) $\chi_{(2)}^2$	Trend (score test)
Primary outcome [1]	Complications	43 (20.1%)	37 (17.1%)	34 (15.5%)	$p = 0.449$	$p = 0.213$
	No complications	171 (79.9%)	179 (82.9%)	185 (84.5%)		
GSEs with/without complications	GSE	77 (36.0%)	71 (32.9%)	64 (29.2%)	$p = 0.324$	$p = 0.134$
	No GSE	137 (64.0%)	145 (67.1%)	155 (70.8%)		
Further treatment	Further treatment	46 (21.5%)	37 (17.1%)	36 (16.4%)	$p = 0.339$	$p = 0.176$
	No further treatment	168 (78.5%)	179 (82.9%)	183 (83.6%)		

**TABLE 34** Effect of location of indicator fibroid on outcome

Outcome		Submucosal [n = 46 (20.5%)]	Intramural [n = 136 (60.7%)]	Subserosal [n = 33 (14.7%)]	Pedunculated [n = 9 (4.0%)]	Significance $\chi_{(3)}^2$
Primary outcome [1]	Complications	7 (12.1%)	40 (67.0%)	10 (17.2%)	1 (1.7%)	$p = 0.174$
	No complications	39 (23.5%)	96 (57.8%)	23 (13.9%)	8 (4.8%)	
GSEs with/without complications	GSE	14 (16.3%)	57 (66.3%)	13 (15.1%)	2 (2.3%)	$p = 0.399$
	No GSE	32 (23.2%)	79 (57.2%)	20 (14.5%)	7 (5.1%)	
Further Treatment	Further treatment	10 (21.7%)	27 (58.7%)	7 (15.2%)	2 (4.3%)	$p = 0.991$
	No further treatment	36 (20.2%)	109 (61.2%)	26 (14.6%)	7 (3.9%)	

tertiles in order to look for a trend over time. No centres were excluded. These groups are compared for complications, GSEs with/without complications and further treatment required after UAE using  $\chi^2$  and trend analysis. In general the more experience the operator had the less likely (smaller ORs) it was that there were complications ( $p = 0.50$ ), GSEs ( $p = 0.24$ ) or further treatment ( $p = 0.06$ ) (Table 32).

There is a general trend for fewer complications, GSEs and further treatment required over time,

although none of these reaches statistical significance (Table 33).

### Fibroid location

Location of the indicator fibroid was investigated in order to investigate any effect of fibroid type on complications, GSEs or further treatment post-UAE (Table 34). Most of the reported fibroids were intramural. These had a slightly higher chance of complications and GSEs, but not further treatment, although none of the effects reached significance.

## Post-UAE fertility

Since their UAE treatment there were 37 pregnancies reported by 27 women, 18 reported on both questionnaire and clinical forms, 14 reported by questionnaire only and four reported by clinical forms only (these four women had not returned their questionnaires).

Thus 4.2% of women in the UAE cohort or 4.8% of 'fertile' women (those who had not experienced the menopause or had not been sterilised) achieved pregnancies. A breakdown of the baseline characteristics and stated aspirations in relation to pregnancy events post-UAE is shown in *Table 35*. The average age of the 27 women who achieved pregnancies was 37.6 years (SD = 3.3), 21 (77.8%) women were nulliparous, the mean time to the first pregnancy event post-UAE was

3 years (SD = 1.8) and 20 (74.1%) had expressed a wish to have any/more children.

There were 19 successful live-births in 16 (2.3%) of the women, no still births, 15 miscarriages in 13 of the women (one woman had two live-births and two miscarriages), two ectopic pregnancies and one termination. Twenty of the patients had only one pregnancy (10 resulted in live-births), five had two pregnancies and one each had three and four pregnancies.

Fifteen of the 19 live-births were delivered by Caesarean section, six being due to complications of pregnancy or delivery: placenta previa grade 4; adhesions resulting from a previous myomectomy; baby not engaged due to fibroid; reduced fetal movements; premature rupture of membranes and pre-eclampsia.

**TABLE 35** Breakdown of the baseline characteristics and stated aspirations in relation to pregnancy events post-UAE. Summary: age at first pregnancy post-UAE = 37.6 years (SD = 3.3), 77.8% nulliparous, 74.1% hoped to have any/more children

Patient <sup>a</sup>	Date UAE	Age (years)	Parity	Fertility <sup>b</sup>	Event <sup>c</sup> 1	Event <sup>c</sup> 2	Event <sup>c</sup> 3	Event <sup>c</sup> 4
1	1999	36	0	Unk	Ectopic (early) 2001			
2	1999	39	0	Yes	Misc			
3	2000	33	1	Yes	Misc (20) 2000	Live (N) 2002		
4	2000	41	1	Yes	Misc			
5	1998	36	0	Yes	Live (C/S)			
6	1999	35	0	Yes	Misc			
7	1997	38	0	Yes	Live (C/S) 1999			
8	1999	35	0	Unk	Live (C/S) (35) 2001			
9	2000	35	1	Unk	Live (C/S) (37) 2004			
10	2001	34	0	Yes	Misc			
11	1999	37	1	Yes	Misc			
12	1998	40	1	Yes	Misc (9)	Live (C/S) 2000		
13	1998	32	0	Yes	Live (C/S) (39) 2000			
14	1999	34	0	Yes	Live (C/S) 2005			
15	1998	35	0	No	Live (C/S) 2000	Live (C/S) 2004		
16	2000	43	0	Yes	Misc (10)			
17	1999	34	1	Yes	Live (C/S) (39) 2000			
18	1999	46	0	Yes	TOP 2001			
19	2002	43	0	No	Live (C/S) (38) 2003			
20	1999	29	0	Yes	Live (C/S) (40) 2000			
21	2000	38	0	Yes	Misc (6)			
22	1997	34	0	Unk	Live (N) (41) 2001			
23	1998	28	0	Other	Live (C/S) (42) 2001	Live (N) 2004		
24	1998	30	0	Yes	Live (C/S) (38) 2001	Misc (8) 2005		
25	1997	40	0	Other	Misc (5)			
26	1998	32	0	Yes	Ectopic (6) 2001	Misc (5) 2002	Misc (6) 2003	
27	1998	35	0	Yes	Live (C/S) (38) 2000	Misc (12) 2001	Misc (11) 2001	Live (N) (40) 2002

<sup>a</sup> Patient IDs have been replaced to preserve anonymity.

<sup>b</sup> Fertility aspirations: Yes = hoped to have any/more children; No = did not want any/more children; Other = not sure; Unk = no questionnaire or not filled in.

<sup>c</sup> Event: Misc, miscarriage; TOP, termination of pregnancy; birth type (if live: type of delivery – C/S = Caesarean section, N = natural) (number of weeks gestation) year of birth.

Fertility issues were also raised in the free-text comments section at the end of the questionnaire and these are reported in Chapter 9.

### **Key findings – UAE cohort only**

The main factor influencing choice of UAE was the desire to avoid a hysterectomy. The reasons for this include economic considerations (“can’t afford the time off work post-surgery”), social considerations (some social groups place great emphasis on uterine preservation), preservation of fertility (definitely want a pregnancy or wish to keep options open) and the desire for a less invasive alternative to avoid the complications of surgery and general anaesthesia. Some women also were aware of others for whom hysterectomy had been unsatisfactory.

Although UAE was a new procedure, and this study sample was taken at the beginning of its use, there was little evidence of a significant learning curve amongst the radiologists involved, all of whom were trained and experienced in procedures requiring similar skills.

There were 27 (4.2%) women who achieved one ( $n = 20$ ) or more ( $n = 7$ ) pregnancies post-UAE. The average age at pregnancy was 38 years (SD 3.3) at an average of 3 years post-UAE; 78% of these women were nulliparous and 74.1% expressed a wish to have any/more children. Of the total 37 pregnancies there were no still births, 15 miscarriages, two ectopic pregnancies, one termination and 19 successful live births [from 16 (2.3%) women], of whom 79% were delivered by Caesarean section, six due to complications of pregnancy or delivery.

# Chapter 8

## Health economics

### Introduction

UAE has been shown to be effective in reducing the size of uterine fibroids and relieving symptoms. However, due to the nature of the procedure, although the uterus is conserved, complete symptom resolution cannot be guaranteed; in some instances, additional procedures may be required due to unresolved or recurrent symptoms. In comparison, hysterectomy is the only procedure that results in complete resolution of symptoms by removing the uterus. In addition to efficacy, the two procedures differ substantially with regard to treatment-associated complications, time to recovery, resource use and QoL. These factors need to be taken into account when making decisions on the choice of treatment.

Compared with hysterectomy, UAE is a less invasive procedure. It is performed under local anaesthetic and, on average, requires an overnight hospital stay and up to 4 weeks of recovery time. However, in some UAE cases technical failure occurs because the uterine arteries could not be catheterised and embolised. In many of these cases a repeat procedure is required, but occasionally technical failure cannot be resolved. This results in unresolved symptomatic fibroids. Post-procedural UAE-specific side-effects such as post-embolisation syndrome, chronic discharge, natural fibroid expulsion and temporary amenorrhoea are common and self-limiting, requiring supportive treatment only. Treatment-related complications of UAE also occur. However, the risk of major or severe complications that may have long-term implications or even be life threatening is low. Hysterectomy is a major surgical procedure and, on average, requires 5 days of hospitalisation and a long recovery time that varies between 4 weeks and several months. In addition, the risk of major or severe complications following such surgical procedures is not insignificant.

UAE has obvious advantages over hysterectomy with regard to reduced hospital stay, lower risk of major or severe treatment-related complications and shorter recovery time. However, UAE does not always result in complete symptom resolution and women who have undergone UAE may experience

unresolved symptoms or recurrence of symptoms over time, requiring additional procedures such as repeat UAE, myomectomy or hysterectomy. It is unclear whether the benefits associated with UAE compared with hysterectomy outweigh the potential complications of these additional procedures.

The aim of this economic analysis was to evaluate the relative cost-effectiveness of UAE and hysterectomy in women with symptomatic uterine fibroids from the perspective of the UK NHS, using epidemiological data on long-term complications and outcomes from the HOPEFUL study cohort.

### Literature review

An extensive literature review was carried out to review the current evidence on the cost-effectiveness of UAE and hysterectomy and to identify all relevant cost and utility data relating to UAE and hysterectomy. Major electronic databases including MEDLINE and BIDS EMBASE were searched using keywords such as uterine fibroids, hysterectomy and embolisation (see Appendix 15 for full listing of keywords). Subsequently, a citation search was carried out on all studies that were found relevant.

### Cost-effectiveness studies

Only three studies were found to evaluate the relative cost-effectiveness of UAE and hysterectomy (see Appendix 15 for a flowchart of the studies considered). The cost and effectiveness of UAE and vaginal hysterectomy were assessed from the perspective of one hospital in France, based on the data from two randomly selected cohorts (UAE  $n = 37$ , Hyst,  $n = 31$ ). Clinical effectiveness was measured as the rate of clinical success, defined as 'significant diminution or disappearance of the clinical symptoms', over a period of 6 months, and direct medical costs including costs of hospitalisation, medication and additional examinations were calculated. Despite a lower clinical success rate (UAE 92%, Hyst 100%), the results showed that UAE was more cost-effective than vaginal hysterectomy (cost-effectiveness ratios were €2300

and €2789, respectively), from the perspective of one hospital.<sup>69</sup>

In a second study, a decision model was developed to evaluate the cost-effectiveness of UAE compared with that of hysterectomy from a societal perspective in the USA. The model was designed to simulate the clinical pathway of a hypothetical cohort of women aged 40 years with a diagnosis of uterine fibroids and no desire for future pregnancy followed up until menopause. Data on QoL were obtained from the literature and expert opinion, and direct medical costs were estimated from Medicare reimbursement data. This study showed that compared with hysterectomy, UAE was the dominant strategy – more effective (8.29 versus 8.18 QoL years) and less costly (US\$6916 versus US\$7847). However, the results were sensitive to increasing procedural costs of UAE, increasing recovery time following UAE and reducing the recovery time following hysterectomy.<sup>70</sup>

Most recently, the cost-effectiveness of UAE was evaluated based on data from an RCT in the UK.<sup>33</sup> At 12 months, the trial reported similar measures of QoL – no significant differences were found in any of the eight components of the SF-36 score in the two arms, but the cost associated with UAE was substantially less than that associated with hysterectomy (difference in mean costs £951; 95% CI £329 to £1480).

### Quality of life

QoL search filters in combination with uterine fibroids, embolisation and hysterectomy yielded 55 studies from MEDLINE, none of which was found to compare the QoL in women following UAE or hysterectomy for uterine fibroids. The QoL following UAE and hysterectomy has been evaluated in separate cohorts, using symptom-specific questionnaires such as the UFS-QOL questionnaire.<sup>71,72</sup> However, these disease-specific measures are not directly transferable to calculating quality-adjusted life-years (QALYs), which require generic preference-based utility measures of QoL; hence these cannot be readily used in economic analysis.

The REST<sup>33</sup> trial is the only study to date that compared QoL using preference-based questionnaires. QoL in women with uterine fibroids was measured, using the SF-36 and EQ-5D at baseline and at 12 months following UAE and hysterectomy. The trial reported substantial improvements in each component of the SF-36 score relative to baseline, but no significant differences were found between the two treatment

arms in any of the eight components of the SF-36 at 12 months.

## Methods

A decision model was developed to estimate costs from the perspective of the UK NHS, and health outcomes in terms of QoL and QALYs associated with UAE and hysterectomy. Based on the data from the HOPEFUL cohort and the literature, costs and outcomes were evaluated over the time horizon from the initial procedure to menopause. In the HOPEFUL cohort, the mean age at initial procedure was 44 years; therefore, the base-case analysis modelled women from the age of 44 years to the menopause, which was assumed to be 55 years.

### Model structure

A probabilistic decision model was developed to simulate the clinical pathways associated with women undergoing UAE and hysterectomy. A two-stage approach was adopted – the first stage of the model represents the clinical pathway in the short term immediately following the initial procedure; the second stage of the model represents the clinical pathway in the longer term, taking into account the probability of symptom recurrence over time. The basic model structure consisted of two arms, replicating the clinical consequences of each strategy (*Figure 30*).

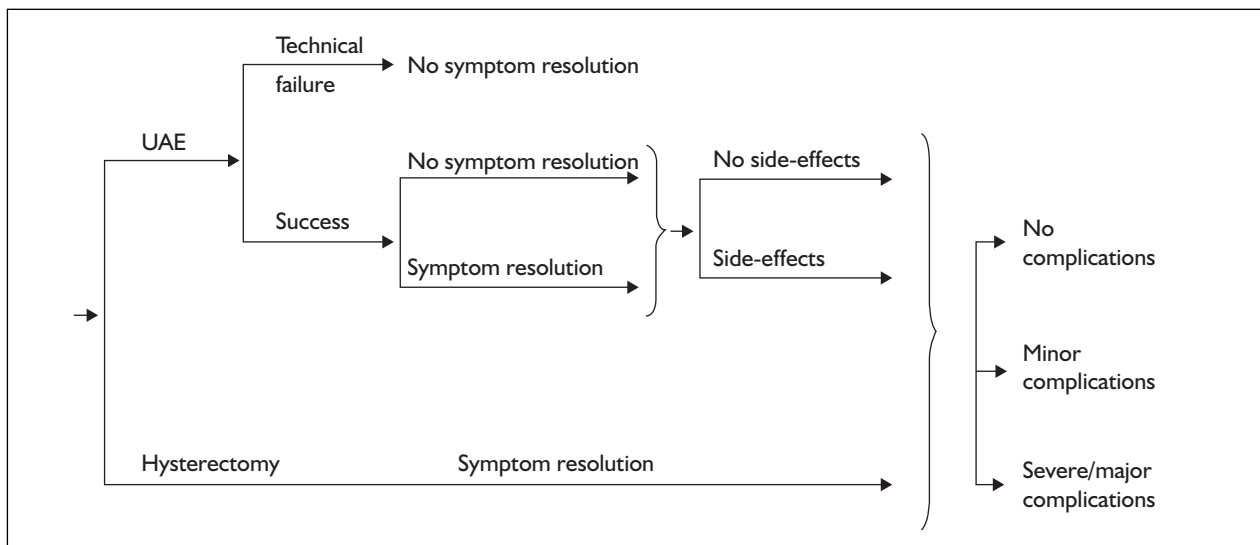
### Technical failure

In the UAE arm, the model took into account the probability of technical failure when the procedure could not be carried out, resulting in unresolved symptoms of uterine fibroids. This may happen when catheterisation and embolisation of the uterine arteries could not be performed. As a result, repeat or additional procedures may be required, which would potentially impact on the overall costs and QoL associated with the choice of a UAE procedure. Technical failure has been documented consistently in observational case series and RCTs.<sup>73–76</sup> It has been suggested that the rate of technical failure was associated with the experience of the radiologist in performing UAE. The inclusion criteria for the UAE arm of the HOPEFUL study required women to have undergone a UAE procedure; therefore, it was not possible to determine the technical failure rate in the HOPEFUL study.

### Symptom resolution

The reported UAE treatment success rate in the literature ranged from 87 to 100%.<sup>77</sup> For the





**FIGURE 30** Stage I – model structure, short term

purpose of modelling, treatment success was defined as the proportion of women in the HOPEFUL cohort who did not experience an additional procedure within the first year of the initial procedure. It was assumed that the majority of women who underwent a successful UAE would result in symptom resolution; however, for the remaining women, symptoms would remain unresolved. Similarly, an unsuccessful UAE procedure due to technical failure would also result in unresolved symptoms at this stage. Subsequently, these women may require additional procedures and would enter Stage II of the model. Following a hysterectomy procedure, it was assumed that all symptoms would be resolved.

### General side-effects

GSEs that are specific to UAE have been well documented, in particular post-embolisation syndrome, which describes flu-like illness, high temperature, high white blood cell count and feeling of general malaise.<sup>77</sup> In addition, other side-effects including chronic discharge, natural fibroid expulsion and temporary amenorrhoea have been recorded in the HOPEFUL cohort (Table 10, p. 37). Generally, these events are self-limiting, require symptomatic treatment only and rarely lead to more serious complications.

### Complications

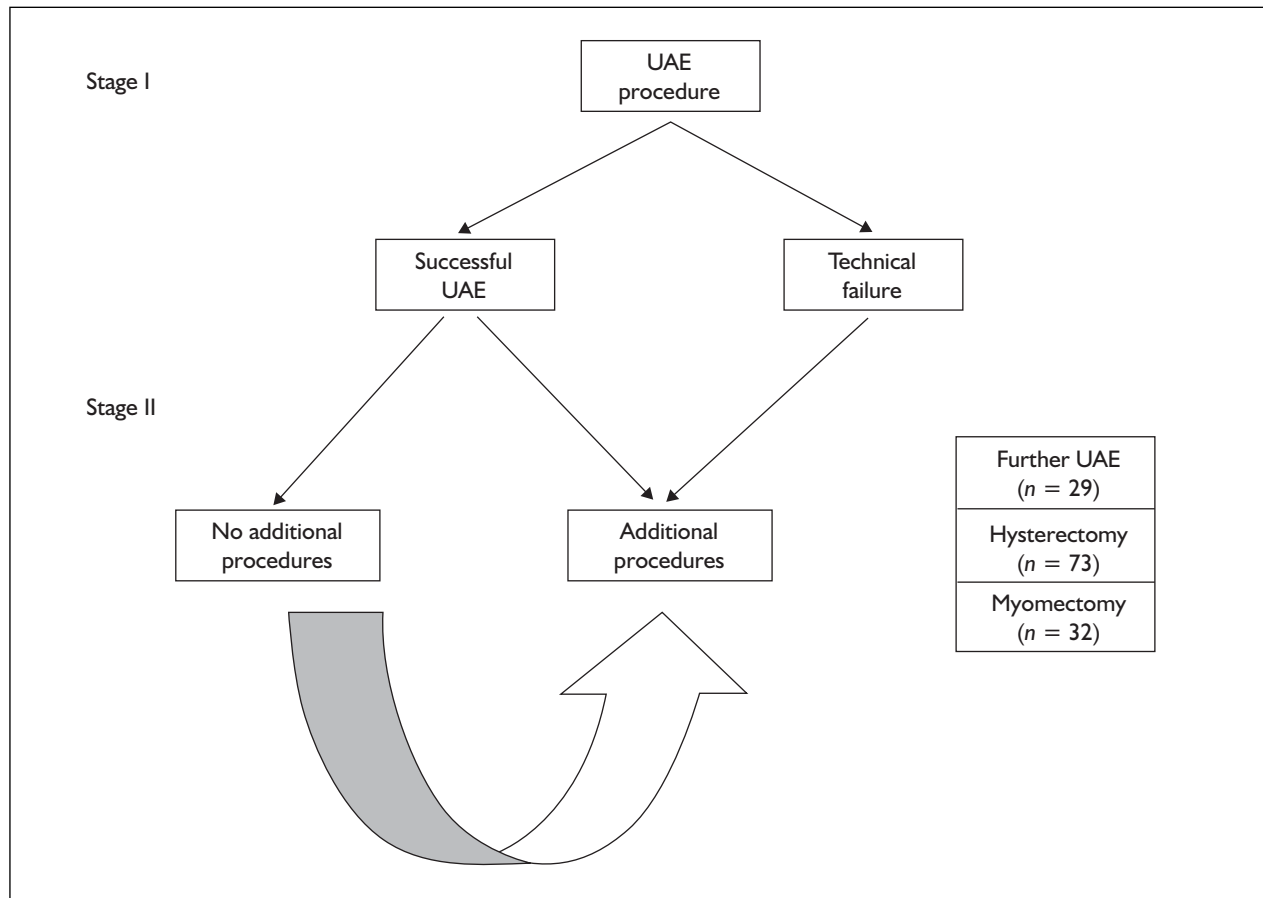
Safety defined by treatment-related complications has been used in several studies<sup>34–36</sup> as the primary study outcome when comparing UAE with hysterectomy. Treatment-related complications were also used as the primary outcome measure of the HOPEFUL cohort. All women who undergo either UAE or hysterectomy may experience

complications. In HOPEFUL these were categorised into (1) minor complications that may require treatment but have no long-term implications, (2) major complications that are not life threatening, may require treatment and may have long-term implications and (3) severe complications that are life-threatening and may have long-term implications (Box 1, p. 34). Few patients in the HOPEFUL cohort reported severe complications; therefore, major and severe complications were aggregated into one arm of the model.

### Additional procedures

The second stage of the model represents the time from the year following the initial procedure until menopause (Figure 31). In each of the subsequent years, women in the UAE arm may fall into one of two possible distinct states:

1. No additional procedures – women in the UAE arm who had their symptoms resolved and required no additional procedures would enter this state. Over time, those who remained free of symptoms and those who developed recurrent symptomatic fibroids, but required no immediate intervention, would remain in this state.
2. Additional procedures – women who did not have their symptoms resolved and required additional procedures would enter this state. Over time, women in the ‘no additional procedures’ state who developed recurrent symptomatic fibroids that resulted in a subsequent intervention such as further UAE, myomectomy or hysterectomy would move into this state and remain in this absorbing state.



**FIGURE 31** Additional procedures

Women who underwent hysterectomy would have their symptoms resolved completely and would not require additional procedures in the years following hysterectomy.

**Parameters of model**

The main data source relating to the key parameters of the model was the HOPEFUL cohort. Other parameters, costs and QoL data that were not recorded in the HOPEFUL cohort were obtained from the literature.

**Probabilities**

The probabilistic parameters for the model are shown in *Table 36*.

**Technical failure**

Technical failure could not be determined in the HOPEFUL cohort and the associated probability was estimated from the literature. The rate of technical failure associated with UAE varied in the literature. In general, observational case studies have reported lower rates of technical failure (0.5% to 2.5%) compared with randomised controlled trial (5.0% to 5.3%).<sup>34–36,73–76</sup> It was assumed that the rate of technical failure reported

in observational studies would be similar to that observed in clinical practice, and the median of the rates reported in observational studies was used in the model.

**General side-effects**

GSEs that were specific to UAE were recorded in the HOPEFUL cohort. The associated probability was estimated from the HOPEFUL minimum regression model on GSEs (*Table 24*, p. 58); the probability of developing UAE-specific GSEs was estimated from the regression equation.

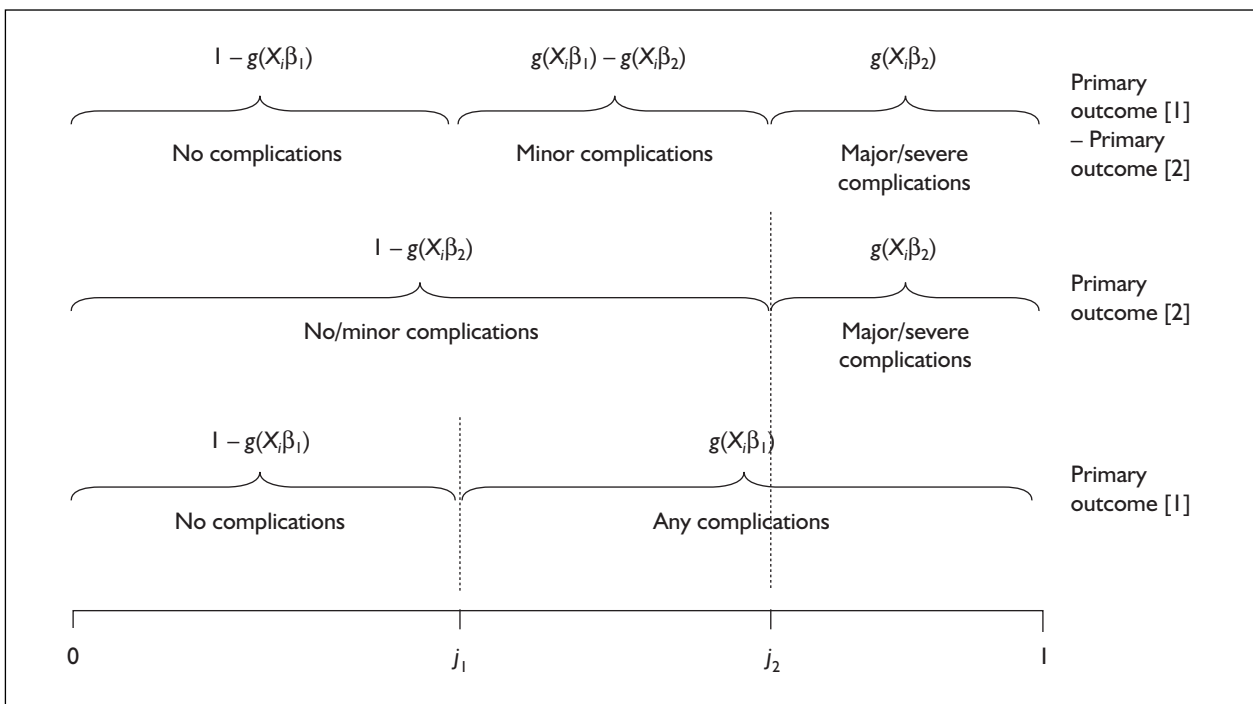
**Complications**

The parameters relating to complications in both the UAE and hysterectomy arms were also estimated from the HOPEFUL cohort (*Tables 19 and 21*, pp. 54 and 56). The probabilities relating to no complications, minor complications and major or severe complications in each intervention arm were estimated from the HOPEFUL minimum regression models on primary outcomes [1] and [2] (*Figure 32*). The minimum regression model on primary outcome [1] estimated the ORs associated with any complications relative to no complications; the probabilities of no complications in both the

**TABLE 36** Estimated probabilities (base-case estimates – age at procedure was 44 years and all other covariates set at their mean values)

Parameter	Description	UAE	Hyst
<i>Stage I</i>			
pFailUAE	Technical failure	0.015 <sup>a</sup>	NA
pGSE	GSEs	0.296 <sup>b</sup>	NA
pNoComp	No procedure-related complications	0.787 <sup>c,d</sup>	0.641 <sup>c,d</sup>
pMinor	Minor procedure-related complications	0.159 <sup>c</sup>	0.172 <sup>c</sup>
pMajorSevere	Major or severe procedure-related complications	0.054 <sup>d</sup>	0.187 <sup>d</sup>
<i>Stage II</i>			
pRecur	Transition probability for additional procedures	0.0384 <sup>e</sup>	NA

Sources:  
<sup>a</sup> Median of rates reported in observational studies.<sup>73–76</sup>  
<sup>b</sup> HOPEFUL data based on minimum regression model for GSEs (Table 24, p. 58).  
<sup>c</sup> HOPEFUL data based on minimum regression model for primary outcome [1] (Table 19, p. 54).  
<sup>d</sup> HOPEFUL data based on minimum regression model for primary outcome [2] (Table 21, p. 56).



**FIGURE 32** Regression models

UAE and hysterectomy arms were subsequently estimated from the regression equation

$$1 - g(X_i, \beta_1)$$

where  $g(X_i, \beta_1)$  is the inverse logistic transformation.

Similarly, the minimum regression model on primary outcome [2] estimated the ORs associated with experiencing major or severe complications

relative to minor and no complications; the probabilities of experiencing major or severe complications were estimated using the regression equation

$$g(x_i, \beta_2)$$

Finally, the probability of experiencing minor complications could be derived by subtraction:

$$g(x_i, \beta_1) - g(x_i, \beta_2)$$

### Additional procedures

In the year following the initial procedure in the UAE arm, women who experienced technical failure and did not receive UAE and women who had UAE but did not result in symptom resolution would receive additional procedures. In subsequent years, the probability of additional procedures was determined by the transition probability, which was estimated from time-to-event analysis.

In the first instance, the data were analysed using the non-parametric Kaplan–Meier analysis. The Kaplan–Meier analysis confirmed the findings of the life-table analysis (*Figure 28*, p. 76).

It was believed that age was predictive of additional procedures; therefore, the risks of additional procedures relative to the age variable and other variables that were found to be predictive of complications from the previous minimum regression models were examined using the Cox proportional hazards model. The Cox model indicated that age at procedure was an important predictor of additional procedures; increasing age was associated with a declining risk of additional procedures (Appendix 15).

In order to extrapolate this hazard beyond the HOPEFUL data to the stage of menopause, parametric models were used to estimate the baseline risk. The Weibull distribution was explored and rejected as the model showed that the hazard of additional procedures did not vary over time (Appendix 15). Subsequently, a parametric model using the exponential distribution for constant transition probabilities was used to fit the data (Appendix 15). The baseline transition probability was estimated using the equation

$$1 - \exp(-\lambda u)$$

where  $u$  is the interval length of the cycle for analysis (1 year).

### Costs

There is limited literature on NHS costs for UAE and treatment of uterine fibroids in the UK to enable estimates of costs to be made. Direct health service costs related to the interventions and complications were included in the model (*Table 37*). All the costs were calculated at 2006 values (UK£).

The costs associated with a UAE procedure had been estimated in a previous study.<sup>33</sup> This was

estimated by applying unit costs to healthcare resource use such as staff time, embolising agent, MRI scan and length of hospital stay. Similarly, the costs associated with a hysterectomy procedure included costs associated with staff time, MRI scan and hospital stay. The cost of complications including pulmonary embolus, thrombosis and septicaemia were obtained from the Department of Health's NHS Reference Costs.<sup>78</sup> No cost data could be found in the literature on complications including organ failure, structural damage caused by treatment, minor infections, haematoma requiring treatment, adverse drug reactions, permanent amenorrhoea, retention of urine requiring catheterisation and fibroid extraction requiring assistance. Therefore, clinical opinions on the average treatment strategy for these complications were used to determine the associated healthcare resource use and the subsequent costs. Some complications such as permanent amenorrhoea and retention of urine did not incur additional interventions, hospital stay or outpatient visits; therefore, no costs were estimated for these complications.

Based on the costs associated with individual complications recorded, average weighted costs were calculated for major or severe complications and minor complications. In addition, a weighted cost of additional procedures was also calculated, taking into account the unit costs of procedures including UAE, hysterectomy and myomectomy, and the relative proportions of women who underwent such additional procedures.

One of the potentially major differences between the two interventions was recovery time. A recent RCT<sup>33</sup> comparing UAE with hysterectomy in the management of symptomatic uterine fibroids reported a significant difference in 'time return to work' between the two arms (20 days in the UAE arm compared with 62 days in the hysterectomy arm).

### Utilities

Utilities are scaled between zero (representing death) and one (representing perfect health), representing an individual's preferences for a given health state. These are generally measured in preference-based health status measurements, which allow individuals to indicate the direction and strength of their preference for a particular health state. For instance, EQ-5D is a commonly used preference-based questionnaire and was used in a recent RCT comparing UAE and hysterectomy.<sup>33</sup> The health states of the women were derived from five dimensions: mobility, self-

TABLE 37 Unit cost data for model input

	Estimated cost (£) <sup>a</sup>	Assumptions and reference source
<b>Procedures</b>		
UAE	1,617	<ul style="list-style-type: none"> <li>• £1.53 per minute of procedure (mean procedural time of 71 minutes)<sup>33</sup></li> <li>• £74 per bottle of embolic agent (4 bottles required)<sup>33</sup></li> <li>• £152 per MRI scan<sup>33</sup></li> <li>• £486 per hospital bed stay per day (2 days)<sup>33</sup></li> </ul>
Hysterectomy	3,003	<ul style="list-style-type: none"> <li>• £3.08 per minute of procedure (mean procedural time of 86 minutes)<sup>33</sup></li> <li>• £152 per MRI scan<sup>33</sup></li> <li>• £486 per hospital bed stay per day (5 days)<sup>33</sup></li> </ul>
Myomectomy	3,003	Assumed to incur the same cost as hysterectomy
<b>Severe complications</b>		
Pulmonary embolus	1,845	NHS Reference Costs 2005 <sup>78</sup>
Organ failure	20,364	£1,378 per ITU bed stay per day <sup>79</sup> (14 days) <sup>b</sup>
Other severe complications	6,475	Weighted average cost associated with severe complications
<b>Major complications</b>		
Permanent amenorrhoea (<40 years)	–	No intervention given <sup>b</sup>
Blood transfusion required	260	<ul style="list-style-type: none"> <li>• £120 per unit of blood (2 units)<sup>c</sup></li> <li>• £20 cross-matching<sup>c</sup></li> </ul>
Structural damage caused by treatment	3,588	£486 per hospital bed stay per day <sup>33</sup> (7 days) <sup>b</sup>
Septicaemia, emergency myomectomy/hysterectomy	3,019	<ul style="list-style-type: none"> <li>• Average treatment cost associated with septicaemia, myomectomy and hysterectomy</li> <li>• £2,966 per case of septicaemia<sup>78</sup></li> </ul>
Thrombosis	921	NHS Reference Costs 2005 <sup>78</sup>
Other major complications	1,783	Weighted average cost associated with major complications
<b>Minor complications</b>		
Minor infections	6	Antibiotics for 14 days <sup>80</sup>
Haematoma requiring treatment	1,538	£486 per hospital bed stay per day <sup>33</sup> (3 days) <sup>b</sup>
Adverse drug reaction	87	£85 per outpatient visit <sup>78</sup>
Permanent amenorrhoea (>40 years)	–	No intervention given <sup>b</sup>
Temporary inability to pass urine	–	No intervention or additional stay required <sup>b</sup>
Fibroid extraction, requiring assistance	1,538	£486 per hospital bed stay per day <sup>33</sup> (3 days) <sup>b</sup>
Other minor complications	419	Weighted average cost associated with minor complications
<b>Average minor complications cost</b>	419	
<b>Average major/severe complications cost</b>	2,073	
<b>Average additional procedure cost</b>	2,703	Weighted average cost of UAE, hysterectomy and myomectomy
<b>Average annual salary</b>	17,549	Annual Survey of Hours and Earnings, Office for National Statistics <sup>81</sup>
ITU, intensive therapy unit.		
<sup>a</sup> Estimated costs are presented in 2006 values, taking into account the appropriate inflation index.		
<sup>b</sup> Average treatment pattern based on expert clinical opinion.		
<sup>c</sup> Clark P, Scottish National Blood Transfusion Services Dundee: personal communication, 2008.		

care, usual activities, pain or discomfort and anxiety or depression based on choices from three levels (no problem, some problem and major problems) per dimension. A tariff derived from the time trade-off technique was then applied to the health states measured by EQ-5D, generating

a utility value. A QALY combines time with utility value in a particular health state.

Since such data were not collected for the HOPEFUL cohort, where possible, QoL effects following treatment and the specific impacts of

**TABLE 38** Quality of life estimates

Parameter	Description	Utilities	Period	Source
<b>Utilities</b>				
uMenorrhagia	Prior to procedure	0.705	1 year	REST <sup>33</sup>
uSuccessUAE	Following UAE procedure	0.825	1 year	REST <sup>33</sup>
uHysterectomy	Following hysterectomy	0.825	1 year	REST <sup>33</sup>
uMyomectomy	Following myomectomy	0.825	1 year	Assumed to equal hysterectomy
<b>Utility decrements</b>				
decAddProced <sup>a</sup>	Additional procedures	0.009	1 year	Based on expert opinion
decMajorSevere	Major or severe complications	0.165	28 days	Based on expert opinion
decMinor	Minor complications	0.083	14 days	Based on expert opinion
decGSE	General side effects	0.041	7 days	Based on expert opinion
decProdU	Loss of productivity in UAE arm	0.041	20 days	Based on expert opinion
decProdH	Loss of productivity in Hyst arm	0.041	62 days	Based on expert opinion

<sup>a</sup> Utility decrement associated with additional procedures took into account the proportion of women who may undergo secondary UAE, myomectomy and hysterectomy; utility decrements related to possible complications, GSEs and utility decrements related to loss of productivity associated with individual procedures.

complications on QoL were obtained from studies of similar patient groups undergoing UAE and hysterectomy in a review of the literature (Table 38).

### Symptom resolution

Utility values associated with menorrhagia prior to interventions and following UAE and hysterectomy were taken from the REST trial. The utility values associated with successful UAE or hysterectomy are greater than that with menorrhagia, indicating an improvement in QoL following symptom resolution.

### General side-effects

Women who experienced GSEs following a UAE procedure would have reduced QoL compared with those who did not experience any side-effects. Utility data relating to GSEs in women who underwent UAE were not available from the literature. Therefore, major assumptions were made on the relative utility decrements over the estimated time required to manage these side-effects. It was assumed that a UAE-specific GSE was associated with a utility decrement of 0.04 from the utility of a successful procedure over a period of 7 days, relative to those who did not experience side-effects following the procedure.

### Complications

Similar to those for GSEs, utility data relating to complications in women following treatment for uterine fibroids were not available from the literature; therefore, major assumptions were made on relative utility decrements over the estimated time required to manage these

complications. It was assumed that utility values associated with successful procedures would also be representative of women who experienced no complications following a procedure. However, it is believed that women who experienced major or severe complications would have a lower QoL than those who were free of complications; therefore, it was assumed that major or severe complications would result in a utility decrement of 0.16 from the utility of a successful procedure over a period of 28 days. Similarly, a utility decrement of 0.08 over a period of 14 days was applied to those who experienced minor complications.

### Additional procedures

It was assumed that the QoL in women who required additional procedures would return to that of menorrhagia; therefore, the utility value for menorrhagia for a period of 1 year was incorporated prior to treatment. Following an additional procedure, women would have a QoL similar to that following a first successful procedure. However, additional procedures would incur a similar risk of treatment-related GSEs and complications. Therefore, a weighed utility decrement based on utility decrements previously estimated to be associated with potential complications (decMajorSevere over 28 days and decMinor over 14 days, Table 38), UAE-specific side-effects (decGSE over 7 days, Table 38), and the relative proportions of women who underwent each additional procedure was applied (Figure 31).

Time to recovery is also an important factor when comparing UAE and hysterectomy, and a

significant difference between the two procedures has been reported.<sup>33</sup> Although not formally recorded in the HOPEFUL cohort, the qualitative analysis gave similar findings. Therefore, utility decrements associated with the reduced health state during the recovery period were also incorporated into the model following each procedure. Data from the REST<sup>33</sup> trial showed that women who underwent UAE were associated with a significantly shorter time to recovery compared with those who underwent hysterectomy (20 days compared with 62 days). Similar to the method applied to utility decrements associated with complications, utility decrements of 0.04 over 20 days and 0.04 over 62 days were applied to the UAE and the hysterectomy group, respectively.

### Cost-effectiveness analysis

The mean costs and QALYs associated with UAE and hysterectomy were calculated for the modelling period. All costs and QALYs were discounted at 3.5%.

Based on the structure of the model, the analysis was carried out in two stages: Stage I represents year one during which the initial UAE or hysterectomy was carried out and Stage II represents subsequent years until menopause is reached, during which additional procedures may be carried out in women in the UAE arm as required.

In Stage I, the cost associated with the UAE and hysterectomy procedures and management of complications, and the QALY associated with the treatment outcomes, taking into account any treatment-related complications, were estimated.

In Stage II, women in the hysterectomy arm were assumed to be completely resolved of all symptoms and no additional procedures would be performed. Therefore, no further costs would be incurred at this stage for the hysterectomy, and the QALY was assumed to remain as that at the end of year one and would be discounted annually until the end of the modelling period. In the UAE arm, symptomatic fibroids may recur and women may be given additional procedures over time. A weighted cost that took into account the probabilities of additional procedures such as further UAE, myomectomy and hysterectomy over time was calculated. In addition, decrements in QALYs – relating to returning to the menorrhagia state due to recurrent symptoms and relating to complications associated with further fibroid treatment in the subsequent years – were also taken into account.

The time-to-event analysis has shown that age at initial procedure is an important predictor of additional procedures in Stage II of the model (Appendix 15). Therefore, results for two age groups were presented – the older women based on the mean age at initial procedure in the HOPEFUL cohort (44 years) and the younger women (age at initial procedure, 35 years).

### Sensitivity analysis

Standard univariate sensitivity analysis was carried out to explore areas of structural uncertainty in the analysis.

#### Conservation of the uterus

One of the key differences between UAE and hysterectomy is that UAE is a uterus-conserving treatment, whereas hysterectomy results in the complete removal of the uterus. Therefore, compared with women who underwent hysterectomy, women who underwent UAE may still be able to experience future pregnancies. Sensitivity analysis was carried out based on the assumption that uterus preservation might be associated with greater QoL compared with those without uterus; estimated utility values of 0.01 and 0.05 were tested in separate analyses.

#### Procedural success

Sensitivity analysis was also carried out to test the scenario when younger women (assumed to be 30 years old) with less severe symptomatic fibroids decide to seek UAE treatment. The benefit of UAE, in terms of improvement of QoL, would be less than that of women with more severe symptoms. The cost-effectiveness of UAE in this group was compared with no active treatment, when women were assumed to be monitored, but received no intervention over time.

#### Costs associated with loss of productivity

Indirect costs associated with loss of productivity were estimated by applying an average wage to the estimated time loss from employment due to both UAE and hysterectomy procedures in the management of uterine fibroids. This approach is termed the human capital approach, and has been commonly adopted to estimate the cost of time loss at employment due to ill health, based on the assumption that the value per unit time lost at employment due to ill health was equivalent to gross earning. Sensitivity analysis was carried out by incorporating the costs associated with loss of productivity during the recovery period following the two procedures.

**Discounting rate**

Following the recommendations from NICE, all costs and QALYs were discounted at 3.5% in the base-case analysis.<sup>82</sup> However, it has been argued that this would give a lower weight to future health effects, and a 1.5% discount rate for health effects should be adopted.<sup>83</sup> Sensitivity analysis was carried out by adopting the alternative discount rate of 1.5% to the QALYs where appropriate.

**Probabilistic analysis**

Probabilistic analysis was undertaken to assess the uncertainty around the point estimates of all model input parameters. Appropriate distributions were assigned to all model parameters.

Probabilities relating to UAE-specific side-effects, complications and the transition probability relating to recurring fibroids were estimated from regression models; therefore, it was assumed that these parameters would fit a normal distribution on the log-odds scale. In order to estimate the uncertainties in these probabilities, the variance of the linear predictor was calculated:

$$\text{var}(LP_0) = X_0^T V X_0$$

where  $X_0$  is the column vector of covariates for a given patient,  $X_0^T$  is the transpose of  $X_0$ , and  $V$  is the variance-covariance matrix of the coefficient parameters. This was applied to a normal distribution with mean equal to the point estimate of the linear predictor. Subsequently, the uncertainties in the probabilities were estimated from the inverse logistic transformation of random draws from this distribution.

The uncertainty around the estimated cost data was also assessed. In the absence of data, it was assumed that the standard error was equal to half of the mean value. The gamma distribution was assigned to the estimated cost data using the methods of moments approach.

The beta distribution was assigned to point estimates of probabilities relating to the probability of technical failure, utility values and utility decrements using the methods of moments approach. Where possible, the standard error was calculated from the data source. An assumption of the standard error equal to one-tenth of the mean value was applied when no data were available.

**Parameter importance**

In addition to examining the overall uncertainty in the model using probabilistic analysis, the importance of individual parameters towards the

overall uncertainty of the results was also assessed. An analysis of covariance was performed on all input and output parameters for the probabilistic analysis (equivalent to linear regression based on the assumption of a linear relationship between the individual input parameters and the incremental costs and QALYs).

**Results****Cost-effectiveness analysis**

The results from both the base-case analysis (age at initial treatment 44 years) and for younger women (age 35 years) is presented in *Table 39*.

The base-case analysis showed that UAE was associated with substantially lower mean cost (£1769 versus £3462), and greater QALYs (0.820 versus 0.815) than hysterectomy in the first year; however, this observed difference in QALYs between the treatments at this stage (Stage I) is small (*Table 39*). In the subsequent years (Stage II), the UAE arm incurred additional costs associated with secondary procedures (£907), whereas no additional costs were incurred in the hysterectomy arm as symptoms were completely resolved. When the associated utility decrements were applied to the model in Stage II, the QALYs in the UAE arm became less than that of the hysterectomy arm (7.384 versus 7.426). Overall, for women who underwent an initial procedure for symptomatic uterine fibroids at the age of 44 years, UAE is associated with lower costs than hysterectomy. UAE showed a gain in QALYs following initial procedure (Stage I difference 0.005), but when both Stages I and II were taken into account, the overall QALYs were found to be less in the UAE arm than the hysterectomy arm (overall difference 0.038).

Similar results were found in women who underwent the procedure at a younger age (35 years). The first stage of the model is not influenced by age, therefore the results remained identical with the first stage of the base-case analysis. However, women who received an intervention at an earlier age would take longer to reach menopause, the end of the modelling period, and were more susceptible to additional procedures compared with older women. Therefore, it is unsurprising that compared with the older age group (44 years) the younger age group (35 years) incurred greater costs (£1831) and greater QALYs (11.639) at Stage II. Overall, when both Stages I and II were taken into account, UAE became more costly (difference £138) and less effective, with a lower QALY (difference 0.081).



**TABLE 39** Cost-effectiveness analysis<sup>a</sup>

		UAE	Hyst	Difference
<b>Base case (age at procedure 44 years)</b>				
Stage I – initial procedure (modelling period of 12 months)	Cost (£)	1769	3462	-1693
	QALY	0.820	0.815	0.005
Stage II – additional procedure (modelling period of 11 years)	Cost (£)	907	0	907
	QALYs	7.384	7.426	-0.043
Stages I and II – overall results (modelling period of 12 years)	Cost (£)	2676	3462	-786
	QALYs	8.203	8.241	-0.038
<b>Younger women (age at procedure 35 years)</b>				
Stage I – initial procedure (as base case)	Cost (£)	1769	3462	-1693
	QALY	0.820	0.815	0.005
Stage II – additional procedure (modelling period of 20 years)	Cost (£)	1831	0.00	1831
	QALYs	11.639	11.725	-0.086
Stages I and II – overall results (modelling period of 21 years)	Cost (£)	3600	3462	138
	QALYs	12.459	12.540	-0.081

<sup>a</sup> The modelling period represents the time from first procedure to menopause.

**TABLE 40** Sensitivity analysis – conservation of uterus

		Utility of conservation of uterus	
		0.01	0.05
<b>Age at procedure 44 years</b>			
Stage II – additional procedure	Costs (£)	907	907
	QALYs	7.472	7.825
Stages I and II overall result (modelling period of 12 years)	Difference in costs (£)	-786	-786
	Difference in QALYs	0.050	0.403
<b>Younger women (age at procedure 35 years)</b>			
Stage II – additional procedure	Costs (£)	1831	1831
	QALYs	11.778	12.322
Stages I and II overall result (modelling period of 21 years)	Difference in costs (£)	138	138
	Difference in QALYs	0.057	0.611

## Sensitivity analysis

### Conservation of the uterus

When the utility associated with conserving the uterus was included in the analysis, the overall QALYs associated with the UAE arm increased and UAE became the dominant strategy (Table 40).

Based on the assumption that conservation of the uterus was associated with a utility value of 0.01, the QALYs at Stage II in women who underwent the initial procedure at 44 years were 7.472, whereas the QALYs in those who underwent the initial procedure at a younger age (35 years) were 11.778. Overall, compared with hysterectomy, the UAE arm was associated with greater QALYs: differences in QALYs of 0.050 and 0.057 in the older and younger age groups, respectively. When

the utility value for conserving the uterus was assumed to be 0.05, the difference in QALYs between UAE and hysterectomy was amplified: 0.403 and 0.611 in the older and younger age groups, respectively. Threshold analysis found that no difference in QALYs between UAE and hysterectomy would be observed when the utility values for the conservation of uterus were assumed to be 0.004 and 0.006 for the analysis of the older and younger age groups, respectively.

### Procedural success

Sensitivity analysis was also carried out to test the scenario when young women (assumed to be 30 years old) with less severe symptomatic fibroids decide to seek UAE treatment. It was assumed that the gain in QALYs from successful treatment in

**TABLE 41** UAE versus no treatment

		UAE	No treatment	Difference
Age at procedure 30 years				
Stages I and II (modelling period 26 years)	Cost (£)	4212	0	4212
	QALY	14.357	13.373	0.984

this scenario would be less than that in older women with more severe symptoms; therefore, the base-case QALY gain as a result of procedural success was reduced from 0.12 (utility for successful procedure minus utility for menorrhagia) to 0.06. In this scenario, UAE was compared with no active treatment incurring no direct medical costs. Although UAE was shown to be associated with greater costs, it was associated with greater QALYs, generating an incremental cost-effectiveness ratio of £4280 per QALY gained (Table 41).

#### **Costs associated with loss of productivity**

The indirect costs associated with loss of productivity had been estimated to be £962 in the UAE arm and £2981 in the hysterectomy arm. When these costs were included in the analysis, the difference in costs between UAE and hysterectomy increased by almost three-fold (base-case cost difference £907 versus cost difference when including loss of productivity to base case £2805).

#### **Discounting rate**

The implementation of a discount rate of 1.5% for health effects gave no substantive differences in the results. The QALYs in Stage I remained unchanged as no discounting was applied to the costs and QALYs in the first year. In Stage II, the QALYs associated with the UAE and hysterectomy group were 8.261 and 8.309, respectively. Overall, the difference in QALYs between the UAE and hysterectomy groups was 0.043 compared with 0.038 observed in the base case.

#### **Probabilistic analysis**

The results of probabilistic analysis following 1000 replications of the model are presented on the cost-effectiveness plane, showing the mean difference in costs and QALYs between UAE and hysterectomy (Figure 33). The majority of the point estimates fell in the two southern quadrants of the cost-effectiveness plane, suggesting that UAE is associated with lower costs, but little difference in QALYs can be detected between UAE and hysterectomy.

Using the results from the probabilistic analysis, Figure 34 shows the cost-effectiveness acceptability curves for UAE and hysterectomy. The probability of UAE and hysterectomy being cost-effective is shown against the ceiling ratio for the willingness to pay. Overall, the probability of cost-effectiveness is greater with UAE than hysterectomy when the maximum willingness to pay is less than £30,000.

#### **Parameter importance**

The contribution of individual parameters to the model was examined and the results are presented in Figure 35. Results from the analysis of covariance showed that costs of hysterectomy, UAE and managing major or severe complications were important for explaining the uncertainty of incremental cost, whereas the utility values associated with UAE and hysterectomy were the important variables in explaining the variation in the incremental life years. Parameters that were derived from the HOPEFUL data such as the probabilities of complications, GSEs and additional procedures had little effect on the uncertainty of the overall results.

## **Discussion**

UAE is less costly than hysterectomy, but the effect of UAE on the overall QoL when compared with hysterectomy is less clear cut. In the base-case analysis, UAE was associated with lower QALYs than hysterectomy; however, the size of the difference in QALYs in the two groups was small. When considering UAE in younger women (35 years old), UAE became slightly more costly than hysterectomy over time when additional procedures were taken into account. Although the overall QALYs are greater in the younger age group compared with the older age group, they remained slightly lower than those of the hysterectomy group.

The main difference between UAE and hysterectomy is the conservation of the uterus with UAE. Women who underwent UAE may

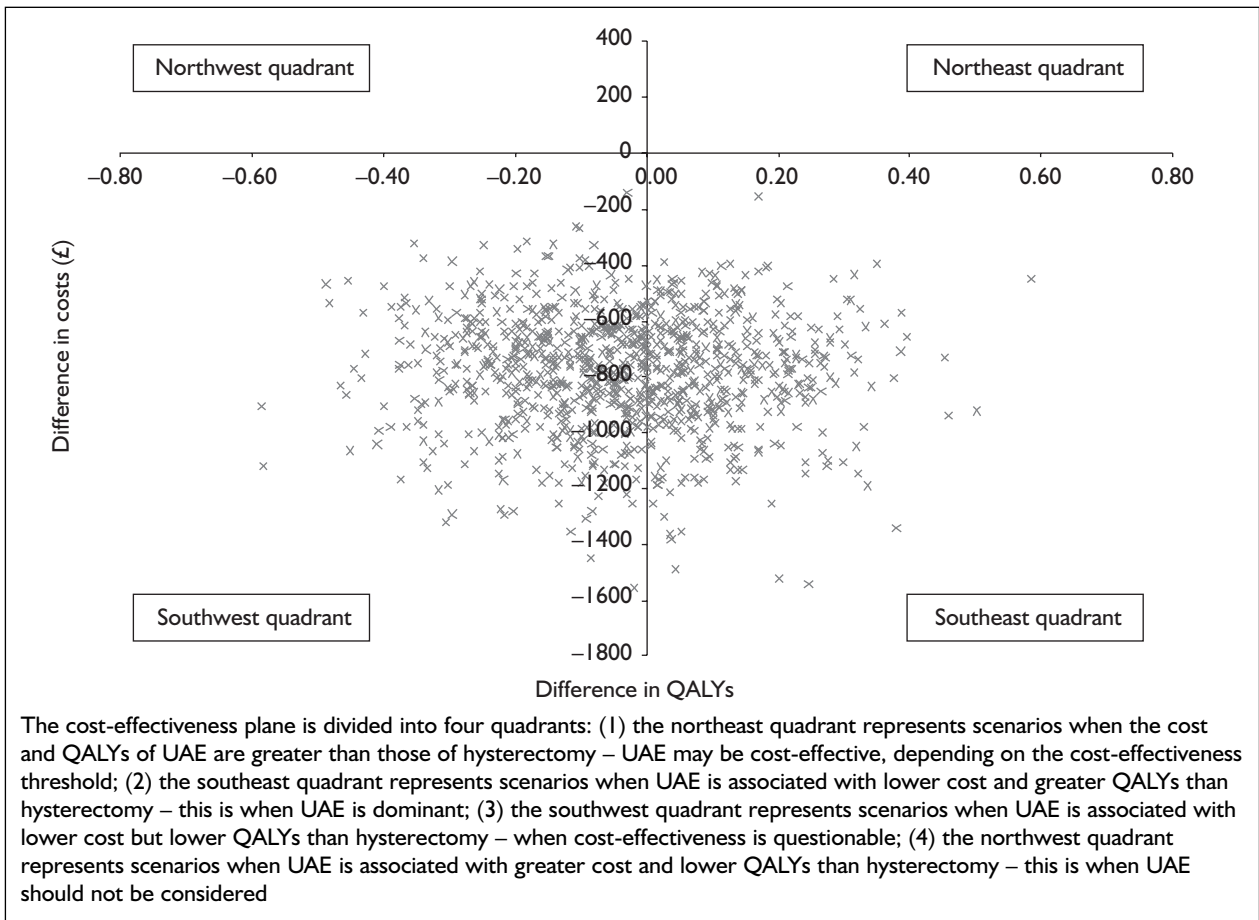


FIGURE 33 Probabilistic analysis

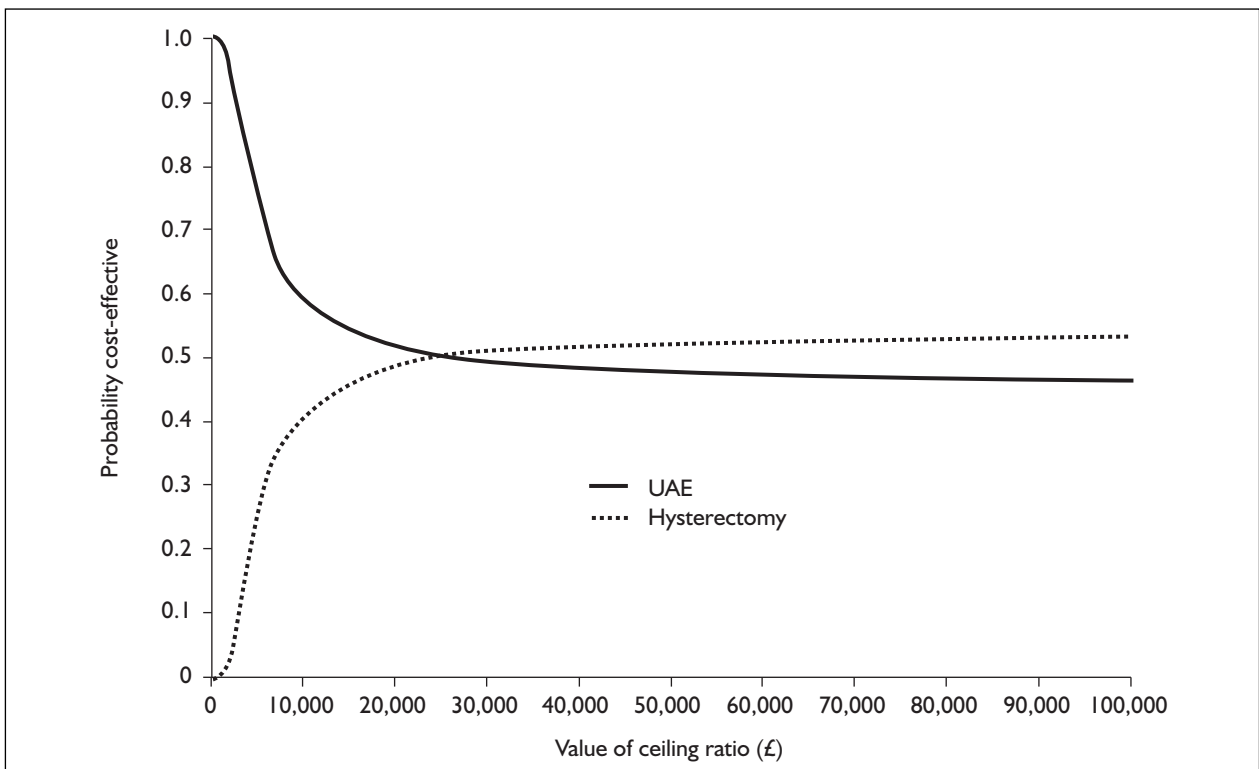
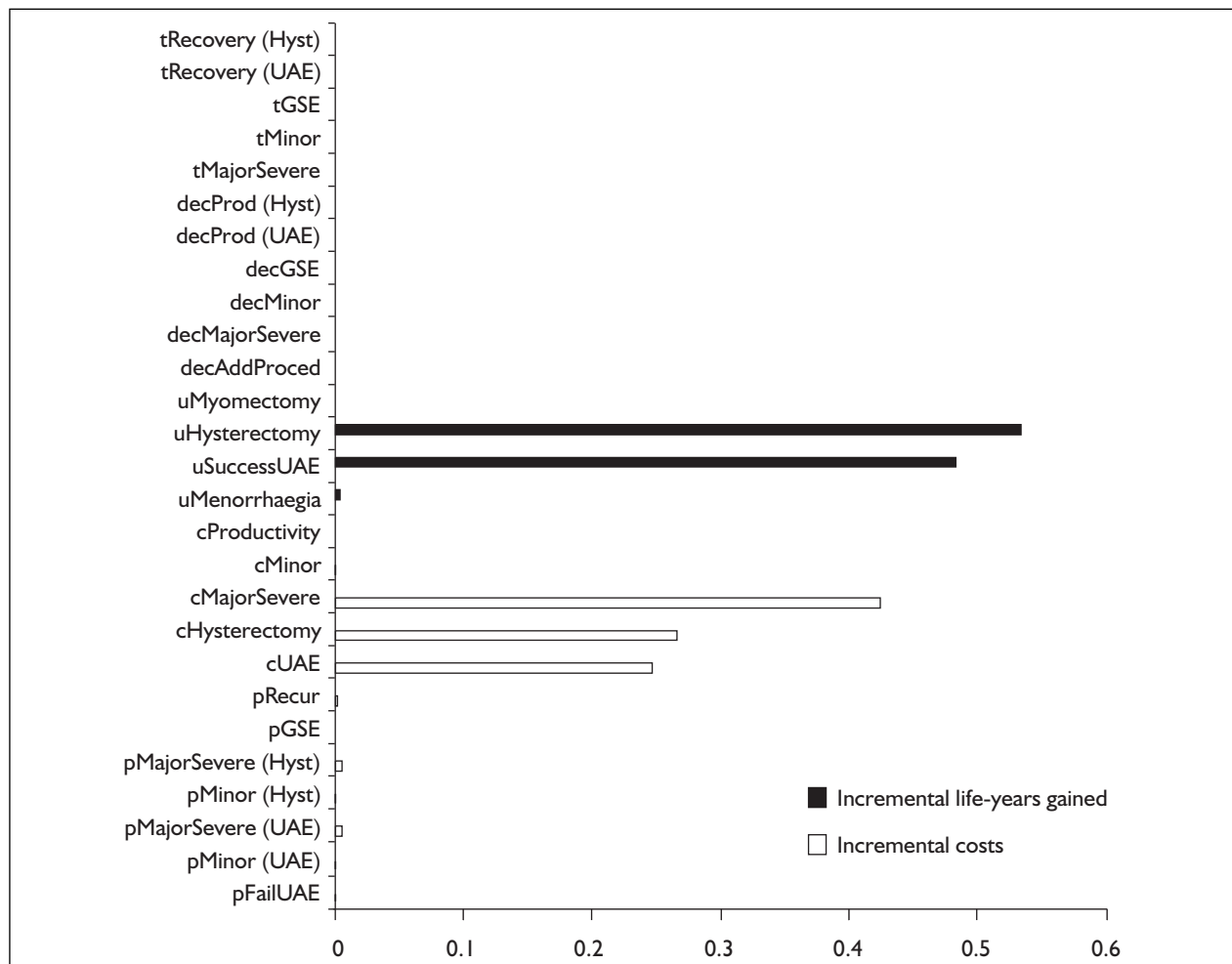


FIGURE 34 Cost-effectiveness acceptability curve



**FIGURE 35** Individual parameter contributions to total model sum of squares. Parameters with prefix 't' represent time, 'dec' represent utility decrements, 'u' represent utility, 'c' represent costs, and 'p' represent probability.

still have normal pregnancies, which is not the case for hysterectomy. Although the rate of miscarriage is high following UAE, this may not be different from an age-matched population with fibroids. The individual and social implications of maintaining fertility and the potential for future pregnancies are difficult to determine. It is difficult to value the advantages of UAE over hysterectomy for some women, regardless of whether pregnancy is achieved or not. The sensitivity analysis attempted to examine the potential gain in QALY associated with this advantage. In the absence of such data, the analysis was based on major assumptions made on the associated utility values (0.01 and 0.05). However, threshold analysis showed gains in QALYs for UAE compared with hysterectomy, when utility for conservation of uterus exceeds 0.0043. This low threshold value indicates that UAE would become preferential when the conservation of the uterus is taken into account,

even when the utility value placed on the conservation of the uterus is modest.

Not all symptomatic fibroids require intervention. In cases when the symptoms are mild and the size of the fibroids is small, women may not require treatment and would be observed and monitored over time. If women aged 44 and 35 years who developed symptomatic fibroids received no active treatment, their QALYs at menopause (cumulative QALYs discounted over time) would be 7.051 and 10.725, respectively. Young women with less severe symptoms would benefit less from UAE than those who are older with more severe symptoms. Sensitivity analysis showed that early UAE intervention incurs substantially greater costs and gain in QALYs.

Another key difference between UAE and hysterectomy is the time to recovery following the

procedures. In the sensitivity analysis, the costs associated with loss of productivity due to recovery were also examined. The indirect costs were estimated based on the human capital approach, which may overestimate the true cost to society. An alternative technique known as the friction cost method has been proposed. This method assumes that over a short-term period, employers may use existing capacity in their labour pool to compensate for an individual's lost work time due to ill health; in the longer term, workers who withdrew from work due to ill health may be replaced following a 'friction period'. Therefore, the friction cost method would result in lower and more representative costs associated with loss of production.

The probabilities in the model relating to severe, major and minor complications were estimated from the logistic regression models. Since there is a clear and intentional ordering to these complications, the application of ordered and multivariate regression models have also been explored (Appendix 15). Both models were found to generate similar results.

## Conclusions

UAE is a less expensive option to the health service than hysterectomy, even when the costs of repeat procedures and associated complications are factored in. The QoL implications favour UAE in the short term due to the less invasive nature of the procedure and the lower complication rate. However, this advantage may be eroded over time as women undergo additional procedures to deal with recurrent fibroids. In particular, for younger women who are exposed to the risk of recurrent fibroids and subsequent additional procedures over a longer period, UAE is no longer preferred. However, the sizes of the differences in costs and QoL between UAE and hysterectomy are small. Overall, the balance of whether UAE improves QoL is likely to rest with the woman and her attitudes towards the resolution of fibroid symptoms and the preservation of her uterus. Given the standard of hysterectomy treatment for this condition, offering women UAE as an alternative treatment for fibroids is likely to be highly cost-effective for those women who prefer womb-conserving treatment.



## Chapter 9

# Analysis of additional free-text comment

### Introduction

The HOPEFUL study questionnaire used predominantly precoded questions, with responses feeding directly into a range of statistical analyses, to form the basis for the earlier chapters of this report. At two points respondents were invited to amplify their response to a question, and were provided with some space for free-text comment. Analysis of this free-text comment, from Q24(a) and (f), is reported in Chapter 6.

In addition, at the end of the questionnaire, the following prompt was given to encourage respondents to record anything that they thought was important, but which they felt had not been covered adequately elsewhere:

“If there is anything else about your treatment/s for fibroids and your health which is important to you, please tell us in the space below: (for example this might include your feelings about your fertility, your uterus or ovaries).”

The nature of additional free-text comments added at the end of a comprehensive questionnaire is very different from that of the precoded responses in the main body of the questionnaire. The value of providing space for additional comment is that it allows:

- respondents to raise new issues that have not been dealt with elsewhere
- respondents to clarify or elaborate on issues dealt with earlier
- researchers to access some of the feelings, concerns, experiences and interpretations that could not be recorded within the pre-coded response options.

These comments thus offer us insight into experiences and concerns, which may be helpful in informing decisions, and the implementation of decisions, that follow from this study.<sup>51</sup>

A total of 711/986 (72.1%) responders wrote a free-text response to this prompt [Hyst  $n = 267/397$  (67.3%), UAE  $n = 444/589$  (75.4%)]. The average number of words written was 67 (Hyst  $n = 59$ , UAE  $n = 71$ ).

The free-text responses were analysed as described in Chapter 3. Patient ID numbers have been removed to protect identities when responses of direct quotes are presented. The women's ages at the time of questionnaire completion and the type of treatment they received, hysterectomy (H) or UAE (U) are included with each quote.

With such an open invitation for additional comment it was inevitable that the responses covered a wide range of topics. There were, however, some broad patterns in the topics raised, and these have been used to structure the reporting of these free-text data.

The findings are presented first for women who had had a hysterectomy and second for women who had initially had treatment with UAE. This separation has been made to make it easier to gain a sense of the overall final comments from each group as whole, and then to compare the whole picture of each treatment, rather than continually to be making comparisons on individual points. It is also because different themes dominated the responses of the two groups of women.

### Free-text comments about the experience of hysterectomy

Five broad themes were identified, into which all of the responses could be placed:

- communication
- HRT
- choice
- fertility, femininity and sexuality
- general positive and negative comments.

The analysis within the main themes will be presented in turn, using extracts of responses to illustrate the interpretations made.

#### Communication

This label covers a huge range of experiences and specific circumstances. Within this study, it has been possible to identify three sub-themes, which catch the essence of the comments falling within the theme of communication. Although arranged

under three subheadings, the messages from the three sets of comments are closely related:

- still wondering
- worries about ovarian cancer
- wish I'd been told.

### **Still wondering**

Communication is a two-way process requiring the active involvement of both health professional and health service user. There is certain information that a clinician may need to communicate to a patient, but there will also be certain information that a patient may want to be given but, for a range of reasons, may not get round to asking for at that point.

One limiting factor found in this study was the hesitant behaviour of some of the women who had had a hysterectomy, who did have questions but had never voiced them:

“When I went for check up at 6 weeks later the nurse who examined me seemed worried about something she felt was not right. She called a surgeon to examine me, but after his examination he sort of dismissed her worries as nothing. As he was quite an abrupt man I was too timid to ask what was wrong and it has worried me ever since, as I now have quite a swollen abdomen.” (H, 71 years)

“After my hysterectomy my world collapsed. I feel more could have been explained or tried before taking such a life-altering operation, as I was only in my late 20s and was too afraid to ask questions as I was a shy type of person and believed the doctor knew best. I think I have ovaries but I am not sure. But would like to know. But don't know how to find out these things. Any information would be appreciated.” (H, 47 years)

Other women are still wondering if their bowel or bladder problems were caused or exacerbated by their hysterectomy, or if HRT caused their irritable bowel syndrome.

While many are still wondering about various issues, others feel that they were given plenty of information before surgery.

“My consultant explained what would happen during the operation, answered my questions and gave me a number to ring if I had further questions. This was very reassuring.” (H, 55 years)

### **Worries about ovarian cancer**

Many women reported concerns about their ovaries, perhaps partly because ‘ovaries’ was mentioned in the free-text prompt. However, this

does seem to be an area where women would like more information in order to make an informed decision whether or not to keep their ovaries when having a hysterectomy. Some women who keep their ovaries report no problems and are happy to have a natural menopause rather than using HRT.

“... I insisted on keeping my ovaries at the time as I did not want to go into an early change and I believe I did the right thing ...” (H, 54 years)

Two women, now aged 52 and 54 years, reported that they were not told that their hysterectomies could trigger an early menopause even though they kept their ovaries and were disappointed when this happened.

Many comments from women who chose to keep their ovaries reveal a fear of developing ovarian cancer, which they seem to believe is more difficult to detect after hysterectomy.

“I was able to keep my ovaries and I am now worried that you can get cancer of the ovaries and it would not be detected.” (H, 41 years)

“My only concern is not having my ovaries taken out, but I understand why this was done, but I had to take HRT after 12 months. If I had had them taken out, I wouldn't have this nagging thing in the back of my mind about ovarian cancer.” (H, 56 years)

“I wanted to keep my ovaries to avoid early menopause which is the case, since I have only just begun hot flushes 10 years after my op. But my concern since, has been that the ovaries might develop ovarian cancer so I try to have a scan now and then to check. I had to pay for this scan but found it beneficial.” (H, 53 years)

“I am now concerned that I could develop ovarian problems as the consultant would not remove them as they were healthy at the time ...” (H, 53 years)

“The only thing that concerns me is both my ovaries. My mother-in-law had a hysterectomy a few years before me with both ovaries left and last year found out she has ovarian cancer too far advanced to have surgery. Is there anything I could do to prevent this or be checked?” (H, 63 years)

This is an area where further development of communication between healthcare professionals and patients is needed. At the time of decision-making, the retention of ovaries seems to have been discussed mostly in connection with possible early onset of menopause. The possibility of developing ovarian cancer at some future point, and unrelated to the current intervention, may not at that time be uppermost in the mind of either patient or clinician. However, in view of the extent



of concern identified in this study, it appears to be a topic that needs to be introduced early on, with full discussion of concerns, risks and options.

### **Wish I'd been told**

Similar to the theme of 'Still wondering', with its focus on lack of information, the theme of 'Wish I'd been told' includes in addition an element of indignation, as women reflect with hindsight that there was something obvious that they should have been told but weren't.

"Nobody explained in any depth the possibilities of loss of sexual feeling or how bad the excessive sweats would be. Although I was on HRT this did nothing to improve matters. Apparently there was nothing wrong with my ovaries and I feel I have been robbed of my womanly feelings unnecessarily. Thankfully I married a very understanding man. It appears the cervix was removed, actually this was not mentioned either at the time of the operation or beforehand."  
(H, 56 years)

"One thing that did bother me was that I was never told they had taken my cervix. It took several smears to come back with no cells seen before the doctor told me I had 'no cervix and it's just a vault'. This terminology I found upsetting – but at least I don't have to have smears any more."  
(H, 45 years)

"I was not given any information about what to expect after the treatment. I was not satisfied with any oral information given."  
(H, 49 years)

Many of the women commented that they had not been given adequate information on how to use HRT.

"I feel more could have been done to explain the HRT treatment to me as I felt I had to read, decide and make my own decisions."  
(H, 57 years)

"After my hysterectomy I feel I was not given information about after care after having a hysterectomy, i.e., HRT or long-term health."  
(H, 46 years)

"... Not enough information about going through the 'change' menopause without ovaries, and the implications of taking HRT and for what length of time I would need to take medication."  
(H, 58 years)

This leads on to other comments made about HRT.

### **HRT**

The views of women about taking HRT were widely divided. Some found it excellent and others wished that they had never used it.

"I would like to continue on HRT until I retire!"  
(H, 59 years)

"I wish I had never had HRT."  
(H, 58 years)

"HRT was very good and made me have more energy and feel good."  
(H, 57 years)

"I had bad reactions to HRT, but was not offered any advice or alternative treatment by my doctor when I stopped taking HRT."  
(H, 63 years)

"My biggest worry is how to ensure I can continue to take HRT indefinitely."  
(H, 46 years)

"I would not recommend HRT to anyone."  
(H, 52 years)

"The only concerns I have are the continued use of HRT and the negative publicity this drug attracts."  
(H, 56 years)

"The only problem is little information about HRT. A patch was given to me the day after the op and I was told that it was for life and that was it. I still can't get any information as to how long I need to take it or what symptoms I will get if I remove it now I am 55."  
(H, 55 years)

"My total hysterectomy was the best day's work. I had excellent counselling before and after the operation. The total removal of my uterus and ovaries has alleviated concerns about later cancers. The HRT treatment has alleviated any mood swings, improved my general well-being and helped although not eliminated night sweats. I hope to wean myself off the patches over the next year due to concern about breast cancer."  
(H, 58 years)

Overall, the problems relating to HRT were predominantly issues of communication. Women were reporting lack of information: in advance of starting it; as they were using it; and as they were looking to stop using HRT, either because it did not suit them, or because they had been using it for many years. Clearly, there is no definitive pattern that can be predicted about individuals' responses to starting to use HRT, but it is possible to describe a typical range of responses and decisions and to facilitate the raising of initial questions and provide a channel through which later questions can be asked. This raises questions about the appropriate division of work on this subject between secondary and primary care teams.

### **Choice**

Some women report that they wish they had been given the choice of an alternative treatment before having a hysterectomy and seem to have felt pressurised into having the hysterectomy or having their ovaries removed.

"My choice was hysterectomy or nothing. I would have valued a medical opinion and felt unsure after if I had made the right decision. Needed reassurance afterwards that the op was appropriate ... Felt I was

blackmailed into agreeing to removal of healthy ovaries at the same time as a condition of having the hysterectomy.” (H, 63 years)

Others were not sure whether, if UAE had been available at the time, they would have tried it.

“At the time of the hysterectomy I was not offered any other treatment – but knew if I had I would still have chosen a hysterectomy – for me it was the best thing and I felt so much better afterwards.” (H, 53 years)

The following is a selection of responses that focused on the issue of choice.

“I would have liked a better choice and been able to have the UAE treatment first.” (H, 53 years)

“My choice was hysterectomy or nothing ... needed reassurance afterwards that it was appropriate.” (H, 63 years)

“I think the treatment offered and used would depend on the age of the patient.” (H, 65 years)

“I did not want a hysterectomy but had little choice.” (H, 53 years)

“At the time of my treatment, if there had been another option and choice, I would have hopefully gone for that treatment.” (H, 64 years)

“If today I had the same condition, I would probably choose an alternative treatment to hysterectomy.” (H, 56 years)

These comments need, however, to be interpreted carefully. UAE was not available before 1997 and the hysterectomy cohort had their hysterectomies during 1994 and 1995. Therefore, it is unlikely that the hysterectomy respondents had information about alternative treatments for fibroids at the time of their treatment and perhaps not until they received an invitation to participate in the study. They therefore may be responding primarily to the idea that something less invasive or final than a hysterectomy might exist, and be unaware of any problems associated with different procedures.

### **Fertility, femininity and sexuality**

Comments on the issues of fertility, femininity and sexuality were noticeable by their frequency, their openness, and their variety. Examples of comments are presented here under four broad headings:

- family complete
- sexual issues
- feelings about loss of fertility
- feelings about being a complete woman.

### **Family complete**

The women in this study having a hysterectomy were 2.7 years older on average than those in the UAE group at the time of their index treatment (7.3 years older on average at time of questionnaire completion), and would have been aware throughout their period of decision-making that loss of fertility would automatically follow a hysterectomy. It is not surprising, therefore, that many of the comments confirmed that the decision to have a hysterectomy had been made after their family was complete, or as a pragmatic response to not already having had children.

“... Having had a previous sterilisation, having no more children was already decided, prior to this. Now having 10 grandchildren is wonderful.” (H, 63 years)

“I had already decided to stop after only 1 child as I had a very bad pregnancy, spending 7 months in hospital, but with a lovely daughter born ...” (H, 58 years)

“As for the option of having children at 44 years old when I had the hysterectomy I had already accepted that it wouldn’t happen.” (H, 54 years)

“My quality of life since the hysterectomy has been much better – we decided years before not to have any more children (my husband had a vasectomy) so that was not an issue ...” (H, 60 years)

“I have no hang ups from having had a hysterectomy. For me it was the best thing – I did not want children at the age of 40 and my whole demeanour changed. I think the treatment offered and used would depend on the age of the patient.” (H, 65 years)

### **Sexual issues**

Most reported comments about sexuality were negative, including comments about:

- decreased sex drive
- decreased sexual desire
- decreased interest in sex
- decreased feeling for sex
- complete or total lack of libido.

It is unclear whether ‘feeling for sex’ is meant to indicate sexual desire or sensation. However, several women speak openly about problems with sexual sensation following hysterectomy, including vaginal dryness, reduced feeling on penetration and less intense orgasms. Some women indicate that the loss of sexuality seriously affected their relationships and their own emotions. Words such as “saddened”, “loss”, “robbed”, “dead” and “depressing” and some of the quotes below help describe this emotional and physical adjustment.

“Removal of uterus changed the nature of my orgasm; even the best are no longer as intense. Previous to the hysterectomy an orgasm often resulted in noticeable uterine contractions.” (H, 54 years)

“Having my sexual desire reduced and feeling on penetration reduced as I had only been re-married not quite a year this has seriously affected me in this marriage.” (H, 56 years)

“After the operation, having intercourse was never the same as before with regard to reaching a climax or orgasm. I felt everything was dead inside, which was depressing. It has improved over the last 5 years...” (H, 58 years)

“I noticed a complete lack of libido as soon as I was in a position to resume a normal sex life.” (H, 64 years)

Not all experiences in this area were deemed negative:

“Since the hysterectomy I have lost all sexual urges which is a relief – it has enabled me to concentrate on much more useful/enjoyable/fulfilling aspects of life.” (H, 60 years)

“I have lost interest and feeling for sex and am really not bothered about it – which is a shame, but not a major problem.” (H, 58 years)

“I live life to the full, enjoy working, have a very good sex life, which I could not enjoy earlier as I found sex uncomfortable most of the time.” (H, 50 years)

“Heavy periods interfered with every aspect of my life, and holidays were a nightmare. A normal sex life was impossible.” (H, 54 years)

These last two comments point out the practical fact that, prior to the hysterectomy, sexual activity had already been a huge problem, although a different one.

### **Feelings about loss of fertility**

Having a hysterectomy brings infertility by definition. This is known in advance, and there is no uncertainty as to whether or not any chance of reproduction remains. Despite this, and despite the fact that many women in the hysterectomy cohort had already completed their families or had grown used to the prospect of not having any children, the clinical finality of their loss of fertility was still something to mourn.

“My family was complete when I had the hysterectomy, but it still troubled me occasionally to think that all my child-bearing equipment had been removed.” (H, 63 years)

“Because I was only 44 when I had a total hysterectomy and my husband and I had completed our family, I still didn’t like the thought of never being able to have any more children. If given the

choice of UAE (and still being able to have children) I would have made that decision, not a total hysterectomy...” (H, 53 years)

“I was 53 years old at the time of the operation so didn’t have negative feelings about loss of uterus or ovaries, but on hindsight I would have appreciated continuing my life with these organs...” (H, 64 years)

“I tried to be fatalistic about the necessity for a hysterectomy but felt a failure at ‘not doing it myself’. Also, ridiculously at 56, I had an emotional struggle accepting the fact that my choice for more children was taken from me...” (H, 65 years)

“The only time I have had any feelings about my hysterectomy was on the morning of the operation. I felt as though I was losing a dear friend who had served me well, being the cradle which had nurtured my children. I can only describe it as a deep grief and wondered whether I would get over it. But I must confess after the operation I never gave it another thought...” (H, 60 years)

### **Feelings about being a complete woman**

Associated with feelings about fertility were feelings about being a complete woman. There were some negative comments, such as:

“Did not feel like a woman as everything has been taken away from me.” (H, 49 years)

However, there were more positive comments, such as:

“I can now say that I don’t regret having the ‘op’ ... I never once missed not having a period – good riddance – and did not in the least feel that I was anything other than a complete woman. Despite everything I and my family went through it has all been worthwhile.” (H, 53 years)

“From as soon as the day after the operation I felt 100% better and have never regretted the operation. It helped me regain my life and made me much more energetic, and feel more feminine. I have no regrets and no problems since...” (H, 44 years)

“When I had my op, for a short while for obvious reasons I felt I was not a complete woman. After I got over the emotional side I really felt good, and am glad I had this done, it’s made life a lot easier.” (H, 56 years)

“I did not experience any psychological concerns about the removal of my uterus as I gather some women do.” (H, 56 years)

“I had no negative feelings regarding my fertility or sexuality...” (H, 56 years)

“Parting from my womb has not bothered me at all...” (H, 61 years)

“I felt so unwell before my hysterectomy and so well afterwards. I was concerned it would affect me

adversely as a woman, but no problems and still feel feminine.” (H, 61 years)

These positive comments weigh against the more commonly anticipated reports of feelings of loss of womanhood.

### General positive and negative comment

Much of the negative comment recorded by the hysterectomy cohort relates specifically to particular problems such as taking HRT, loss of fertility and lack of choice at the time. There was no identifiable pattern to these comments, but many have been incorporated into the sections above. Whether they are due to surgery or not, women mentioned many different health problems that followed their surgery, including: weight gain; bowel and bladder problems; cardiac problems such as high BP and angina; thyroid and cholesterol problems; breast cancer; migraines; osteoarthritis; painful joints; Barrett’s oesophagus; gall stones; diabetes; psoriasis; and asthma.

Much of the positive comment was more general and concerned women’s overall feeling after having a hysterectomy.

“Although a big operation with a long recovery period – it was the best thing I ever did.” (H, 45 years)

“Since having my hysterectomy I have started to enjoy my life. It has been hassle free and I feel more comfortable in those situations (socialising with friends and family) than I did previously.” (H, 48 years)

“No problem. No smear test. No more period. No HRT. No heavy bleeding. ‘I am happy with myself.’” (H, 61 years)

“Following the hysterectomy I felt more confident and could plan my life more efficiently.” (H, 62 years)

“It was miraculous how I felt from when I awoke from the anaesthetic – GREAT – soon had shower – never looked back – a new woman – a transformation.” (H, 61 years)

“Having my hysterectomy gave me a new lease of life. I had endured years of heavy periods with embarrassing flooding – through clothes – clots. The hysterectomy was easily coped with and I had little or no pain or discomfort and very quickly got back to an improved unembarrassing lifestyle. I wish I had had the op 10 years before.” (H, 64 years)

“I have never had a problem coping with the treatment. Relieved the discomfort/pain has not returned and was able to return to work full-time, without having discomfort during menstruation.” (H, 58 years)

“I had no qualms whatsoever! Losing my womb, ovaries and cervix only meant that to me my life was

going to be 100% better!! And it was ... 25 day periods were no joke and I was glad to get rid of them.” (H, 57 years)

These are highly positive comments, and give a strong impression of success and relief from difficult symptoms.

## Discussion of hysterectomy findings

### Need for realistic balance in communication of possible outcomes

Communication, HRT, choice, fertility, femininity and sexuality are important and connected themes in the free-text comments of women who had hysterectomies. Individual factors such as personality, life circumstances, symptoms before hysterectomy and other health concerns influence each woman’s response to hysterectomy, resulting in a wide range of negative and positive views. Health professionals who communicate a balanced view of the many potential reactions to hysterectomy may help prevent feelings of uncertainty and disappointment, such as those found in women’s comments under the communication subthemes of ‘Still wondering’ and ‘Wish I’d been told’. By providing more information about both the risks and benefits of hysterectomy, women may be better prepared to deal with actual health risks, such as the potential for bone loss or osteoporosis that may result from hormonal changes following hysterectomy.

### Development of fears about ovarian cancer

Women’s comments in the subtheme ‘Worries about ovarian cancer’ point to a need for early consideration of the decision to keep or remove ovaries during hysterectomy, with a full discussion of concerns, risks and options for follow-up. Ovarian cancer is a risk for anyone with ovaries and is known to be difficult to detect until the cancer has spread. However, some women who had hysterectomies but kept their ovaries seem to fear that they are more likely to develop ovarian cancer and that it will be less detectable in them than in the general population. Other women express the belief that even though they kept their ovaries, their hysterectomy triggered an earlier menopause. Reliable evidence needs to be communicated on these issues to dispel any unnecessary fears.

### Facilitation of questioning

Women found it very reassuring when, prior to the surgery, consultants explained the hysterectomy

procedure, answered their questions and invited them to contact them with further questions. Some women may not ask their questions due to hesitant, shy or timid behaviour but may be more likely to express their concerns if doctors invite their questions during consultation or give them opportunities to ask in the future. Several women still had very basic questions about what exactly had been removed during surgery: they had never known.

While providing information prior to surgery is helpful in decision-making, women should be encouraged to address any questions or follow-up treatment needs to their consultant or their GP. Some women wonder about issues regarding their hysterectomy many years later but never ask for or receive adequate information. Some women felt they had no choice but to have a hysterectomy. While they vary in their desire for a choice of treatments, some women do state that they wish they had information about alternative treatments before having a hysterectomy. Others state that they are completely happy with their hysterectomy even if they had not been given a choice, or if they had experienced a time of adjustment after the surgery. Interest, in hindsight, in the alternative treatment of UAE is, however, unlikely to be informed by the range of possible negative outcomes of UAE that this study has identified.

### **Variety of possible outcomes to prepare for**

Many women have questions about the use of HRT, especially the length of time they should use it and any potential long-term effects. They also wonder if having a hysterectomy can make them more prone to certain health problems, such as getting ovarian cancer if they have kept their ovaries. They have various reactions after hysterectomy regarding changes to their sexuality, femininity or fertility. Some women are prepared to accept the loss of their fertility and changes to their sexual relationships and their feelings about their womanhood. Some feel more feminine after hysterectomy, perhaps due to the end of the heavy and prolonged bleeding that interfered with their sex life prior to hysterectomy. A few women stated that they were glad to be rid of the organs that caused these problems. They feel more confident, able to socialise and can plan their lives more efficiently without worrying about the embarrassment of heavy bleeding. Defiant and positive statements were made, which challenge the notion that removal of reproductive organs removes womanhood. Others felt more of an emotional loss and could have used more

preparation or information in order to cope with these changes.

### **Channels for asking questions**

Questions occur to women close to the time of their surgery, but also many years later, in connection with the operation and with follow-up experiences, in particular the use of HRT, and issues connected with sexual function. While initially the responses will be available mostly within secondary care, in subsequent years some women feel unsupported and unable to ask their questions. It would be useful to make sure that women having hysterectomies know who they can approach with such questions, and that they feel confident that their questions will be welcomed and answered knowledgeably.

### **Free-text comments about the experience of UAE**

Eight main themes were identified that encapsulate the majority of the responses. Responses that related mainly to either unfulfilled expectations or specific problems caused by the treatment, were fed into the analysis of Q24(a) and (f) reported in Chapter 6, and have not been examined again here. The eight main themes identified were:

- UAE was a successful treatment.
- Interest in keeping parts of their body where possible.
- Pain and its treatment.
- UAE was not a successful treatment.
- Follow-up.
- Treatment by staff was good/bad.
- Needed to do own research.
- Fertility.

### **UAE was a successful treatment**

There were many highly complimentary comments about the results of UAE. For those for whom it worked well it was a positive, life-changing experience, and they could not speak too highly of it.

“The treatment should be given far sooner – it gave me back my life!!!” (U, 56 years)

“UAE dramatically changed my life. I am now on progesterone cream which I buy from America. It suits me. I was absolutely delighted with my treatment. I was in hospital 24 hours, went home next day and straight back to work. Hardly any pain afterwards.” (U, 55 years)

“Thanks to everyone concerned. Respect. Treatment highly recommended” (U, 47 years)

“And thanks – it was the best thing that ever happened. If I could have had this procedure earlier in my life I would have saved loads of money on sanitary protection, and iron pills. Heavy periods ruled my life. Best procedure since sliced bread” (U, 55 years)

“I feel that I have been given my life back. Before UAE I was very lethargic, very short of breath, always had indigestion, always looked as though I was 6 months pregnant, no drive to do anything, had tremendous water retention and my hair regularly moulted more than usual, and I was always moody and tearful. Now – I feel as though I am only 18, I have sustained energy, no pain in lower back, no water retention, have dropped dress sizes and feel like I have had a personality transplant! I am more positive in my attitude and am now considering options for perhaps starting a family of my own. I am now running my own estate agency business which was only a dream before. I would heartily recommend that all women should take this route first (wherever possible).” (U, 41 years)

The main positive responses were about the dramatic effect UAE had had on heavy and prolonged periods. Regaining a much more limited and predictable period pattern had enabled women to start living life more fully. UAE had therefore both physical and psychological benefits, as described in the following response:

“I have recommended UAE to many. It has many social and economic advantages as well as clinical ones.” (U, 48 years)

The woman above who said she is now ‘considering options for perhaps starting a family of my own’ currently gives high praise to UAE, because of its effect on her periods, and she appears confident that she will be able to start a family when she wants to. The issue of fertility is addressed in the section ‘Fertility’ (p. 107). In this study there were 19 successful live-births in 16 (2.3%) of the women who had UAE.

### **Interest in keeping their body parts where possible**

In addition to reducing symptoms associated with periods, some women who had UAE were very keen to avoid any unnecessary removal of body parts. For some this was associated with retaining the possibility of having children, and this is discussed later in this section. For some it was associated with retaining ‘womanhood’, and for others it was a more general desire to keep their body intact as far as possible. Feelings about retaining womanhood and keeping their body intact were expressed both by women keen to have children and by those who were not.

“I found the idea of a hysterectomy very upsetting – loss of womanhood etc.! UAE had none of that emotional loading.” (U, 48 years)

“Although I was not single minded about having children, I was unwilling to have a hysterectomy while there was still the opportunity. It also seemed wrong to get rid of part of my body which had not been used for its purpose, through major surgery, if I could avoid this.” (U, 51 years)

“Due to the large size of the fibroid and an increasing tummy size, to some extent I felt pregnant. So after surgery, although I knew I had not murdered a baby, I suffered a period of what I can only describe as bereavement. However this did not affect my overall delight and complete satisfaction with my treatment. I would not hesitate to recommend this treatment. I am happily still very attached to my uterus and ovaries.” (U, 43 years)

“One doctor at the hospital told me ‘just have it out, can’t you feel how bulky your womb is’. I did not want a big operation such as a hysterectomy. No removal of body parts if possible.” (U, 58 years)

“Although I had no plans for a family I was nevertheless emotionally attached to my uterus and ovaries which were healthy and not in themselves causing the problems.” (U, 46 years)

These examples of responses within this theme show how the desire to retain the womb can go well beyond the need for it to be available to fulfil its technical role in pregnancy. The third quote shows that it is even possible for some women to become emotionally attached to the part of their body that is actually causing them problems.

### **Pain**

Weighing against the highly positive comments on the experience of UAE were more negative comments. One area where negative comment was recorded was that of pain. This section presents some of the comments associated with levels of pain experiences but, as with the general picture of comments about UAE, there is a mix of negative and positive comments that makes a simple conclusion or message impossible. These quotes show some of the negative comments about pain.

“Without harping on – hospital gave me some type of pain relief which was ineffective. When I told the nurse she accused me of fabricating – I was in total pain after the operation.” (U, 52 years)

“Prior to the procedure I was told about how painful it might be afterwards and how the pain would be controlled – this was more painful than I thought it would be and I feel it was not controlled as well as it could have been, i.e. the drugs were allowed to wear off before being topped up, especially at night when

there were fewer qualified staff around to administer pain relief.” (U, 50 years)

“I was treated very shabbily by the nursing staff after my UAE. They withheld pain killers because they had not been trained in post-UAE care and the anaesthetist did not monitor or discuss my care or the lady in the next bed with the staff. She screamed and wept and so did I.” (U, 55 years)

“I would recommend the treatment but would tell about high level of pain and length of full recovery time.” (U, 43 years)

“The fibroid embolisation treatment was extremely painful post-operative – and I was not told of this pre-operative. I needed large amounts of pethidine and Voltarol P/R and Diazepam for 72 hrs + post-op. I suggest that patients are given self-control of their opiates infusion so that they can better regulate their pain relief requirements.” (U, 41 years)

“The actual treatment was quick and pain-free. The pain following treatment was much worse than I expected – especially the day/night following discharge from hospital.” (U, 50 years)

Other women had a different experience and found the pain negligible.

“I would like to say that I would encourage women to have the embolism operation as it is not painful in any way.” (U, 43 years)

“I consulted several women who’d had UAE and felt frightened by their stories of pain etc. But I went ahead. I prepared for the treatment for about a year in advance through yoga (pelvic strengthening) nutrition and homeopathy. I found the treatment very painless, recovered within days, and had immediate positive results and almost 100% shrinkage.” (U, 54 years)

“The one thing that I was surprised about this treatment was the negative view by the pre-assessment nursing staff, who clearly felt it was their duty to tell me how risky and painful this op would be. I feel they need more education themselves so that they could offer a more balanced view.” (U, 49 years)

This last comment shows the only way forward in this area of widely different experiences. A challenge in this field is to present a balanced view that is not so full of caveats and different possibilities that it is of no use to the women making the choice.

### **UAE was not a successful treatment**

In addition to some negative comment regarding pain, there was some more general negative comment. But, again, the picture is not simple.

“Treatment did not work in long term. UAE worked and improved symptoms for a few months following

UAE but following re-growth of fibroids I had to have a hysterectomy.” (U, 34 years)

“Fibroids still grew, haemorrhaging more frequently, required alternative surgical treatment – hysterectomy.” (U, 46 years)

“The questionnaire does not adequately cover degrees of improvement and relapse. Initially my treatment seemed successful but more fibroids grew to ‘replace’ the ones that had diminished in size.” (U, 48 years)

These comments clearly state that the treatment was not successful, and add no further information.

The following comments give insight into a more complex picture, where a certain degree of satisfaction can be experienced even when the treatment was not successful.

“Although UAE did not work for me, the procedure is pain-free and has a quick recovery. Would recommend to others. Bit of a mystery why it didn’t work for me.” (U, 46 years)

“Although UAE didn’t work for me and was a very painful treatment I felt it was worth trying.” (U, 35 years)

“I had high expectations of the UAE treatment, perhaps too high.” (U, 38 years)

“I am perfectly happy after having a hysterectomy, but did feel that I wanted to give UAE treatment a try, unfortunately for me it was unsuccessful.” (U, 47 years)

The precoded responses in the questionnaire have collected comprehensive data on outcomes. This free-text data complements the quantitative data by providing insight into how individuals felt as a result of the outcomes, and how the process fitted into the context of their lives.

Three of the four women whose responses are included above said that they did not regret having UAE/would recommend it to others, even though it had not worked for them. This immediately complicates the relationship between outcome and satisfaction, and shows that the decision-making process is neither straightforward nor objective.

An important element in the decision-making process is knowledge about possible outcomes, which can be gained only by appropriate follow-up of patients. At the time when the women in this study had their UAE it was a relatively under-studied procedure without comprehensive data on outcomes. The following comment challenges whether adequate follow-up data collection was happening.

“I do not believe that my UAE was successful; it helped in the short-term, but was, for me, a far too temporary solution. It’s hardly surprising that the success rates for UAE are so high if no follow-up is carried out...” (U, 39 years)

### Follow-up

There were a few other comments specifically about follow-up, although there were many more that were implicit in suggesting that not enough information on outcomes further down the line had been given.

“Although the treatment was mostly successful, at times since the treatment I get very bloated. I also think there should be some follow-up in terms of another scan in later years to see if the fibroids have remained the same or increased in size.” (U, 53 years)

“The research for fibroids is incomplete. Don’t they want to know the actual size of the fibroid I have now? I am more comfortable now than before treatment, but I often get pain for no reason. Perhaps fibroids need to be scanned at this stage to conclude the research.” (U, 49 years)

“... So far I have had no problems that I am aware of. Although I think it would be a good idea to have a check up to see if everything inside is ok.” (U, 45 years)

“I cannot have three months off work and look after myself, so I have not had a hysterectomy. I’ve daily pain in ... and nobody seems to have any solution. There has been no follow-up, no advice and no help.” (U, 59 years)

Systematic and prolonged follow-up would have benefited these women individually, and would have collected data on outcomes that would support decision-making for women in the future.

### Satisfaction with care

Many women were satisfied with their care, for example:

“The treatment and care I have received both in hospital and after-care has been second to none.” (U, 34 years)

“I met everyone who was treating me – specialist, radiographer, researchers and all spent time with me. This gave me confidence.” (U, 54 years)

“Treatment before, during and afterwards were excellent.” (U, 48 years)

However, others felt more negative. A recurring theme was the lack of knowledge that there seemed to be among health professionals about this treatment.

“Lack of information and choice – thoroughness differs from hospital to hospital. Always felt I was

walking in the dark. Treatment was not person centred but focused on symptoms only. Likely to see different doctors, registrars, surgeons in one hospital. No strategy for outcomes based on dates. Difference in opinions on treatments.” (U, 42 years)

“I was angry that it took 2 years to diagnose fibroids. I was angry that I had to fight so hard to see X, who I saw privately, in order to avoid his registrars etc, as these people had no clue about my pain, about how my life was being destroyed by heavy bleeding every single day or how to treat the condition. Giving a contraceptive pill was not the answer! I was angry that the first gynaecologist suggested a hysterectomy – she thought I had either endometriosis or adenomyosis or both, without due care and thought. Seven or eight years later I am still angry with the medical profession. UAE saved my life and without removing organs vital to my overall health (I was in my thirties) like my uterus.” (U, 44 years)

“I think that a gynaecologist should have also been involved when the initial operations were done. I was number xx in the country and I only saw Mr X, the UAE specialist. I think with hind sight, I should have asked a lot more questions, for example what will happen to my womb, are there likely to be further problems. Also after care, I was misinformed, on how well you are likely to be and also the pain/temperature etc. I am sure by now most of the misinformed information has now been corrected and mistakes that occurred at the beginning have now been sorted out.” (U, 50 years)

This last person suggests that “most of the misinformed information has now been corrected and mistakes that occurred at the beginning have now been sorted out”. Initially UAE was a new and experimental procedure carried out under research conditions and information about possible side-effects and outcomes was not readily available to the first patients undergoing the treatment. Now that 10 years have elapsed, more information is readily available and patients are, in general, more carefully counselled prior to their treatment.

### Women needed to do their own research

Because of the difficulty of lack of readily available and reliable information on UAE, many women had the treatment only by doing their own research and by pushing for it themselves.

“... But at the time I had to do my own research, and request a referral from my GP – I was not offered the treatment, only a hysterectomy – ‘You might as well have a hysterectomy seeing as you’ll be in the menopause anyway in a few years’ – which I felt was insensitive and condemning me to a major operation which I didn’t want.” (U, 50 years)



“The first consultant I saw gave me no choice but it would be a hysterectomy – at that time I felt it was like ‘taking a sledge-hammer to crack a nut’. I did some research and found out about UAE. I decided that I would prefer to have that done.” (U, 58 years)

“The gynaecologist department in the hospital did not advise me about UAE until I requested the process. This was confirmed by meeting women on the ward having hysterectomies who had fibroids and had not heard of UAE. I thought this was a bad policy.” (U, 55 years)

“Excellent – good job I was in the healthcare profession or I would now be without a uterus as my gynaecologist said this was the only solution.” (U, 44 years)

“I had to find out about UAE for myself. I very much resented the with-holding of this information.” (U, 53 years)

“If I had not heard about UAE on ‘Woman’s Hour’ I would not have known to ask about it when the consultant told me I needed a hysterectomy.” (U, 44 years)

This shows high motivation to find an alternative to hysterectomy.

In addition to the key perceived benefits of retaining body parts, and maintaining the *status quo* as far as possible, the other key reason for opting for UAE as opposed to hysterectomy for the treatment of fibroids was to preserve the chance of having children.

## Fertility

This section brings together elements from all of the others, and adds the further and highly emotionally charged dimension of whether or not the treatment has affected the ability to conceive. There was a range of responses regarding fertility, from women seemingly unaware that they might not be able to conceive when they try to; to people who are still hopeful of conceiving and are only starting to suspect that something might be wrong; to women who are upset and indignant, and who feel they have been misled by the medical profession regarding any continuing chance of conceiving.

The following women seem almost light-hearted about the likelihood of their conceiving. They clearly think it is possible, and is something that can be put off until wanted.

“Desperately hoping to have a child in next few years – not trying at present, just practising!!” (U, 36 years)

“Nothing was removed so I am still a whole woman, able if I choose to have a family.” (U, 34 years)

“I am in a relationship and take a progesterone contraceptive pill – just in case!” (U, 46 years)

The women whose responses are included next have begun to sense that something is not right, but are still unwilling to blame UAE explicitly for their subsequent inability to conceive.

“I now wonder whether UAE may have affected my chance of having children. It wasn’t such an issue at the time and a choice had to be made.” (U, 35 years)

“This treatment was a godsend to me as someone who is desperate for a baby, even though I haven’t been able to conceive in the last two years.” (U, 40 years)

“Very pleased with the outcome It would be very interesting if you could do more research on fertility chances in relation to UAE. In my case opting for UAE was very influenced by there being a chance that I would be able to get pregnant – this hasn’t happened but could be due to my age...” (U, 44 years)

Other women are more outspoken and direct about their lack of progress in conceiving.

“After my UAE treatment, I thought I would conceive, up to date, nothing has ever happened.” (U, 44 years)

“Disappointed it seems to affect my fertility – despite investigations showing no obvious reason.” (U, 45 years)

“Soon after UAE my periods ceased. I feel none of the treatments really helped my infertility. I was still unable to conceive and uterus still big even now that I have not had a period for a long time.” (U, 50 years)

Other women express anger at what they consider was misinformation on fertility issues prior to their treatment.

“REALLY NOT GIVEN ENOUGH INFORMATION ABOUT FERTILITY. Not given any information on the UAE treatment – was just told they were going to ZAP!” (U, 35 years)

“I would have liked to have been told more about what problems I am currently having about conceiving. We have been trying for a baby for 10 months and we were not told we would have this much trouble conceiving.” (U, 35 years)

“I decided to undergo the UAE treatment after reading an article in *The Guardian* because the procedure does not involve radical surgery. However the information on fertility after the procedure was unclear. This needs to be clearer for younger women who might wish to have a family.” (U, 50 years)

“I was upset to find out at a later consultation (approximately 1 year after the UAE) that the treatment was now considered a ‘contraceptive’ measure. This had not been explained to me at the time of the UAE and I was assured my fertility would

remain intact. I was informed by the gynaecologist later that it was 98% certain I would not be able to conceive. I should have been informed of the risks to my fertility at the time of the UAE.” (U, 46 years)

“I did not have fibroids when I was offered this treatment. I am now very concerned about my fertility and I am currently trying for a baby without any success. I was not properly informed at my consultation regarding the fact that it could prevent me having a baby.” (U, 31 years)

“I am worried that I may not be able to get pregnant as there wasn't much data at the time concerning this. I have been trying since the treatment with no success. Definitely concerned about the fertility aspect and would like to know if other women have gotten pregnant after embolisation. I don't have any children and worry I'm getting too old or that the treatment has affected my ability to conceive.” (U, 42 years)

These are very strong expressed feelings and there is clearly much resentment about the lack of full information that had been made available to them at the time of their decision-making. It should be pointed out that the advice at the time of their treatment was that women wishing to conceive should not undergo UAE and for some centres this was an exclusion criterion. Further study of post-UAE fertility is necessary.

## Discussion of UAE findings

For those for whom UAE worked well it was a positive, life-changing experience, and they could not speak too highly of it. The main positive responses were about the dramatic effect that UAE had on heavy and prolonged periods. Regaining a much more limited and predictable pattern of periods had enabled some women to start living life more fully. UAE had physical benefits in reduced pain and blood loss, psychological benefits in allowing a freer lifestyle and economic benefits in reducing the amount of sanitary supplies and clean clothes that needed to be bought.

For those who had not had such a successful outcome, problems centred on disappointment regarding lack of fertility, the continuation of symptoms and feelings about misinformation concerning the process and likely outcome of UAE.

### UAE is a process not a one-off event

UAE is multifaceted in its implications for women. The main broad dimensions of impact that were evident in this study were fertility, womanhood, pain and heavy blood loss and lifestyle, each of which has a range of subdimensions, and each has important subjective meaning to women in

addition to any objective measures that can be applied.

With these very important dimensions of impact that may need to be addressed both before and following the intervention, it is understandable that not all questions a woman may have will necessarily be voiced at one time. It is not possible to try to predict a woman's reactions to UAE, or even particularly straightforward for her to predict these herself. Also, as individuals' experiences of UAE are so varied, regarding levels of pain, period of recovery and how well it works, preparation can be difficult, as it is not clear what to prepare for.

Because of the time over which concerns emerge, and because of the range of important dimensions that are involved, it is important that UAE is regarded as a 'process' rather than a one-off event. Women need to be facilitated in thinking through the implications, and in voicing concerns at any point. There needs to be accessible support and information identified for women to refer to in the years following treatment: not just if they need further medical or surgical intervention, but regarding seemingly smaller issues.

### Fertility issues

As the main alternative treatment for fibroids was hysterectomy, it is inevitable that concerns about fertility would feature heavily in women's decision-making. This was the area where most dissatisfaction was expressed among those who had had UAE.

With hysterectomy there is no further chance of reproduction. With UAE there can be. Many of the women hoped that not only would UAE maintain their chance of reproduction, but that it would improve it. The picture is of women going into this procedure with trust and hope, but who were then left to discover over time that fertility after UAE is not guaranteed. Some expressed anger at what they consider was misinformation on fertility issues prior to their treatment.

It is vital to be realistic about the chances of improving or maintaining fertility following UAE, as this is both a key dimension on which decisions will be based, and an area where the potential for disappointment and resentment is high.

### Pain

Mixed messages are coming from the data. For some the experience of having UAE was painful, for others it was not. For some there was no pain in subsequent months, but for others levels of pain

were high. It is not possible to provide a simple message to those weighing up their options.

### **Clinical simplicity**

Measurements of the fibroids can be taken before the procedure, predictions can be made of likely reduction in size, and follow-up measurements can be taken to assess objectively what the technical outcome has been. The relationship between the change in size of the fibroids and the qualitative change in symptoms is neither direct nor guaranteed. This lack of fit needs to be made clear to patients, so that they do not develop unrealistic hopes, and so that their decision-making is not misled by ideas of proportionate improvements in symptoms.

The image of a defined reduction in size of the cause of their symptoms helps to present a clean picture of clinical embolisation as a neat and simple intervention that would have a proportionate effect on their symptoms. Information about size and shrinkage of fibroids needs to be presented not only mathematically but also in relation to the probable associated effects on symptoms.

### **The womb is not just to use but to have**

Feelings about retaining womanhood and keeping their body intact were expressed both by women keen to have children and by those who were not. The desire to retain the womb can go well beyond the need for it to be available to fulfil its technical role in pregnancy. This is a desire that impacts on decision-making and so should be included in the factors to be considered. However, women themselves cannot necessarily judge what their reactions will be following treatment. It would be useful to have available a collection of reflections of women who had undergone either UAE or hysterectomy so that women trying to decide what to do can hear the range of responses to each treatment.

### **Communication**

Many of the negative experiences reported by women who had UAE could be said to link with the over-arching theme of communication. To support effective and relevant communication in this area, health professionals need knowledge about the intervention and its effects, and they need to be receptive to the concerns and information needs of patients.

An important element to inform women's decision-making in this area is knowledge about possible outcomes. This can be gained only by

appropriate follow-up of patients. At the time when the women in this study had their UAE it was a relatively under-studied procedure without comprehensive data on outcomes. A recurring theme among responses was the lack of knowledge that there seemed to be among health professionals about this treatment. There are now studies that have looked further at outcomes, and the current study provides detailed follow-up data on a range of dimensions which can be used to inform future decision-making.

The main areas where women felt they were ill-informed were regarding the likelihood of becoming pregnant post-UAE, and the chances that they would need a further intervention if UAE was found to be only temporarily or not at all effective. The intervention and outcome of UAE are challenging to describe comprehensively and clearly without giving a long list of negative and positive possibilities.

### **Didn't work but I'd recommend it to others**

An apparent anomaly highlighted within the statistical analysis, which is also evident within the free-text data, is that many women for whom UAE had not worked did not regret having it, and would recommend it to others. This complicates the relationship between outcome and satisfaction, and shows that the decision-making process is neither straightforward nor objective.

It appears contradictory, but some women made it clear that, even though UAE had not worked for them, and they had to have a further UAE or a hysterectomy, they had been pleased to have taken the chance that it seemed to offer at the time. With women happy to have a further UAE, and saying that they did not regret having tried UAE before going for a hysterectomy, it becomes clearer why they would be able to recommend UAE to someone else, even though it had not worked for them. It also implies that the negative effects of UAE were for those women outweighed by the potential benefits it seemed to offer.

## **Conclusions**

The interventions of hysterectomy and UAE for the treatment of fibroids are two completely different procedures on many dimensions. It is a matter of personal preference what weight an individual would place at which point within each dimension. It can be difficult to make a reasoned and conclusive comparison as there are several

dimensions to take into account; individuals react very differently to various parts of the process and women may not be able to predict how they will react; there are both physical and emotional issues involved.

Presentation of comprehensive and reliable evidence is needed at the outset to inform the decision-making process and to avoid causing resentment and disappointment later on. Ideally this evidence would be a mix of quantitative and qualitative material.

Evidence on such subjects as likelihood of reduction in period length/pain, patterns of follow-up treatment needed and chances of becoming pregnant could be presented in tabular form. This could be backed up by free-text comment from individuals who had been through each of the kinds of outcome described, being careful to include both positive and negative comment where it existed.

Such comprehensive and diverse outcome evidence is needed because it is not simple to define what a successful outcome is. In the case of hysterectomy it is more straightforward as it is not complicated by further periods or by questions over fertility. With UAE it is much more complicated, and therefore important that the definition of a successful outcome is open to scrutiny. Ideally it would relate to different points in time following the intervention, and separately to different dimensions within the outcomes, such as early complication, further intervention needed, successful pregnancy and size of fibroid. Follow-up over a long period is needed, with scope for collection of qualitative as well as quantitative data.

A crucial element of the process is management of expectations. In the UAE cohort in particular there were several areas where expectations were unrealistically high. The challenge is to present balanced information that is not so full of caveats and different possibilities that it is of no use to women making their decision. The mixing of

quantitative data with personal reflection would be a way of easing an individual's way through weighing up the reality of different possible outcomes.

Because of the long-term nature of women's concerns and questions about the effect of their treatment, or their continued use of HRT, there is a clear need for continuing opportunities to ask questions. The balance of work between secondary and primary care, in facilitating and responding to questions, needs to be considered. Most of the questions that women had several years after treatment were questions that could be answered within general practice. Some, however, concerned details of the intervention, which they had not been given at the time.

The transition from secondary care back to primary care is an opportunity to facilitate the voicing of remaining questions about the intervention, and to explain the kinds of issues that could routinely be handled in primary care.

This study has collected the kind of quantitative and qualitative material that could usefully be communicated in lay language to someone considering the options for treatment for fibroids.

## **Key findings – free-text**

The free-text data indicated that many women, in both cohorts, felt that their treatment had been a complete success. In the UAE cohort there were several areas where expectations were apparently high, some women said that the outcome had not fulfilled their expectations. Disappointment was expressed mainly about continuation or return of symptoms. A particular concern was the low level of fertility experienced following UAE, and many women felt that they had been misled on this issue. Women's concerns and questions about the effect of their treatment, and their subsequent use of HRT, continued well beyond their contact with the hospital teams.

# Chapter 10

## Discussion

### Introduction

This study was an observational multi-centre retrospective cohort study of the safety and efficacy of two interventions for the treatment of symptomatic uterine fibroids. The standard treatment is the surgical removal of the uterus (hysterectomy) and the newer less invasive uterus-conserving treatment is UAE. We included an economic analysis to estimate the cost-effectiveness of UAE compared with hysterectomy using data from this study on longer-term outcomes. In addition, due to the complex nature of this treatment area, we included a qualitative analysis of free-text data derived from women's comments on the HOPEFUL patient questionnaire to enhance our findings further.

The results of the study represent the experiences of women who received their treatment according to available practice in the UK during the period 1994–5 for hysterectomy (VALUE<sup>50</sup>) and 1996–2002 for UAE. Eighteen NHS hospital trusts collaborated in this study (17 sites in England and one in Scotland). There were a total of 1734 eligible women traced, 972 received UAE as their index treatment and 762 received hysterectomy. The majority of the hysterectomy group underwent total abdominal hysterectomies (86.7%). The UAE group all underwent embolisation using PVA particles with size distributions in the ranges 250–355, 355–500 and 500–710  $\mu\text{m}$ .

This study was commissioned due to a lack of RCT evidence about the long-term efficacy and safety of UAE compared with surgical options for the treatment of symptomatic fibroids. Fully informed randomisation between major surgery, which terminates reproductive function, and an intervention which aims to deal primarily with the specific cause of symptoms while theoretically preserving fertility, is problematic. An alternative surgical comparison with UAE would have been against myomectomy, as the objective of that operation is to remove some or all of the fibroids, thus preserving the uterus and possible fertility. However, no such comparative cohort existed to study and the complication rates for myomectomy are considered to be similar to those for

hysterectomy. In the long term, however, myomectomy like UAE will be associated with some requirement for further fibroid treatments, in contrast to hysterectomy. In addition, myomectomy rates have been falling, making direct comparisons increasingly difficult. The question of whether myomectomy or UAE is the better option for women with fibroids who wish to retain their uterus remains unanswered. A randomised study looking at the efficiency, safety and fertility of these women needs to be undertaken and this is recommended in the NICE heavy menstrual bleeding guidelines.<sup>32</sup>

This study sought to collate systematically clinical data retrospectively from experience within the UK to provide comparable preliminary data in an unselected observational setting. A rigorous attempt has been made to compare directly benefits and costs of the two procedures (UAE and hysterectomy) where possible. At the time the study began, UAE was not routinely offered to women within the NHS due to this uncertainty about longer-term outcomes. However, it was available in over 50 centres in the UK with patients' consent for audit or research, primarily in London and south-east England.

UAE and surgery have since been subjected to randomised trials of short-term efficacy amongst women willing to be randomised, and are summarised in *Table 1*, pp. 14–15. Since the treatments are so different, with known differences in important outcomes, the population of women truly indifferent to all of these outcomes is likely to be small. A comparison between women who had no choice and were treated with hysterectomy and others who chose embolisation once it had become available is an important investigation at a time of declining hysterectomy rates.

### Methodological/design issues

The limitations of an observational retrospective cohort study design such as this are acknowledged. A prospective RCT of the two treatments would clearly provide the highest quality evidence to examine this question by minimising biases and allowing more direct pre- to post-treatment

comparisons to be made. However, recruitment to such trials in these circumstances is difficult and it would require a decade to achieve several years' follow-up on patients prospectively. The advantage of the current design is that it enables a large number of patients' longer-term experiences to be examined in order to contribute valuable data for informing decisions on recommendations for practice.

There are important methodological considerations to be addressed due to the retrospective study design. The first consideration concerns the comparability of the women in the two treatment cohorts at baseline. Without randomisation it is likely that the patients in the two treatment cohorts will differ in any of a number of ways that may have a confounding influence on outcome measures. Biases that are plausible in this study relate to the higher education and lower parity of the women choosing embolisation and the availability of choice in that arm. Moreover, this study has examined the results of UAE in a cohort of patients who were some of the first to undergo the procedure and may suffer from the initial limited experience of radiologists and possibly a more careful selection and follow-up of patients. Many of these differences have been adjusted in the analyses, but inevitably not all.

Analysis was performed using multiple logistic regression on the risks of complications, with predisposing determinants of risk (patient's age, previous illness, ethnic origin and obstetric history) as possible confounders. This method investigated the adjusted and unadjusted odds of complications for these *a priori* confounders. It is nonetheless impossible to be sure that this study does not suffer from residual unknown bias or selection. We have endeavoured, by rigorous design, protocol and analyses, to minimise these effects.

A second important consideration concerns the identification of relevant outcome measures that can be assessed in both cohorts retrospectively to allow a direct comparison between the two treatments. Clinical outcomes of relevance relate to both the safety of the procedures and the efficacy of the treatment to resolve or reduce symptoms. Because hysterectomy surgically removes the uterus and therefore the source of all fibroid symptoms, it is difficult to compare directly improvements in symptoms between the two interventions as the primary study outcome. Furthermore, the retrospective design means no pretreatment measures of QoL/symptoms are available to compare with post-treatment values in both groups.

Primary outcome therefore was a comparison of safety as defined by the complication rate. To overcome the issue of different treatment-specific complications, safety was assessed by clinical severity. Events were categorised into severe/major/minor *a priori* by the project team. Specific GSEs of treatment in the UAE group that may be anticipated were also investigated. Secondary outcomes related to treatment efficacy. Data were gathered retrospectively primarily by patient questionnaire on resolution of fibroid symptoms and satisfaction with treatment compared between treatment groups. In addition, further measures of efficacy in the UAE group only including fibroid/uterine size reduction, resolution of menstrual symptoms and any further treatments for fibroid symptoms were investigated. Additional issues of relevance to the UAE treatment group only were investigated, including factors influencing choice of treatment, factors influencing outcome of UAE treatment and fertility post-UAE.

## Results

### Baseline characteristics

Of the 1734 eligible patients, data were collected on 1108 (63.9%) consenting (or deceased) patients [Hyst  $n = 459$  (60.2%), UAE  $n = 649$  (66.8%)]. The average length of follow-up was 8.6 years (SD 3.4) for the hysterectomy cohort and 4.6 years (SD 2.0) for the UAE cohort. At least 2 years' follow-up was attained for 91.5% of the UAE cohort and 87.1% of the hysterectomy cohort and 5-year follow-up was available for 46.5% of the UAE group and 86.7% of the hysterectomy cohort.

As expected, the two cohorts presented a different baseline profile for many of the *a priori* confounders. These included educational level (UAE higher), ethnicity (UAE more ethnically diverse, but still with only a small number of non-white women in the cohort), parity (UAE more likely to be nulliparous), menopausal status (more post-menopausal women in the hysterectomy cohort) and smoking (less common in the UAE cohort). Medical co-morbidity was higher in the hysterectomy cohort, whereas the incidence of prior pelvic surgery was higher in the UAE cohort. Prophylactic antibiotics were more likely to be given to patients in the hysterectomy cohort.

In spite of all attempts to collect complete data, there were missing data items in one or more of the *a priori* confounding variables for 53.1% of the women, although there were less than 10% missing items in total. In order to utilise all the available

data, missing values were estimated using well-tested multiple imputation methods. These methods provide the most unbiased estimate of the main comparison available, since to exclude women with any missing data affects the precision enormously while also omitting subjects, which could bias the estimates.

### Primary outcomes (safety)

The crude incidence of *a priori* defined complications (severe, major or minor) was higher for the hysterectomy cohort (26.1 versus 17.6%). The crude incidence of severe/major complications was also higher for the hysterectomy cohort (11.3 versus 3.9%). The complication rates for hysterectomy found in the HOPEFUL study were found to be higher than those reported in VALUE.<sup>12</sup> The VALUE team carried out an ascertainment exercise to compare the data submitted by clinicians with a review of 1453 cases obtained from operating theatre records in randomly selected hospitals. Case note review suggested that forms submitted under-reported major operative haemorrhage and postoperative complications. In addition, the team validated 429 submitted forms against a random selection of patient notes. They discovered that reporting of operative complications was reasonably accurate, but that there was under-reporting of postoperative complications. As HOPEFUL used both patient records and questionnaires for data collection, complications are more likely to be complete and would be expected to be higher than for VALUE, which was an audit alone.

The OR for all complications for UAE versus hysterectomy was 0.48 (95% CI 0.26 to 0.89) after using multiple logistic regression and adjusting for significant confounders (at the 10% level), clustering by centre and missing values (by multiple imputation). This was importantly less than the crude OR. The odds for severe or major complications against minor or none was 0.25 (95% CI 0.13 to 0.48), again importantly reduced by adjustment for confounding. The extra risk of complications associated with hysterectomy is primarily associated with severe and/or major complications. Analysis of the actual complications shows that the excess in the hysterectomy group was mainly attributable to an increased incidence of the need for blood transfusion (7.4 versus 0.4%) and structural damage (3.5 versus 0.8%).

Multiple logistic modelling indicated that obesity and medical co-morbidity predisposed to complications in both groups whereas the use of prophylactic antibiotics was protective, especially

when analysing all complications. Patients undergoing UAE are more likely to experience minor complications if any.

Expected GSEs of UAE including chronic although self-limiting discharge, spontaneous fibroid expulsion and post-embolisation syndrome were reported by 32.7% of the women, with 8.9% of these additionally experiencing complications as defined above. The majority of the women with complications and related GSEs (4.0% of the total) suffered chronic discharge caused by disintegrating fibroids/infection, chronic discharge leading to assisted fibroid expulsion, or both. In total, 41.3% of the UAE cohort experienced some adverse effects (complications and/or GSEs) of their treatment, although most were GSEs that the patients were informed about prior to the procedure. The duration of these adverse effects varied from a few hours to persisting for several months. Multiple logistic modelling of GSEs for the UAE cohort, adjusting for complications and confounders, found that prophylactic antibiotics were also protective against GSEs, in addition to being protective for both cohorts against complications. GSE reporting varied widely between centres, probably due to some centres undertaking their own research and directly asking women specific questions about GSEs whereas others did not.

### Secondary outcomes (efficacy)

Secondary outcomes concerning efficacy were available retrospectively from patient questionnaires. The general health of both cohorts was similar at baseline. Of those women completing questionnaires, 75% of the hysterectomy cohort reported improved health status (average 9 years post-surgery) compared with 65% of the UAE cohort (average 5 years) ( $p < 0.0001$ ). Relief of fibroid symptoms (89 versus 80%,  $p < 0.0001$ ) and feeling better since their index treatment (81 versus 74%,  $p < 0.0001$ ) was also significantly higher for the hysterectomy cohort than the UAE cohort. However, paradoxically, only 70% of the hysterectomy cohort would recommend their treatment to a friend compared with 86% of the UAE cohort ( $p = 0.007$ ).

The expectations of the UAE cohort were less likely to be fulfilled (71% UAE versus 86% Hyst,  $p < 0.0001$ ), possibly due to the high expectations of women in the UAE cohort. There was no difference between the cohorts for reported problems (17% Hyst versus 18% UAE,  $p = 0.18$ ). From the free-text analysis of expectations not

fulfilled it is apparent that the management of expectations is particularly important for the UAE cohort. Many of the women are self-referred and have high, maybe unrealistic, expectations, some choosing UAE in the hope of achieving pregnancy.

Hysterectomy removes the uterus, thus completely resolving the fibroid-related symptoms. UAE may either technically fail, completely or partially resolve symptoms, or may only resolve them initially, with a possible recurrence of symptoms; 18.3% of the UAE cohort underwent one or more further fibroid treatments [defined here as further UAE (4.5%), myomectomy (4.9%) and hysterectomy (11.2%)]. After adjusting for differential time of follow-up using survival analysis to first further treatment, the UAE women had a 23% (95% CI 19 to 27%) chance of requiring further treatment for fibroids. Our observed further treatment rate of 23% is consistent with the EMMY<sup>34–36</sup> and REST<sup>33</sup> studies. The 11.2% hysterectomy rate is higher than in the US FIBROID registry, but their data have only been published to 12 months and there are other indications for hysterectomy that may not imply UAE treatment failure as many women have more than one coexisting uterine pathology, such as uterine fibroids and adenomyosis.

### UAE-only cohort

The main factor influencing choice of UAE was the desire to avoid a hysterectomy. The reasons for this include economic considerations (“can’t afford the time off work post-surgery”), social considerations (some social groups place great emphasis on uterine preservation), preservation of fertility (definitely want a pregnancy or wish to keep options open) and the desire for a less invasive alternative to avoid the complications of surgery and general anaesthesia. Some women also were aware of others for whom hysterectomy had been unsatisfactory.

Although UAE was a new procedure, and this study sample was taken at the beginning of its use, there was little evidence of a significant learning curve amongst the radiologists involved, all of whom were trained and experienced in procedures requiring similar skills.

There were 27 (4.2%) women who achieved one ( $n = 20$ ) or more ( $n = 7$ ) pregnancies post-UAE. The average age at pregnancy was 38 years (SD 3.3) at an average of 3 years post-UAE. Some 78% of these women were nulliparous and 74.1% expressed a wish to have any/more children. Of the total 37 pregnancies, there were no still births,

15 miscarriages, two ectopic pregnancies, one termination and 19 successful live-births [from 16 (2.3%) women], of whom 79% were delivered by Caesarean section, six due to complications of pregnancy or delivery. The observed high miscarriage rate (40.5%) is greater than expected for women of this age group. For women aged less than 35 years, the clinical miscarriage rate is 6.4%, for age 35–40 years it is 14.7% and over the age of 40 years it is 23.1% ([www.womens-health.co.uk/miscarr.asp](http://www.womens-health.co.uk/miscarr.asp)). However, it is comparable with miscarriage rates of 57.1% reported in women of this age with fibroids.<sup>84</sup>

### Health economics

UAE is a less expensive option than hysterectomy during the first year post-treatment when the fiscal and QoL costs of complications and GSEs are taken into account. The differences in costs and QALYs are eroded in subsequent years due to the additional cost incurred in the UAE arm associated with secondary treatments for unresolved symptoms or recurrent fibroids. UAE becomes more expensive than hysterectomy when younger women are treated due to the longer period prior to the menopause and the greater possibility of further treatments being required during that time. Improvements in QoL were small for both treatments.

The main difference between UAE and hysterectomy is that UAE conserves the uterus. A woman’s individual preference will affect the benefits and cost-effectiveness of her treatment. UAE is more cost-effective when a woman wishes to retain her uterus, but hysterectomy may be more cost-effective if she has a preference for its removal. The attitude of the individual woman towards the preservation of her uterus is likely to be the prime determinant regarding her choice of treatment for fibroids.

### Free-text data

The free-text data indicated that many women, in both cohorts, felt that their treatment had been a complete success. In the UAE cohort there were several areas where expectations were apparently high, whereas some women said that the outcome had not fulfilled their expectations.

Disappointment was expressed mainly about continuation or return of symptoms. A particular disappointment was the failure to become pregnant following UAE, and many women felt misled. But this was a cohort of women among whom the treatment of infertility was not the purpose. Whether that had been a stronger implicit purpose than was recognised is unknown,



indeed there is evidence that the expressed intention to become pregnant would have been a contraindication (*Table 3*, p. 20). Women's concerns and questions about the effect of their treatment continued well beyond their contact with the hospital teams, in particular whether subsequent use of HRT would encourage return of fibroid symptoms.

### **Interpretation**

Embolisation is less invasive and involves a shorter recovery time than hysterectomy. The uterus is preserved and hence also the potential for future fertility. However, after adjusting for differential time of follow-up using survival analysis to first further treatment, the UAE women had up to a 23% (95% CI 19 to 27%) chance of requiring further treatment for fibroids. The short-term unpleasant anticipated side-effects of the treatment, reported by 32.7% of UAE patients in this study, also requires consideration.

The crude incidence of prior defined severe, major and minor complications was higher in the

hysterectomy group. The possibility of further reduction of complications and GSEs by wider use of prophylactic antibiotics is raised, but further work is required before a definitive statement about antibiotics can be made.

There were insufficient data in this study to enable us to determine whether any particular groups of women or types of fibroids are more at risk of failure of embolisation, although the US Registry has suggested that submucosal fibroids respond best to UAE, particularly as a cause of menorrhagia. This does not mean, however, that fibroids in other anatomical sites will not respond.

UAE is a less expensive option for the health service compared with hysterectomy even when the fiscal and QoL costs of complications and further procedures are included. The balance of improvement in QoL for UAE or hysterectomy overall is small and is likely to rest with the woman and her attitudes towards the resolution of fibroid symptoms and the preservation of her uterus.



# Chapter 11

## Conclusions

### Introduction

This study was an observational multi-centre retrospective study of the safety and efficacy of two interventions for the treatment of symptomatic uterine fibroids. UAE was compared with the standard of hysterectomy treatment. Any possible biases due to using this methodology were minimised by rigorous design, protocol and analyses. Statistical adjustment for known and suspected confounders, clustering by centre and adjustment for missing values (using multiple imputation) resulted in an improvement of the estimated relative benefit of UAE over hysterectomy in terms of safety. Although further treatments were required by up to 23% of women post-UAE (11% had hysterectomies), women prefer to be given the choice of uterus-conserving treatment.

This study provides comparable medium-term follow-up for the two cohorts. There may remain unidentified biases in the comparison that may affect the outcome. UAE was a new treatment at the start of the study period whereas hysterectomy was well established. The careful follow-up of women post-UAE may have been more assiduous than post-hysterectomy with more concern for their long-term welfare. Hence this comparison may be on the conservative side, and whatever biases remain may tend to underestimate the relative benefit of UAE compared with current routine practice.

For women with fibroids, complications are less common when treated with UAE compared with hysterectomy, although treatment failure is possible after embolisation, either due to non-resolution of symptoms or to recurrence of fibroids. Women are enthusiastic about both treatments after the procedure, although some post-UAE women in this study were disappointed since their (possibly unrealistically high) expectations were not met. In the longer term, both treatments are safe and no unexpected problems were detected for embolisation after a long follow-up period (average 5 years). The cost-effectiveness analysis favours embolisation even after taking account of complications, expected side-effects associated with the procedure and

subsequent re-treatments for women with a preference for uterus preservation. For younger women the cost to the NHS may become slightly more than for hysterectomy due to the longer period prior to the menopause and thus the increased potential requirement of further fibroid treatment.

The evidence from this study is that UAE is more cost-effective than hysterectomy and the results of the trial support the provision of information about UAE to women with symptomatic fibroids whose symptoms are not managed with medical therapies. Comprehensive advice about side-effects and other consequences of the treatment choice should be provided and monitoring put in place to enable women's questions to be addressed. Women would benefit from seeing interventional radiologists in an outpatient setting both before and after UAE treatment.

### Implications for healthcare

#### Safety

Even after adjusting for confounding, clustering by centre and missing values women treated with UAE rather than hysterectomy for symptomatic fibroids had half the odds of having a complication following treatment (odds of UAE versus hysterectomy 0.48, 95% CI 0.26 to 0.89). When considering only the severe/major complications, the OR was reduced to one-quarter (0.25, 95% CI 0.15 to 0.43). The extra risk of complications for hysterectomy is primarily associated with the severe/major complications, mainly attributed to blood transfusions and structural damage. Multiple logistic modelling indicated that women who were obese or had pre-existing medical co-morbidity were more likely to suffer from complications while prophylactic antibiotics were protective against complications.

A significant proportion of women experienced GSEs post-UAE (32.7%). It is suggested that the use of prophylactic antibiotics may reduce this proportion. The chances of further fibroid treatment is also non-trivial (23%, 95% CI 19 to 27%, after adjusting for differential follow-up

time), but for women wishing to retain their uterus this may be a risk worth taking, particularly as the morbidity associated with the procedure is lower.

### Cost-effectiveness

The HOPEFUL study has enabled the probabilities of complications, side-effects and further treatment to be calculated for women with symptomatic fibroids treated either by UAE or hysterectomy with a medium-term follow-up of at least 2 years (UAE average 5 years, hysterectomy average 9 years). In addition, evidence of costs and utilities from other studies have been incorporated into the cost analysis and show that UAE is a less expensive option to the health service compared with hysterectomy, even after the fiscal and QoL costs of complications and further procedures are taken into account.

The overall medium-term aggregate costs of UAE are less than for hysterectomy, particularly for older women, and the benefits are equivalent. For women, the immediate inconvenience associated with UAE is substantially less than for hysterectomy. There is a theoretical possibility that the minimally invasive nature of UAE will lead to a lower threshold for treatment which might lower the net gain in QoL. However, there is no indication that the present policy of offering UAE to patients who might benefit from hysterectomy will change in the future. This aspect needs careful monitoring, however. The possibility of younger women being treated for symptomatic fibroids would lead to a higher comparative cost for these women than for no treatment or hysterectomy due to the possibility of recurrent symptoms over time, requiring further treatment prior to menopause.

The QoL implications in the short term are also predicted to favour UAE due to the less invasive nature of the procedure and the lower complication rate, although these differences are small. However, this advantage may be eroded over time as up to 23% of women undergo additional procedures to deal with recurrent fibroids. In particular, in younger women who are exposed to the risk of recurrent fibroids and subsequent additional procedures over a longer period, UAE may no longer be as cost-effective, although this would depend on the QoL placed by an individual young woman on uterine preservation.

Overall, the balance of whether UAE improves QoL is likely to rest with the woman and her attitudes towards the resolution of fibroid symptoms and the preservation of her uterus.

Even a small desire to retain the uterus gives rise to a net improvement in QoL associated with UAE. Given the standard of hysterectomy treatment for this condition, offering women UAE as an alternative treatment for fibroids is likely to be highly cost-effective for those women who prefer womb-conserving treatment. For a strong preference the choice is unequivocal.

### Communication/information

Women who have had UAE are currently self-selected but the level of satisfaction is high for symptomatic fibroids and particularly in younger women this choice is sensible. This trial suggests that UAE therefore should be considered to be among the options offered to women seeking treatment for their fibroids. It is important to improve the management of expectations, particularly regarding fertility following UAE. Reliable evidence of short-, medium- and long-term outcomes and of treatment failure is needed to inform decision-making and to avoid causing resentment and disappointment later on. The challenge for the future is to present information that is balanced, but not so full of caveats and uncertainty that it is of little use to women making their decision.

To complement the statistical analysis, the free-text comment provided insight into the nature and strength of the women's concerns, and into the range of feelings about both positive and negative outcomes. Most of the problems, disappointments and sometimes angry comments could be addressed by improved communication rather than by anything more expensive or radical in terms of change of practice. The way in which participants described their experiences showed that, for them, the intervention was not an event, but a process, and this needs to be reflected in the communication strategy in this area. Because of the long-term nature of the effects of each of these interventions, the balance of support between work in secondary and in primary care needs to be considered, so that women know where their first line of communication is at all points. Women would benefit from seeing interventional radiologists in outpatients both before and after UAE treatment.

Examples of issues that participants in this study worried about, which could be handled effectively in primary care if anticipated, were the practicalities of using HRT and worries about developing ovarian cancer. Both of these issues need to be introduced within the process of decision-making, but follow-up queries could be handled within primary care, if the handover of

responsibility from secondary to primary care is clearly signposted. It is important that the economic drivers for providers to propose UAE rather than hysterectomy for women with symptomatic fibroids, do not take advantage of a woman's desire to have children, by including retained fertility as one of the key differences between the two interventions. Full information on success and failure rates needs to be examined and made available.

### Impact on NHS

Our results concur with the recommendations of the NICE Clinical Guidelines on Heavy Menstrual Bleeding,<sup>32</sup> which states that women with fibroid symptoms should be given a choice of treatment options, including embolisation. Exactly which women will benefit most from UAE will depend on subsequent research to define more precisely the characteristics of the fibroids most amenable to treatment. Changes in treatment patterns may have an impact on resources, particularly a reduction in the need for surgical beds for fibroid-related hysterectomy.

### Implications for further research

In the absence of large RCTs, this study adds to the current literature by confirming the medium-term safety of UAE because this study has greater than 12 months' follow-up for almost all of the 1108 patients (some as much as 10 years). This provides large enough numbers to collect data on complications and even on rare events, which is a recognised lack in RCTs. On reading the methods of the REST<sup>33</sup> and EMMY<sup>34–36</sup> trials, they both planned to recruit more patients than they were able to and this is an inherent problem with RCTs, particularly for preference-laden treatments. HOPEFUL also provides solid data to generate hypotheses. These are vital questions for women with fibroids.

### Who will benefit from UAE?

Conclusions regarding which subgroups of women will be treated most successfully by UAE (size, position and number of fibroids) are not possible from this study. It has been suggested that sub-6-cm submucosal single fibroids causing menorrhagia respond best to embolisation (US Registry<sup>38–41</sup>). However, this has not been adequately tested against fibroids in other anatomical locations, of different sizes causing menorrhagia with or without bulk symptoms. Indeed, the possibility of important effect modification according to the type of symptoms,

ethnicity, age and expectation of women remains unclear. This would have important implications when informing patients, and for health economics.

### What techniques are the most useful?

The best method of achieving effective embolisation is also still not clear, with a number of different agents being used which vary from being relatively cheap (gelfoam) to very expensive (spherical particles). At the time of the HOPEFUL study, all women were treated with traditional PVA particles, occasionally with the addition of coils or gelfoam. There is much discussion amongst radiologists as to whether using expensive microcatheters is the best way to avoid arterial spasm, which may cause inadequate embolisation and complications. Randomised studies would be useful to determine the optimal UAE technique. In addition, comparison between treatments for women who are amenable to myomectomy or UAE requires investigation, particularly if the expectation of uterus retention among women with fibroids increases.

### What advice can be given to women who desire future fertility?

The true likelihood of pregnancy and live-births could not be addressed reliably in the current study design. Our observations suggest that live-births after UAE are possible, but the actual probabilities and factors that allow some to carry a pregnancy to term and others to either not conceive or miscarry early remain poorly understood. The role of embolisation in the infertile patient, particularly those who are undergoing *in vitro* fertilisation, is important. Unpublished data from the EMMY trial suggest that ovarian dysfunction attributable to embolisation is comparable to that of hysterectomy [Meeting of Cardiovascular and Interventional Radiology Society of Europe, CIRSE, Rome, 2006, personal communication AN (HOPEFUL) and J Reekers (EMMY, Amsterdam)].

The joint RCR/RCOG guidelines<sup>31</sup> suggest that UAE should not be offered to women desiring pregnancy. Although appearing high, the miscarriage and Caesarean section rates in HOPEFUL are in line with those expected for women with fibroids in this age group. The number of successful full-term pregnancies in this study suggests that further investigation in this area is warranted, and this is also recommended by the NICE clinical guidelines on heavy menstrual bleeding.<sup>32</sup> This may lead to a review of the current cautious advice. Moreover, it is

interesting that four patients had both miscarriages and live-births, suggesting further that prior UAE may not be a cause of early miscarriage. Randomisation between myomectomy and embolisation could determine the more cost-effective and successful option in this group, and among those women with fibroids about to undertake expensive *in vitro* fertilisation therapy.

### **What role do prophylactic antibiotics have in UAE?**

The role of antibiotics in the prevention of side-effects has strong support from this study, but the results should be viewed with caution. Although there is strong evidence for single-dose antibiotics reducing infection rates after Caesarian section,<sup>85</sup> such evidence does not exist elsewhere, and single perioperative dose regimes are contrary to standard antibacteriological theory. The fact that antibiotics in this study reduced both the infection rate and the incidence of GSEs suggests that other variables might play some part. It is clear in this study that the use of antibiotics is highly confounded with centre, since each centre had a specific policy on its use. The uncertainty that remains warrants randomised trials into these issues since the potential for reducing side-effects and the expected consequences of rendering fibroids necrotic may be important.

### **What are the effects of HRT use after UAE on recurrence of fibroid symptoms?**

Our free-text analysis suggested that a common question amongst women after UAE is whether using HRT would lead to recurrent fibroid symptoms. Currently patients are advised against the use of HRT as its effects after embolisation are unknown. Further research is warranted to help clarify this question.

## **HOPEFUL study conclusions**

The ability to recommend a recently developed less invasive procedure for fibroids has been hampered by a paucity of longer-term comparative data. This study has contributed to reducing that uncertainty using a pragmatic study design incorporating ethical methodology to

minimise biases where possible. The women who underwent UAE and their outcomes reported here represent experience of the very early days of the new procedure so may provide conservative results. The evidence that we have accumulated strongly suggests that UAE is a safe procedure over the medium term, with fewer significant complications than hysterectomy, and has an important role in the effective treatment of symptomatic fibroids. We have highlighted several residual areas of uncertainty that require resolution before its place among the treatment options can be established. Research and monitoring protocols to answer some of the important outstanding uncertainties will also need to be established, in particular whether there are any fibroid characteristics which are less appropriately managed with this technique and whether the troubling side-effects experienced by one in three women having this procedure can be reduced.

Although one in four women may require subsequent treatment for fibroids, UAE still remains cost-effective, although less so for younger women. While this procedure permits preservation of fertility, caution needs to be exercised with regard to counselling women still desirous of pregnancies, and further research into this issue is needed.

There may be implications for the health service arising from this study. Offering women with fibroids UAE as one of their treatment options is likely to increase the demand for the provision of interventional radiology services and reduce the demand for surgical beds.

This study was not randomised because a large randomised study was not feasible. Hence, representing contemporary practice as well as possible, the aggregate conclusions are as robust as they can be at this stage. The place for UAE in the treatment of symptomatic fibroids may change as a result. It is therefore important that comprehensive advice be made available to all women with fibroids, based on these and other data. This study provides information that enables clinicians to counsel patients more accurately.



## Acknowledgements

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This study would not have been possible without the valued contributions of the women who allowed us to collect information from their hospital records and gave their time to share their experiences of their fibroids and treatments. We thank them for enabling us to extend our knowledge in this area. We would particularly like to thank Ginette Camps-Walsh, FEMISA, for her valuable input in constructing and piloting the patient questionnaire and other documentation.

### HOPEFUL study team

Nuffield Department of Obstetrics and Gynaecology, University of Oxford staff at the Oxford Coordinating Office contributing to the HOPEFUL Study: Klim McPherson (Chief Investigator), Allison Hirst (Project Manager/Researcher), Susan Dutton (Project Statistician), Sue Boyt (Project Secretary) and Lara Waldenmaier (Project Secretary/Qualitative Researcher).

Other members of the HOPEFUL study team: Mike Maresh and Tony Nicholson were part of the HOPEFUL study project team attending all project meetings and trial steering committee meetings and were responsible for the clinical content of the study for the hysterectomy and embolisation cohorts, respectively.

### Contribution of authors

Allison Hirst (Project Manager/Researcher) contributed to the design of the study, data collection forms and questionnaires, managed the conduct of the study including administration of all aspects relating to the collaborating centres, carried out the evidence literature review, contributed to the analyses and interpretation of the data and was primarily responsible for writing all sections of the report in conjunction with Susan Dutton (Project Statistician). Susan Dutton contributed to the design of the data collection forms, created and managed the study database including input of all data and its validation, analysed all the data and wrote the statistical methods and results chapters. She contributed to writing the discussion, conclusion and summary chapters of the report in conjunction with Allison Hirst. Susan Dutton and Allison Hirst incorporated the peer-review comments into the revised final version of the report. Andrew Briggs and Olivia Wu (Health Economics, Glasgow) carried out all economic analyses and wrote Chapter 8. Lara Waldenmaier (Project Secretary/Qualitative Researcher) carried out the free-text data analyses with Carol Edwards (Leicester and 'Qualitative Focus') and both wrote Chapter 9 and other qualitative sections of the report. Lara Waldenmaier also carried out the database validation. Klim McPherson (Visiting Professor of Public Health Epidemiology), Mike Maresh (Consultant Gynaecologist) and Tony Nicholson (Consultant Interventional Radiologist) conceived the study, contributed to the conduct of the study and the interpretation of data and contributed to the initial drafting of the discussion and conclusion parts of the report. Mike Maresh and Tony Nicholson also provided advice on clinical aspects relating to the treatments.







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## Appendix I

UAE collaborators: for each centre the lead clinician (principal investigator) and researcher/research nurse are acknowledged

Hospital centre (HOPEFUL Centre Code)	Local principal investigator (PI)	Researcher/research nurse
Glasgow Royal/Gartnavel General Hospitals, Glasgow (21)	Mr John Moss	June Innes
Guy's and St Thomas' Hospital, London (22)	Mr John Reidy	Marlene Anodu/Stephen Thomas
Hull Royal Infirmary/York Hospitals (23)	Mr Steve Killick	Teresa Doto
Royal Berkshire Hospital, Reading (24)	Mr Peter Torrie	Mary Wyman
Royal Free Hospital, London (25)	Mr Neil Davies	Mina Karamshi
St George's Hospital, London (26)	Ms Anna Belli	Nassera Banu
Southampton General Hospital (27)	Mr Nigel Hacking	Carol Gough/Sanchia Triggs
The Churchill Hospital, Oxford (28)	Mr Nigel Cowan	Allison Hirst/Sue Dutton
Royal Surrey County Hospital, Guildford (29)	Mr Woody Walker	Rose Nielsen
Countess of Chester Hospital (30)	Mr Gian Abbott	Jackie Blundell/Maria Stokes



## Appendix 2

Hysterectomy collaborators: for each centre the lead clinician (principal investigator) and researcher/research nurse are acknowledged

Hospital centre (HOPEFUL Centre Code)	Local principal investigator (PI)	Researcher/research nurse
Blackpool Victoria Hospital (01)	Mr Frank Wilcox	Adele Whitehead/Dee Inott
Countess of Chester Hospital (02)	Mr John Williams	Jackie Blundell/Maria Stokes
Derby City Hospital (03)	Mr Howard Jenkins	Jeanette Steward/Keeley Anderson
Gloucestershire Royal Hospital (04)	Mr Mike Read	Sarah Devereux
King George Hospital, Ilford (05)	Ms June Swinhoe	Lesley Polak/Dr Sita Sahoo
Leicester General Hospital (06)	Mr Philip Kirwan	Gillian Walden/Katie Peck
Norfolk and Norwich Hospital (07)	Ms Katherine Stanley	Jill Tinsey
Royal Hospital, Chesterfield (09)	Mr Philip Tromans	Louise Wood
Bradford Royal Infirmary (12)	Ms Sian Jones	Diane Farrar/Maureen Jones/Anne Bates





## Appendix 3

### Trial steering committee members

- Dr Nick Chalmers (Chair) (Radiologist, Manchester Royal Infirmary)
- Dr Mary Ann Lumsden (Division of Developmental Medicine, Reproductive and Maternal Medicine, Glasgow Royal Infirmary)
- Mr Enda McVeigh (Nuffield Department of Obstetrics and Gynaecology, John Radcliffe Hospital, Oxford)
- Dr David Shepherd (Radiologist, The Royal Bournemouth Hospital)
- Professor Doug Altman (Methodologist/ Statistician, Centre for Statistics in Medicine, Oxford).



## Appendix 4

### Initial patient contact letter

#### UAE version

**LOCAL CENTRE  
HEADED PAPER**

May 2004 – version 2

Hysterectomy Or Percutaneous Embolisation For Uterine Leiomyomata:  
HOPEFUL Project

Dear Ms OTHER,

We are writing to you about a research project that is being carried out by the University of Oxford looking at women's experiences of their treatments for uterine fibroid symptoms.

You will recall that when you underwent your fibroid embolisation treatment with us you gave consent for us to keep your details on our clinical database. This was because the technique of fibroid embolisation was so new that we needed to collect as much information as possible about how effective a treatment it is and how safe it is. We are now working with the University of Oxford HOPEFUL Project which has been asked by the Health Technology Assessment (HTA) unit of the Department of Health (DoH) to look at the safety and effectiveness of uterine artery embolisation and to compare it with hysterectomy which has been the standard treatment for fibroids.

We enclose a patient information sheet for you with details of the HOPEFUL Project and are asking for your consent to allow a special research nurse to reexamine your hospital record. She will be collecting details from many other similar patients. We will also be sending a questionnaire to you asking about your treatment for your fibroids and other related health questions.

If, after reading the information sheet, you are happy to give permission for your hospital notes to be examined please sign and return the consent form in the stamped addressed envelope provided.

Thank you very much for your help.

Yours sincerely

CONSULTANT RADIOLOGIST

## Hysterectomy version

**LOCAL CENTRE  
HEADED PAPER**

May 2004 – version 2

Hysterectomy Or Percutaneous Embolisation For Uterine Leiomyomata:  
HOPEFUL Project

Dear Ms OTHER,

We are writing to you about a research project that is being carried out by the University of Oxford looking at women's experiences of their treatments for uterine fibroid symptoms.

You may recall that when you underwent your hysterectomy with us you consented to your details being kept on a clinical database. This was because you had the surgery in one of the hospitals participating in a national audit of all hysterectomies during a 1 year period between 1994 and 1995. Since you had your operation, a new radiological treatment for treating fibroid symptoms has emerged. This is called uterine artery embolisation (UAE). We are working with the University of Oxford HOPEFUL Project which has been asked by the Health Technology Assessment (HTA) unit of the Department of Health (DoH) to look at the safety and effectiveness of this new treatment and to compare it with women who were treated with a hysterectomy.

We enclose a patient information sheet for you with details of the HOPEFUL Project and are asking for your consent to allow a special research nurse to reexamine your hospital record. She will be collecting details from many other similar patients. We will also be sending a questionnaire to you asking about your treatment for your fibroids and other related health questions.

If, after reading the information sheet, you are happy to give permission for your hospital notes to be examined please sign and return the consent form in the stamped addressed envelope provided.

Thank you very much for your help.

Yours sincerely

CONSULTANT GYNAECOLOGIST

# Appendix 5

## Patient information sheet

The HOPEFUL Study “Hysterectomy Or Percutaneous Embolisation For Uterine Leiomyomata?”  
Patient Information Sheet (12th January 2004 – version7)



### The HOPEFUL Study: UAE (Uterine Artery Embolisation) versus Hysterectomy for symptomatic fibroids

Fibroids cause considerable health problems in 25% of white women aged in their 40s, and occur 2–3 times as frequently in Afro-Caribbean women of similar age. Studies have found that women who have fibroids often have a family history, and that fibroid growth is linked to hormone stimulation. When drug therapy fails, women are commonly offered a hysterectomy (or less commonly – myomectomy, which is the surgical removal of their fibroid/s) or, since 1995, uterine artery embolisation (UAE).

Fibroid embolisation is considered a safe procedure, designed to improve a woman’s symptoms and save her having a larger operation. The majority of women treated with UAE are pleased with the results and most fibroids are shrunk to about half the size they were before. But the exact cause for fibroid development and long term effects of UAE are still unclear. The effects on women’s lives in the longer term are also poorly understood.

The HOPEFUL Study based at the University of Oxford is the first UK study to evaluate a novel radiological treatment for bothersome fibroids (embolisation) against the commonly performed gynaecological intervention (hysterectomy), and we hope that the results will benefit many thousands of women in the future.

We invite you to take part in the HOPEFUL Study because you are one of 2,000 women who had fibroids which were managed by one of the two treatments, either:  
Hysterectomy – the whole womb (uterus) is removed, usually with the cervix; this is the commonest gynaecological operation, and about 100,000 are carried out in England and Wales each year; or  
Uterine Artery Embolisation (UAE) – a new way to treat fibroids by blocking off the arteries that feed the fibroid(s), causing it to shrink and become trouble-free; over 10,000 of these have been performed across the world since its introduction in the mid 1990s.

Your participation is voluntary and you are free to withdraw from the study at any time, without giving a reason for your decision, and without your medical care or legal rights being affected. If you decide to withdraw at any point during the study we will not use any of your data obtained up to that point in our study.

Hysterectomy is effective, but clearly may sometimes be considered as too radical. In comparison, UAE treatment is a less invasive procedure: it preserves the uterus, women spend far less time in hospital and can return more quickly to work in or outside the home. However, sometimes complications occur, the fibroid(s) reappear or become bothersome again, and further treatment may be needed – either

repeat embolisation, or hysterectomy. A proper comparative evaluation of the UAE treatment for bothersome uterine fibroids, as a clinical alternative to hysterectomy, is very important.

#### **Why did we begin the study?**

It is essential for a woman and her doctor to have the best possible information about different treatments, so that the best decisions can be made. In this study, research will help us (women, doctors and researchers) to find out whether there are any differences in the effect of treatments, what those differences are, and how they might affect health. In the future, a woman with bothersome fibroids and her doctor should be able to use the information from this study to decide which treatment would be best for her. If you agree to participate, you will know that you will be helping other women to make informed decisions about their treatment.

We are working in close cooperation with 20 hospitals throughout the country, known to treat the highest number of bothersome fibroids. The study will be completed by mid-2006.

#### **What do we ask you to do?**

We ask you to complete a concise postal questionnaire about your health, and about what might affect your health. We are interested in your satisfaction with the treatment you received, your related preferences, choices, experiences and expectations before and after your treatment for fibroids. It is important to know whether you needed to go back to hospital as an inpatient or outpatient (for whatever reason), and whether you had/have any specific complications. We would like to know about the number of children you have had, your smoking habits, because these can contribute to your lifestyle, which in turn may affect your general health. The questionnaire may take up to 30 minutes to complete and you are not obliged to answer every question.

We would also like to ask for your written permission for one of our research nurses to inspect your hospital records to give us the best possible understanding of how you have recovered and benefited from your treatment. In some cases hospital records may be unavailable. In this situation we will use some basic clinical information on your hysterectomy surgery that was provided at the time of the original VALUE study and is already held by the VALUE study researcher working with this project (Mr Michael Maresh). By signing the accompanying Consent Form (January 2004 – version 4) you are giving our researcher permission to do this.

#### **Security and confidentiality**

We are all bound by absolute confidentiality, and all staff working on the study have signed a confidentiality form. Your forms and questionnaires are kept in locked cupboards or filing cabinets in locked rooms. You are identified on the computer by only a Patient ID number (which is on the letter accompanying this summary sheet). In a completely different database we have your names and addresses so that we can write to you. Only the team members have password-protected access to the information you send us. When we analyse what you have told us, everyone is grouped together and nobody can be identified as an individual.

#### **Our funders and our staff**

We thank the Department of Health, Health Technology Assessment, for funding the project and the 20 collaborating hospitals for their interest and participation. We work under the guidance of Professor Klim McPherson, Professor of Public Health Epidemiology at the Nuffield Department of Obstetrics and Gynaecology, University of Oxford. Professor McPherson has undertaken medical research for over 20 years including looking at the use of surgery, oral contraceptives and HRT on women's health.

Our close collaborators are Dr Michael Maresh, Consultant Gynaecologist from the St Mary's Hospital for Women and Children in Manchester, as the representative of the Royal College of Obstetricians and Gynaecologists, and Dr Anthony Nicholson, Consultant Radiologist from Leeds General Infirmary, representing the Royal College of Radiologists.

A FREEPHONE telephone line in the Study centre in Oxford will be available for all your questions, comments and complaints. This number will be clearly given on the patient questionnaire. The staff

working on the study will be happy to provide you with all requested information, including the study results as soon they become available.

We cannot carry out this important study of women's health without your help and we would be very grateful if you would agree to complete our questionnaire and consent to the review of your hospital notes.

You will be sent the patient questionnaire following our receipt of your consent for the study. At that time a FREEPOST envelope will be enclosed for its return for your convenience, and if needed, we shall remind you about the reply on two occasions – two and four weeks after the initial mailing. We look forward to your positive reply.

Two copies of the consent form are provided here and we would be grateful if you could sign both copies keeping one for yourself and returning the other to us in the FREEPOST envelope provided.

*THANK YOU*

HOPEFUL Study

*If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms should be available to you.*





# Appendix 6

## HOPEFUL consent form

The HOPEFUL Study “Hysterectomy Or Percutaneous Embolisation For Uterine Leiomyomata?”  
 Consent Form (January 2004 – version 4)

### The HOPEFUL Study

Prof. Klim McPherson, Dr Michael Maresh, Dr Anthony Nicholson



CONSENT FORM

Patient ID:

**Please tick boxes as appropriate.**

- a) I confirm that I have read and understand the information sheet (12th January 2004 – version 7) for the above study and have had the opportunity to ask questions.
- b) I agree to take part in the HOPEFUL study. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
- c) I understand that parts of my medical hospital notes will be reviewed by a research nurse employed on the study. I give permission for this person to have access to my records.
- d) I agree to the University of Oxford recording and processing information about me. This information will be held and processed for the following purpose: The HOPEFUL Study only.
- e) I understand that this information will be used only for purposes set out in the statement above, and my consent is conditional upon the University of Oxford complying with its duties and obligations under the Data Protection Act.

\_\_\_\_\_  
**Name of Patient**

\_\_\_\_\_  
**Date**

\_\_\_\_\_  
**Signature**

\_\_\_\_\_  
**Researcher**

\_\_\_\_\_  
**Date**

\_\_\_\_\_  
**Signature**



## Appendix 7

### Cause of death recorded on death certificates

Treatment	Cause of death (certificate)	Years since treatment	Age at death (years)
<i>Cardiac causes</i>			
Hyst	I(a) Myocardial infarction	0.62	54
	II Left cerebral vascular accident (L-CVA)		
Hyst	I(a) Intraventricular haemorrhage	1.3	49
	(b) Hypertension		
Hyst	I(a) Ventricular fibrillation	2	66
	(b) Myocardial infarction		
	(c) Hypertension		
	II Hypothyroidism (treated)		
Hyst	I(a) Ischaemic heart disease	3.3	89
Hyst	I(a) Myocardial infarction	7.1	70
	(b) Ischaemic heart disease		
	II Transitional cell carcinoma of the bladder		
Hyst	I(a) Multi-organ failure	7.9	50
	(b) Pulmonary embolism		
	II Ischaemic heart disease		
	Diabetes mellitus		
Hyst	General old age and heart failure (clinical notes only)	9.7	82
<i>Cancer</i>			
Hyst	I(a) Bronchogenic carcinoma	2	50
Hyst	I(a) Metastatic carcinoma	2.1	52
	(b) Carcinoma of breast		
Hyst	I(a) Carcinomatosis	2.9	75
Hyst	I(a) Stomach carcinoma	3	48
Hyst	I(a) Metastatic carcinoma of lung	4.6	49
Hyst	I(a) Carcinomatosis	5	59
	(b) Carcinoma of breast		
Hyst	I(a) Metastatic carcinoma of breast	5.3	80
Hyst	I(a) Metastatic melanoma	6.3	53
Hyst	I(a) Carcinomatosis	6.4	54
	(b) Carcinoma of breast		
Hyst	I(a) Metastatic colon carcinoma	7.6	52
Hyst	I(a) Metastatic carcinoma of lung	8.5	56
Hyst	I(a) Metastatic carcinoma of endometrium	8.9	51
UAE	I(a) Metastatic uterine sarcoma	2.4	43
UAE	I(a) Carcinomatosis – adenosarcoma of endometrium	4.9	53
UAE	I(a) Carcinomatosis	Unk	50
	(b) Carcinoma of duodenum		
UAE	I(a) Carcinomatosis	Unk	41
	(b) Carcinoma of breast		
UAE	I(a) Glioblastoma (G14) of frontal lobe of brain	Unk	50
UAE	I(a) Carcinomatosis	Unk	44
	(b) Carcinoma of breast		
<i>Respiratory</i>			
Hyst	I(a) Type II respiratory failure	8.4	52
	(b) Bronchiectasis		
<i>Open verdict</i>			
Hyst	I(a) Amitriptyline, setraline and dihydrocodeine poisoning	4.1	34
UAE	I(a) Asphyxia	0.9	45
	(b) Hanging		



## Appendix 8

### Second letter to non-consenters (first chase)

**LOCAL CENTRE  
HEADED PAPER**

November 2004 – Version 1

Hysterectomy Or Percutaneous Embolisation For Uterine Leiomyomata:  
HOPEFUL Project

Dear Ms OTHER,

You may recall we recently wrote to you regarding the HOPEFUL Project which is comparing hysterectomy with a newer treatment, uterine artery embolisation (UAE), to treat fibroid symptoms. You may not yet have decided if you would like to participate in this study and we would like to provide you with another opportunity for considering this. We enclose another information sheet on the project and consent forms for you should you wish to take part. The project involves a research nurse gathering information from your hospital notes regarding your treatment for fibroids and also you will be sent a short questionnaire to complete asking about your treatment for your fibroids and other related health questions. Please be reassured that all information provided is completely confidential. If, after reading the information sheet, you are happy to give permission for your hospital records to be examined please sign both consent forms, returning one in the FREEPOST envelope provided and keep the other for your own records.

If you would like to ask any questions before making a decision please call on the telephone number given on this letter and we will be happy to answer any queries regarding the project.

The more women that take part in the project the more information we can find out about these treatments to advise doctors and women in the future. If you feel able to participate your contribution to this research is greatly appreciated. Thank you very much for your help.

Yours sincerely,

CONSULTANT GYNAECOLOGIST/RADIOLOGIST



## Appendix 9

### Non-consenters reasons tick box sheet



#### HOPEFUL STUDY

#### Hysterectomy Or Percutaneous Embolisation For Uterine Leiomyomata?

We are interested in the reasons why some patients may not wish to take part in the HOPEFUL Study and if you have decided you do not wish to do so we would be very grateful if you felt able to tell us why. This only involves ticking the boxes below that apply to you and returning this sheet in the FREEPOST envelope provided. These forms are completely anonymous and will not allow you to be identified in any way.

*I do not wish to consent to take part in the HOPEFUL Study because:*  
(Please tick any box that applies to you, you may tick more than one)

- |   |                          |
|---|--------------------------|
| <b>I don't believe in surveys</b>   | <input type="checkbox"/> |
| <b>It isn't going to benefit me in any way</b>  | <input type="checkbox"/> |
| <b>It isn't anyone else's business</b>  | <input type="checkbox"/> |
| <b>I had forgotten all about my treatment</b>   | <input type="checkbox"/> |
| <b>I am not interested in this topic</b>  | <input type="checkbox"/> |
| <b>I am too busy to take part</b>   | <input type="checkbox"/> |
| <b>I am not well enough to take part</b>  | <input type="checkbox"/> |
| <b>I thought the questionnaire would be too difficult</b>   | <input type="checkbox"/> |
| <b>I thought the questionnaire would be too long</b>  | <input type="checkbox"/> |
| <b>I thought I may have language difficulties and be unable to complete the questionnaire</b>           | <input type="checkbox"/> |
| <b>I don't want my private medical notes looked into</b>  | <input type="checkbox"/> |
| <b>I was not happy with my medical treatment referred to in this project and would rather forget it</b> | <input type="checkbox"/> |
| <b>Other</b>  | <input type="checkbox"/> |
- (Please provide details if you wish)

Thank you for taking the time to complete this. Please return in the FREEPOST envelope provided.





## Appendix 10

### UAE clinical data form and instruction sheet



#### The HOPEFUL Study

Hysterectomy Or Percutaneous Embolisation For Uterine Leiomyomata?

### UAE Clinical Data Form

HOPEFUL Coordinating Centre  
Nuffield Department of Obstetrics and Gynaecology  
The Research Institute  
Churchill Hospital  
Oxford, OX3 7LJ

Funded by HTA Project Grant 03/60/01

**HOPEFUL Clinical Data Collection Form for Uterine Artery Embolisation (UAE) procedure**

- C1. a)** Code of referring Gynaecologist:  **Patient ID:**   
**b)** Code of Interventional Radiologist carrying out procedure:   
*(codes to be allocated by local nurses. Names not to be submitted to Oxford Central Office)*
- C2.** Date of admission:  (dd/mm/yy)

**Section A: Patient ID**

- C3.** Date of birth:  (dd/mm/yy)
- C4.** Patient initials:  (first initial followed by surname initial)
- C5.** Postcode:  (at time of procedure)

**Section B: Pre-procedure assessment**

*(This refers to information available at the time of the UAE procedure and to events preceding the procedure)*

**Clinical details at time of procedure** (if available – leave blank if not given):

- C6. a)** Height<sub>a</sub>  .  cm *or* <sub>b</sub>  / <sub>c</sub>  (ft/in)  
**b)** Weight<sub>a</sub>  .  kg *or* <sub>b</sub>  / <sub>c</sub>  (st/lb)  
*or c)* BMI  .  (if given)
- C7.** Menopause: <sub>a</sub>  (tick if yes)  
 If yes, age at menopause <sub>b</sub>  years  
 or Last menstrual period (LMP): <sub>c</sub>  (dd/mm/yy) or age at LMP <sub>d</sub>  years
- C8.** Smoker:  (1=never, 2=current, 3=ex)
- C9.** BP <sub>a</sub>  / <sub>b</sub>  (systolic/diastolic)
- C10.** History of anaemia requiring: **a)** oral iron?  (tick if yes)  
**b)** blood transfusion?  (tick if yes)
- C11.** Past history of abnormal smear?  (tick if yes)
- C12.** Obstetric history: (prior to UAE) (number of each, 0 if none and leave blank if not known)  
 Live births <sub>a</sub>  Stillbirths <sub>b</sub>  Caesarean Sections <sub>c</sub>

**C13. Gynaecological co-morbidity: (prior to UAE)** (Tick and give details where recorded)

	<i>Gynaecological co-morbidity/history</i>	<i>Yes<sub>a</sub></i>	<i>Details<sub>b</sub></i>
1	History of Pelvic Inflammatory Disease		
2	History of Urinary Tract Infection		
3	Adenomyosis		
4	Endometriosis		
5	Previous myomectomy		
6	Previous endometrial ablation		
7	Previous ovary/fallopian tube procedure		
8	Presence of ovarian pathology		
9	Presence of tubal disease		
10	History of sexually transmitted disease		

**C14. Principal presenting symptoms:**

	<i>Principal presenting symptom</i>	<i>Present</i>	<i>Details</i>
1	Menorrhagia (heavy menstrual bleeding) (with/without anaemia)		
2	Dysmenorrhoea (painful periods)		
3	Abdominal mass causing pressure or pain		
4	Other:		

**C15. Reason for choice of UAE**

	<i>Reason for UAE</i>	<i>Yes</i>	<i>Details</i>
1	Expressed a wish to retain uterus		
2	Expressed a wish to retain fertility		
3	Expressed a wish for future pregnancies		
4	Other:		

**Pre-procedure imaging**

**C16.** Pre-procedure imaging: a  (1=None, 2=US, 3=MR, 4=Other – Specify<sub>b</sub>.....)

**C17.** Date of imaging:       (dd/mm/yy)

**C18.** Fibroid details:

1) Number of fibroids (>2 cm)  (leave blank if not stated)

2) Dimensions of largest/indicator fibroid: 1    2    3    (cm)

or Volume:    (cc)

3) Location of largest/indicator fibroid (tick one):

1 Submucosal  2 Intramural  3 Subserosal

4 Pedunculated (Submucosal/Subserosal)  5 Not stated

**C19.** Dimensions of uterus: 1    2    3    (cm) or Volume:    (cc)

or Equivalent to   weeks pregnant.

**C20.** Medical conditions and their associated medications at the time of the procedure (include HRT, Diabetes):

	Medical condition <sub>a</sub>	Current Medication <sub>b</sub>
1		
2		
3		
4		
5		

**Section C: Embolisation procedure details**

(This refers to information regarding the UAE procedure itself)

**C22.** Procedure date/s:

	Date (dd/mm/yy)	Details	Total Fluoroscopy Time	Total Radiation Dose	Radiation units
1	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>				
2	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>				
3	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>				
4	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>				

**C23. Embolic agent**

	Type	Details	Manufacturer <sub>a</sub>	Size <sub>b</sub>	Amount <sub>c</sub>
1	Spherical PVA				
2	Traditional PVA				
3	Gelfoam				
4	Coils				
5	Other				

**C24. Which arteries were embolised? (tick all relevant)**

Left uterine <sub>1</sub>  Right uterine <sub>2</sub>  Left ovarian <sub>3</sub>  Right ovarian <sub>4</sub>   
 Right uterine-ovarian anastomosis <sub>5</sub>  Left uterine-ovarian anastomosis <sub>6</sub>

**C25. Any unusual uterine/ovarian characteristics documented:** .....

.....

**C26. Any other comments documented:** .....

.....

.....

**C33. a) Prophylactic antibiotics?** <sub>1</sub>  (tick if used) <sub>2</sub>Details: .....

.....

**b) Prophylactic heparin?** <sub>1</sub>  (tick if used) <sub>2</sub>Details: .....

.....

**C34. Pain management during procedure (tick and give details of all relevant)**

	Pain management–Medication	Tick <sub>a</sub>	Details <sub>b</sub>	Total Dose <sub>c</sub>
1	Sedation			
2	Non-PCA narcotics			
3	PCA narcotics			
4	Epidural			
5	Spinal			
6	NSAID			
7	Other			

## Section D: Peri-Procedural Complications

**C35.** Were there any embolisation specific problems before leaving the Angiography room?<sup>a</sup>   
 (tick if yes and give date and details in the table below)

Embolisation Specific Problems		Procedural complications	Yes <sup>a</sup>	Date <sup>b</sup>	Details <sup>c</sup>
Angiography	7	Groin haematoma (req treatment)		<input type="text"/>	
	8	Contrast reaction		<input type="text"/>	
	9	Nephrotoxicity		<input type="text"/>	
	10	Injury to uterine arteries		<input type="text"/>	
	11	Necrosis		<input type="text"/>	
	12	Thrombosis		<input type="text"/>	
	13	Fistula		<input type="text"/>	
	14	Other		<input type="text"/>	
Non-target embolisation	15	Ureter		<input type="text"/>	
	16	Ovarian		<input type="text"/>	
	17	Bowel		<input type="text"/>	
	18	Bladder		<input type="text"/>	
	19	Other		<input type="text"/>	
Adverse drug reaction	33	Sedative		<input type="text"/>	
	34	Analgesia		<input type="text"/>	
	35	Other		<input type="text"/>	

## Section E: In Patient post-procedure and prior to Discharge

(refers to events whilst still an in-patient prior to discharge and details of discharge)

**C36.** Pain management – post procedure (tick and give details of all relevant)

	Pain management—Medication	Tick <sup>a</sup>	Details <sup>b</sup>	Total Dose <sup>c</sup>
2	Non-PCA narcotics			
3	PCA narcotics			
6	NSAID			
7	Other (Specify <sup>b</sup> .....)			

**In hospital events:**

**C37.** Did any of the following complications occur after the procedure but prior to discharge?<sup>a</sup>

(tick if yes and give date and details in the table below)

Complications		Yes <sup>a</sup>	Date <sup>b</sup>	Details <sup>c</sup>
Angiography	7 Groin haematoma (req treatment)		<input type="text"/>	
	8 Contrast reaction		<input type="text"/>	
	9 Nephrotoxicity		<input type="text"/>	
	10 Injury to uterine arteries		<input type="text"/>	
	11 Necrosis		<input type="text"/>	
	12 Thrombosis		<input type="text"/>	
	13 Fistula		<input type="text"/>	
	14 Other		<input type="text"/>	
Non-target embolisation	15 Ureter		<input type="text"/>	
	16 Ovarian		<input type="text"/>	
	17 Bowel		<input type="text"/>	
	18 Bladder		<input type="text"/>	
	19 Other		<input type="text"/>	
Medical complications	27 Pulmonary embolus		<input type="text"/>	
	28 Deep vein thrombosis		<input type="text"/>	
	Other		<input type="text"/>	
Adverse drug reaction	33 Sedative		<input type="text"/>	
	34 Analgesia		<input type="text"/>	
	35 Other		<input type="text"/>	
Death	36		<input type="text"/>	
Other	37		<input type="text"/>	

**C38.** Was there any infection present prior to discharge:  (tick yes if positive culture documented, and then complete the following table)

	<i>Infection</i>	<i>Yes<sub>a</sub></i>	<i>Date<sub>b</sub></i>	<i>Details<sub>c</sub></i>
1	Systemic		<input type="text"/>	
2	Urinary tract		<input type="text"/>	
3	Pelvic		<input type="text"/>	
4	Wound		<input type="text"/>	
5	Chest		<input type="text"/>	
6	Other		<input type="text"/>	

**C39. a)** Pyrexia (>38.0°C on at least one occasion)  (tick if yes)

**b)** If yes, please give details.....

.....

**c)** Was Post-embolisation Syndrome identified?  (tick if yes)

**d)** Were these symptoms identified?

	<i>Symptoms</i>	<i>Yes</i>	<i>Date<sub>a</sub></i>	<i>Duration<sub>b</sub></i>	<i>Details<sub>c</sub></i>
1	Fever		<input type="text"/>		
2	Pain		<input type="text"/>		
3	Nausea		<input type="text"/>		
4	Leukocytosis		<input type="text"/>		
5	Other		<input type="text"/>		

**C40.** Was further treatment required prior to discharge?  (tick if yes and complete the following)

	<i>Further treatment<sub>a</sub></i>	<i>Details<sub>b</sub></i>	<i>Date<sub>c</sub></i>	<i>Outcome<sub>d</sub></i>
1			<input type="text"/>	
2			<input type="text"/>	
3			<input type="text"/>	
4			<input type="text"/>	
5			<input type="text"/>	

**C41.** Date of discharge:  (dd/mm/yy)



**HOPEFUL UAE Follow up Form**

Patient ID:

*(One form to be completed for each follow up occasion including scheduled outpatient appointments related to the UAE index treatment or any associated hospital readmissions)*

F1. Date of follow up:       (dd/mm/yy)

F2. Was the follow up an outpatient appointment  <sub>1</sub> or a readmission?  <sub>2</sub> (tick one only)

F3. a) Was a scan carried out?  (tick if yes and complete the following, else go to question 4)

b) Type of scan imaging:  (1=None, 2=US, 3=MR, 4=Other – Specify<sub>b</sub>.....)

c) Date of imaging:       (dd/mm/yy)

d) Fibroid details:

1) Number of fibroids (>2 cm)  (leave blank if not stated)

2) Dimensions of largest/indicator fibroid: <sub>1</sub>    <sub>2</sub>    <sub>3</sub>    (cm)

or Volume:    (cc)

3) Location of largest/indicator fibroid (tick one):

<sub>1</sub> Submucosal  <sub>2</sub> Intramural

<sub>3</sub> Subserosal  <sub>4</sub> Pedunculated (Submucosal/Subserosal)  <sub>5</sub> Not stated

e) Dimensions of uterus: <sub>1</sub>    <sub>2</sub>    <sub>3</sub>    (cm) or Volume:    (cc)

or Equivalent to   weeks pregnant.

F4. Were there any patient comments noted regarding change in symptoms?  (tick if yes and complete the following – change in symptoms: 1=improved, 2=same, 3=worse)

	Symptoms	Change in symptoms	Comments
1	Heavy periods		
2	Painful periods		
3	Bulk related symptoms e.g. pressure or pain		
4	General		

F5. Was there reported passage of fibroid tissue?  <sub>a</sub> (1=yes, 2=no, 3=unsure)

If yes, please give details: .....

.....

.....

F6. Was amenorrhea reported?  <sub>a</sub> (1=yes, 2=no, 3=unsure)

If yes, please give details<sub>b</sub> .....

.....

.....

F7. Was a pregnancy reported?  <sub>a</sub> (tick if yes)

For each pregnancy, please complete a pregnancy form

F8. a) Was further treatment required for fibroids?  <sub>a</sub> (tick if yes and complete the following)

	Treatment	Date <sub>a</sub>	Details <sub>b</sub>	Reasons <sub>c</sub>	Outcome
1	Medical	<input type="text"/>			
2	UAE – planned	<input type="text"/>			
	UAE – unplanned	<input type="text"/>			
3	Myomectomy – planned	<input type="text"/>			
	Myomectomy – unplanned	<input type="text"/>			
4	Hysterectomy	<input type="text"/>			
5	Other	<input type="text"/>			

F9. a) Was Post Embolisation Syndrome identified?  <sub>a</sub> (tick if yes)

b) Were the following symptoms recorded?

	Symptoms	Yes	Date <sub>a</sub>	Duration <sub>b</sub>	Details <sub>c</sub>
1	Fever (>38°C)	<input type="checkbox"/>	<input type="text"/>		
2	Pain	<input type="checkbox"/>	<input type="text"/>		
3	Nausea	<input type="checkbox"/>	<input type="text"/>		
4	Leukocytosis	<input type="checkbox"/>	<input type="text"/>		
5	Other	<input type="checkbox"/>	<input type="text"/>		

**F10.** Were there any of the following complications since the last follow up?  (tick if yes and complete the following)

Complication		Yes	Readmission	Date	Details
Infection	1 Systemic			<input type="text"/>	
	2 Urinary tract			<input type="text"/>	
	3 Pelvic			<input type="text"/>	
	4 Wound			<input type="text"/>	
	5 Chest			<input type="text"/>	
	6 Other			<input type="text"/>	
Angiography	7 Groin haematoma (req treatment)			<input type="text"/>	
	8 Contrast reaction			<input type="text"/>	
	9 Nephrotoxicity			<input type="text"/>	
	10 Injury to uterine arteries			<input type="text"/>	
	11 Necrosis			<input type="text"/>	
	12 Thrombosis			<input type="text"/>	
	13 Fistula			<input type="text"/>	
	14 Other			<input type="text"/>	
Non-target embolisation	15 Ureter			<input type="text"/>	
	16 Ovarian			<input type="text"/>	
	17 Bowel			<input type="text"/>	
	18 Bladder			<input type="text"/>	
	19 Other			<input type="text"/>	
Medical complications	27 Pulmonary embolus			<input type="text"/>	
	28 Deep vein thrombosis			<input type="text"/>	
	29 Myocardiac infarction			<input type="text"/>	
	30 Cerebrovascular accident			<input type="text"/>	
	31 Renal failure			<input type="text"/>	
	32 Other			<input type="text"/>	
Death	36			<input type="text"/>	
Other	37 <i>specify:</i>			<input type="text"/>	

**F11. Comments** *(Please include the question number and subset number next to any comments to enable us to relate them)*

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**HOPEFUL UAE Follow up Form**

Patient ID:

(One form to be completed for each follow up occasion including scheduled outpatient appointments related to the UAE index treatment or any associated hospital readmissions)

F1. Date of follow up:       (dd/mm/yy)

F2. Was the follow up an outpatient appointment  <sub>1</sub> or a readmission?  <sub>2</sub> (tick one only)

F3. a) Was a scan carried out?  (tick if yes and complete the following, else go to question 4)

b) Type of scan imaging:  (1=None, 2=US, 3=MR, 4=Other – Specify <sub>b</sub>.....)

c) Date of imaging:       (dd/mm/yy)

d) Fibroid details:

1) Number of fibroids (>2 cm)  (leave blank if not stated)

2) Dimensions of largest/indicator fibroid: <sub>1</sub>    <sub>2</sub>    <sub>3</sub>    (cm)

or Volume:    (cc)

3) Location of largest/ indicator fibroid (tick one):

<sub>1</sub> Submucosal  <sub>2</sub> Intramural

<sub>3</sub> Subserosal  <sub>4</sub> Pedunculated (Submucosal/Subserosal)  <sub>5</sub> Not stated

e) Dimensions of uterus: <sub>1</sub>    <sub>2</sub>    <sub>3</sub>    (cm) or Volume:    (cc)

or Equivalent to   weeks pregnant.

F4. Were there any patient comments noted regarding change in symptoms?  (tick if yes and complete the following – change in symptoms: 1=improved, 2=same, 3=worse)

	Symptoms	Change in symptoms	Comments
1	Heavy periods		
2	Painful periods		
3	Bulk related symptoms e.g. pressure or pain		
4	General		

F5. Was there reported passage of fibroid tissue? <sub>a</sub>  (1=yes, 2=no, 3=unsure)

If yes, please give details: .....

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F6. Was amenorrhea reported? <sub>a</sub>  (1=yes, 2=no, 3=unsure)

If yes, please give details, <sub>b</sub> .....

.....

.....

F7. Was a pregnancy reported?  <sup>a</sup> (tick if yes)  
 For each pregnancy, please complete a pregnancy form

F8. a) Was further treatment required for fibroids?  <sup>a</sup> (tick if yes and complete the following)

	Treatment	Date <sup>a</sup>	Details <sup>b</sup>	Reasons <sup>c</sup>	Outcome
1	Medical	<input type="text"/>			
2	UAE – planned	<input type="text"/>			
	UAE – unplanned	<input type="text"/>			
3	Myomectomy – planned	<input type="text"/>			
	Myomectomy – unplanned	<input type="text"/>			
4	Hysterectomy	<input type="text"/>			
5	Other	<input type="text"/>			

F9. a) Was Post Embolisation Syndrome identified?  <sup>a</sup> (tick if yes)

b) Were the following symptoms recorded?

	Symptoms	Yes	Date <sup>a</sup>	Duration <sup>b</sup>	Details <sup>c</sup>
1	Fever (>38°C)	<input type="checkbox"/>	<input type="text"/>		
2	Pain	<input type="checkbox"/>	<input type="text"/>		
3	Nausea	<input type="checkbox"/>	<input type="text"/>		
4	Leukocytosis	<input type="checkbox"/>	<input type="text"/>		
5	Other	<input type="checkbox"/>	<input type="text"/>		

**F10.** Were there any of the following complications since the last follow up?  (tick if yes and complete the following)

Complication		Yes	Readmission	Date	Details	
Infection	1	Systemic			<input type="text"/>	
	2	Urinary tract			<input type="text"/>	
	3	Pelvic			<input type="text"/>	
	4	Wound			<input type="text"/>	
	5	Chest			<input type="text"/>	
	6	Other			<input type="text"/>	
Angiography	7	Groin haematoma (req treatment)			<input type="text"/>	
	8	Contrast reaction			<input type="text"/>	
	9	Nephrotoxicity			<input type="text"/>	
	10	Injury to uterine arteries			<input type="text"/>	
	11	Necrosis			<input type="text"/>	
	12	Thrombosis			<input type="text"/>	
	13	Fistula			<input type="text"/>	
	14	Other			<input type="text"/>	
Non-target embolisation	15	Ureter			<input type="text"/>	
	16	Ovarian			<input type="text"/>	
	17	Bowel			<input type="text"/>	
	18	Bladder			<input type="text"/>	
	19	Other			<input type="text"/>	
Medical complications	27	Pulmonary embolus			<input type="text"/>	
	28	Deep vein thrombosis			<input type="text"/>	
	29	Myocardiac infarction			<input type="text"/>	
	30	Cerebrovascular accident			<input type="text"/>	
	31	Renal failure			<input type="text"/>	
	32	Other			<input type="text"/>	
Death	36			<input type="text"/>		
Other	37	<i>specify:</i>		<input type="text"/>		

**F11.** Comments *(Please include the question number and subset number next to any comments to enable us to relate them)*

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**HOPEFUL UAE Follow up Form**

Patient ID:

(One form to be completed for each follow up occasion including scheduled outpatient appointments related to the UAE index treatment or any associated hospital readmissions)

F1. Date of follow up:       (dd/mm/yy)

F2. Was the follow up an outpatient appointment  <sub>1</sub> or a readmission?  <sub>2</sub> (tick one only)

F3. a) Was a scan carried out?  (tick if yes and complete the following, else go to question 4)

b) Type of scan imaging:  (1=None, 2=US, 3=MR, 4=Other – Specify <sub>b</sub>.....)

c) Date of imaging:       (dd/mm/yy)

d) Fibroid details:

1) Number of fibroids (>2 cm)  (leave blank if not stated)

2) Dimensions of largest/indicator fibroid: <sub>1</sub>    <sub>2</sub>    <sub>3</sub>    (cm)

or Volume:    (cc)

3) Location of largest/ indicator fibroid (tick one):

<sub>1</sub> Submucosal  <sub>2</sub> Intramural

<sub>3</sub> Subserosal  <sub>4</sub> Pedunculated (Submucosal/Subserosal)  <sub>5</sub> Not stated

e) Dimensions of uterus: <sub>1</sub>    <sub>2</sub>    <sub>3</sub>    (cm) or Volume:    (cc)

or Equivalent to   weeks pregnant.

F4. Were there any patient comments noted regarding change in symptoms?  (tick if yes and complete the following – change in symptoms: 1=improved, 2=same, 3=worse)

	Symptoms	Change in symptoms	Comments
1	Heavy periods		
2	Painful periods		
3	Bulk related symptoms e.g. pressure or pain		
4	General		

F5. Was there reported passage of fibroid tissue?  <sub>a</sub> (1=yes, 2=no, 3=unsure)

If yes, please give details: .....

.....

.....

F6. Was amenorrhea reported?  <sub>a</sub> (1=yes, 2=no, 3=unsure)

If yes, please give details, <sub>b</sub> .....

.....

.....

F7. Was a pregnancy reported?  <sup>a</sup> (tick if yes)

For each pregnancy, please complete a pregnancy form

F8. a) Was further treatment required for fibroids?  <sup>a</sup> (tick if yes and complete the following)

	Treatment	Date <sup>a</sup>	Details <sup>b</sup>	Reasons <sup>c</sup>	Outcome
1	Medical	<input type="text"/>			
2	UAE – planned	<input type="text"/>			
	UAE – unplanned	<input type="text"/>			
3	Myomectomy – planned	<input type="text"/>			
	Myomectomy – unplanned	<input type="text"/>			
4	Hysterectomy	<input type="text"/>			
5	Other	<input type="text"/>			

F9. a) Was Post Embolisation Syndrome identified?  <sup>a</sup> (tick if yes)

b) Were the following symptoms recorded?

	Symptoms	Yes	Date <sup>a</sup>	Duration <sup>b</sup>	Details <sup>c</sup>
1	Fever (>38°C)	<input type="checkbox"/>	<input type="text"/>		
2	Pain	<input type="checkbox"/>	<input type="text"/>		
3	Nausea	<input type="checkbox"/>	<input type="text"/>		
4	Leukocytosis	<input type="checkbox"/>	<input type="text"/>		
5	Other	<input type="checkbox"/>	<input type="text"/>		

**F10.** Were there any of the following complications since the last follow up?  (tick if yes and complete the following)

Complication		Yes	Readmission	Date	Details
Infection	1 Systemic			<input type="text"/>	
	2 Urinary tract			<input type="text"/>	
	3 Pelvic			<input type="text"/>	
	4 Wound			<input type="text"/>	
	5 Chest			<input type="text"/>	
	6 Other			<input type="text"/>	
Angiography	7 Groin haematoma (req treatment)			<input type="text"/>	
	8 Contrast reaction			<input type="text"/>	
	9 Nephrotoxicity			<input type="text"/>	
	10 Injury to uterine arteries			<input type="text"/>	
	11 Necrosis			<input type="text"/>	
	12 Thrombosis			<input type="text"/>	
	13 Fistula			<input type="text"/>	
	14 Other			<input type="text"/>	
Non-target embolisation	15 Ureter			<input type="text"/>	
	16 Ovarian			<input type="text"/>	
	17 Bowel			<input type="text"/>	
	18 Bladder			<input type="text"/>	
	19 Other			<input type="text"/>	
Medical complications	27 Pulmonary embolus			<input type="text"/>	
	28 Deep vein thrombosis			<input type="text"/>	
	29 Myocardiac infarction			<input type="text"/>	
	30 Cerebrovascular accident			<input type="text"/>	
	31 Renal failure			<input type="text"/>	
	32 Other			<input type="text"/>	
Death	36			<input type="text"/>	
Other	37 <i>specify:</i>			<input type="text"/>	

**F11.** Comments *(Please include the question number and subset number next to any comments to enable us to relate them)*

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**HOPEFUL UAE Pregnancy Form**

(Only complete for pregnancies after index UAE treatment)

Patient ID:

**P1. a)** Were there any complications during the pregnancy?  (tick if yes)

**b)** If yes, please give details.....

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**P2.** Length of gestation?   weeks.

**P3. Outcome:** 1) Livebirth  Stillbirth  Miscarriage  (tick)

2) Single birth  Multiple births  (tick)

3) If miscarriage, please give date <sub>a</sub>       and any reasons or details:

.....

.....

.....

4) If livebirth or stillbirth date of birth? <sub>a</sub>       (dd/mm/yy)

Was the birth natural <sub>b</sub>  or Caesarian section <sub>c</sub> ? (tick)

Birthweight <sub>d</sub>     (gm) Sex <sub>e</sub>  (1=male, 2=female)

5) If Multiple - second: birthweight <sub>d</sub>     (gm) Sex <sub>e</sub>  (1=male, 2=female)

- third: birthweight <sub>d</sub>     (gm) Sex <sub>e</sub>  (1=male, 2=female)

**4. a)** Were any congenital malformations present?  (tick if yes)

**b)** If yes, please give details

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### HOPEFUL UAE Pregnancy Form

(Only complete for pregnancies after index UAE treatment)

Patient ID:

**P1. a)** Were there any complications during the pregnancy?  (tick if yes)

**b)** If yes, please give details.....

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.....  
.....  
.....

**P2.** Length of gestation?  weeks.

**P3.** Outcome: 1) Livebirth  Stillbirth  Miscarriage  (tick)

2) Single birth  Multiple births  (tick)

3) If miscarriage, please give date <sub>a</sub>  and any reasons or details:

.....  
.....  
.....

4) If livebirth or stillbirth date of birth? <sub>a</sub>  (dd/mm/yy)

Was the birth natural <sub>b</sub>  or Caesarian section <sub>c</sub>  ? (tick)

Birthweight <sub>d</sub>  (gm) Sex <sub>e</sub>  (1=male, 2=female)

5) If Multiple - second: birthweight <sub>d</sub>  (gm) Sex <sub>e</sub>  (1=male, 2=female)

- third: birthweight <sub>d</sub>  (gm) Sex <sub>e</sub>  (1=male, 2=female)

**4. a)** Were any congenital malformations present?  (tick if yes)

**b)** If yes, please give details

.....  
.....  
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.....

**HOPEFUL Data Collection Form for Deceased Patients**

**Patient ID:**

**D1.** Date of birth:  (dd/mm/yy)

**D2.** Date of death:  (dd/mm/yy)

**D3.** Cause of death: .....  
.....  
.....  
.....  
.....  
.....  
.....  
.....

**D4. a)** Was death related to the fibroid treatment? Yes <sub>1</sub>  No <sub>2</sub>  Not sure <sub>3</sub>  (please tick. If "Not sure" please refer to Principal Investigator)

**b)** If yes, give details: .....  
.....  
.....  
.....  
.....  
.....  
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## **Instruction Sheet for HOPEFUL Clinical Data Forms – UAE**

*We have prepared these notes to assist you in completing the data forms but please call us if you have any queries whilst collating the patient data.*

*Many thanks*

*Allison (01865) 225209*

*Sue (01865) 225830*

*Or Freephone (0800) 0283202*

### **General comments:**

- Always ensure Patient ID code is completed.
- If information is unavailable please leave the box blank and write N/R (not recorded) next to the box. This will be treated as a missing value in our data analysis.
- If there is not enough space please \* and add the information at the side or on the blank back page, recording question and part clearly.
- Some question numbers appear to be missing. These questions are found on the Hysterectomy clinical data form. The numbers have been kept consistent across the 2 forms to help us with data inputting and analysis.
- The numbers appearing in some of the tables are for ease of data manipulation after collection, please ignore (unless adding extra information when this can be used as part of the labelling).
- We have structured the data form within sections ordered chronologically so this should assist in your locating the information in the patient's notes.
- A lot of this form will be blank because very few people have complications (~4% for hysterectomy patients), so only record information that is readily available.

### **Question Specific comments:**

- C1: Please compile a list of referring gynaecologists and allocate each a simple number code  
e.g. Joe Bloggs 1, Harry Clark 2  
Include all gynaecologists, even if they have left. The list does not need to be complete at the start as more may be added as you discover them in the notes.  
In C1 a) please insert the code of the patient's referring gynaecologist.  
Please retain a copy of this list with your HOPEFUL files but do not send to us. We should not be able to identify doctors individually.
- Compile a similar list of the Interventional Radiologists and record the code for the radiologist who carried out the embolisation in C1.b
- C6: If height and weight are available please complete these and our computer will calculate body mass index (BMI). Or, if Ht and Wt are not given, but BMI is please fill it in. You have the option to fill in Ht in cm or feet/inches, and Wt in kg or stones/lbs. You don't need to fill in both.
- C16-C26: Information on MR Imaging and Embolisation details can usually be found in the radiology department, although this may vary from one hospital to another.
- C16: If more than one imaging is carried out, please give details from the imaging providing the best information.



- C18: These details are not always available depending on the type of imaging carried out.
- C18.1: If the number of fibroids (regardless of size) is stated please record as 1, 2, 3 or >3. Please ignore the >2 cm.
- C18.2: Sometimes the dimensions are given and sometimes only the estimated volume. You do not need to fill in both. If dimensions are available complete these and our computer will calculate the volume.
- C19: Again you don't need to give both dimensions and volume if dimensions are given. Alternatively, sometimes the uterus size is given as equivalent to number of weeks pregnant, particularly if a scan has not been carried out. The latter may be available from the pre-op assessment or during the operation.
- C20: Please record any medical conditions and associated medications, mentioned in the notes at the time of admission for treatment.
- C22: Sometimes the index UAE procedure is carried out on consecutive days, either planned or unplanned. Do not give details of further UAEs carried out months or years later. These will be covered in the Follow up forms.
- C27-C32: These are found on the Hysterectomy clinical data forms.
- C33: Details should include number of drug doses, but drug names or manufacturer not necessary. (These can usually be found on the drug sheets).
- C34/C36: please note there are two tables dealing with pain management, one for during the operation and one for post operation. Post operative suppositories should be filled in C36.
- C35/C37: Please ignore numbering within these tables – this is for our future data manipulation and analysis. If in doubt about the complication, please ask your consultant (PI) or phone us for advice.
- C39.c/C39.d: It is now recognised that most patients will experience Post Embolisation Syndrome, however in the early days of the procedure, this was not recognised. Some women may have had emergency hysterectomies or other treatments as a result of unrecognised post embolisation syndrome. We are interested in any post-embolisation symptoms identified at the time.
- C40: This refers to further treatment given prior to discharge, and may be related to one of the complications ticked in C37 or C38 or may be an emergency hysterectomy.
- C41: Date of discharge is important as it enables us to compare length of stay in hospital for the two groups.

### Follow Up Forms (F)

- A follow up form should be completed for each scheduled outpatient appointment following the UAE, and for each hospital readmission for treatment related to the original procedure or complications caused by the procedure. If in doubt about whether a readmission is related to the UAE, please ask your consultant (PI) or phone us for advice.
- Three follow up forms are included in each booklet. Please complete as required. Further copies are available on request if needed.
- F1: it is very important to include this as it enables us to differentiate between follow up events.
- F3: See comments on C18/C19.
- F4: Patients often comment on changes in symptoms at follow up, and sometimes these are reported.
- F5: This may be at home or requiring surgical assistance.
- F7: If a pregnancy was reported please complete a pregnancy form for each pregnancy.
- F9: See comments on C39. Post embolisation syndrome can occur up to two weeks after the procedure.

- F10: If there is not sufficient room to fill in all the details reported, please use F11, and label the comments according to the number in the 2<sup>nd</sup> column of the table.
- Any additional comments can also be added in F11.

### **Pregnancy Form (P)**

Complete one form for each pregnancy that occurred after the first UAE. Information is not required for pregnancies occurring before the index treatment. This information can usually be found in the maternity notes.

- Two pregnancy forms are included in the booklet. More are available on request.
- P1: please describe in full any complications during the pregnancy.
- P2: This is important information, if available (it may not be available for miscarriages)
- P3: If the pregnancy outcome was a multiple birth please give details of all the babies.
- P4: Please give details of any congenital malformations if available.

We hope these have been helpful. If there are any problems, please call us.

## Appendix II

# Hysterectomy clinical data form and instruction sheet



The HOPEFUL Study  
Hysterectomy Or Percutaneous Embolisation For Uterine Leiomyomata?

## Hysterectomy Clinical Data Form

HOPEFUL Coordinating Centre  
Nuffield Department of Obstetrics and Gynaecology  
The Research Institute  
Churchill Hospital  
Oxford, OX3 7LJ

Funded by HTA Project Grant 03/60/01

**HOPEFUL Clinical Data Collection Form for Hysterectomy (VALUE subgroup)**

**C1. a)** Code of referring Gynaecologist:  **Patient ID:**   
*(codes to be allocated by local nurses. Names not to be submitted to Oxford Central Office)*

**C2.** Date of admission:  (dd/mm/yy)

**Section A: Patient ID**

**C3.** Date of birth:  (dd/mm/yy)

**C4.** Patient initials:  (first initial followed by surname initial)

**C5.** Postcode:  (at time of procedure)

**Section B: Pre-operative assessment**

*(This refers to information available at the time of the hysterectomy and to events preceding the operation)*

**Clinical details at time of procedure:** *(if available, leave blank if not given)*

**C6. a)** Height<sub>a</sub>  .  cm or <sub>b</sub>  / <sub>c</sub>  (ft/in)

**b)** Weight<sub>a</sub>  .  kg or <sub>b</sub>  / <sub>c</sub>  (st/lb)

**or c)** BMI  .  (if given)

**C7.** Menopause: <sub>a</sub>  (tick if yes)

If yes, age at menopause <sub>b</sub>  years

or Last menstrual period(LMP): <sub>c</sub>  (dd/mm/yy) or age at LMP <sub>d</sub>  years

**C8.** Smoker:  (1=never, 2=current, 3=ex)

**C9.** BP <sub>a</sub>  / <sub>b</sub>  (systolic/diastolic)

**C10.** History of anaemia requiring: **a)** oral iron?  (tick if yes)

**b)** blood transfusion?  (tick if yes)

**C11.** History of abnormal smear?  (tick if yes)

**C12.** Obstetric history: *(prior to hysterectomy) (number of each, 0 if none and leave blank if not known)*

Live births <sub>a</sub>  Stillbirths <sub>b</sub>  Caesarean Sections <sub>c</sub>

**C13. Gynaecological co-morbidity: (prior to Hysterectomy)** (Tick and give details where recorded)

	Gynaecological co-morbidity/history	Yes <sub>a</sub>	Details <sub>b</sub>
1	History of Pelvic Inflammatory Disease		
2	History of Urinary Tract Infection		
3	Adenomyosis		
4	Endometriosis		
5	Previous myomectomy		
6	Previous endometrial ablation		
7	Previous ovary/fallopian tube procedure		
8	Presence of ovarian pathology		
9	Presence of tubal disease		
10	History of sexually transmitted disease		

**C14. Principal presenting symptoms:**

	Principal presenting symptom	Present	Details
1	Menorrhagia (heavy menstrual bleeding) (with/without anaemia)		
2	Dysmenorrhoea (painful periods)		
3	Abdominal mass causing pressure or pain		
4	Other:		

**Pre-procedure imaging**

**C16.** Pre-procedure imaging: a  (1=None, 2=US, 3=MR, 4=Other – Specify b.....)

**C17.** Date of imaging:       (dd/mm/yy)

**C18. Fibroid details:**

1) Number of fibroids (>2 cm)  (leave blank if not stated)

2) Dimensions of largest/indicator fibroid: 1    2    3    (cm)

or Volume:    (cc)

3) Location of largest/indicator fibroid (tick one):

1 Submucosal  2 Intramural

3 Subserosal  4 Pedunculated (Submucosal/Subserosal)  5 Not stated

**C19.** Dimensions of uterus: 1    2    3    (cm) **or** Volume:    (cc)  
 or Equivalent to   weeks pregnant.

**C20.** Medical conditions and their associated medications at the time of the procedure (include HRT, Diabetes):

	Medical condition <sub>a</sub>	Current Medication <sub>b</sub>
1		
2		
3		
4		
5		

**Hysteroscopy findings**

**C21. a)** Was a hysteroscopy carried out?

**b)** If yes, date of hysteroscopy:       (dd/mm/yy)

**c)** If yes, tick which of these were identified:

Submucosal fibroids <sub>1</sub>  Pedunculated submucosal fibroids <sub>4</sub>  Other fibroids <sub>5</sub>  No fibroids <sub>6</sub>

**Section C: Hysterectomy Details**

(This refers to details of the surgical procedure itself)

**C22. a)** Operation date:       (dd/mm/yy)

**b)** Status of senior operator present at operation: Consultant  Non-Consultant

**C27.** Anaesthetic: <sub>a</sub> main  <sub>b</sub> additional

(1=General Anaesthetic, 2=Local Anaesthetic, 3=Epidural, 4=Spinal, 5=Other (Specify.....))

**C28.** Method of Hysterectomy: (tick one in each column)

	Method	Intended <sub>a</sub>	Actual <sub>b</sub>
1	Total abdominal		
2	Subtotal abdominal		
3	Vaginal		
4	Laparoscopic assisted vaginal		
5	Total laparoscopic		
6	Subtotal laparoscopic		
7	Other, (Specify.....)		

**C29.** Reason for any change of method intended: .....

**C30.** Unusual uterine/ovarian pathology: .....

**C31.** Ovaries removed during operation:  (1=none, 2=left, 3=right, 4=both)

**C32.** Endometriosis:  (tick if present)

**C33. a)** Prophylactic antibiotics? <sub>1</sub>  (tick if used)<sub>2</sub> Details: .....

.....

**b)** Prophylactic heparin? <sub>1</sub>  (tick if used)<sub>2</sub> Details: .....

.....

**C34.** Pain management during operation (tick and give details of all relevant)

	Pain management- Medication	Tick <sub>a</sub>	Details <sub>b</sub>	Total Dose <sub>c</sub>
1	Sedation			
2	Non-PCA narcotics			
3	PCA narcotics			
4	Epidural			
5	Spinal			
6	NSAID			
7	Other			

**Section D: Peri-Operative Complications**

**C35.** Were there any of the following complications before leaving the operating theatre?  (tick if yes and complete the table)

Operative Complications		Yes <sub>a</sub>	Date <sub>b</sub>	Details <sub>c</sub>
Operative sequelae	20 Ureteric damage		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
	21 Ovarian damage		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
	22 Bowel damage		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
	23 Bladder damage		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
	24 Haemorrhage (req. Transfusion)		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	Number units required: <input type="checkbox"/> <input type="checkbox"/>
	25 Haematoma (req. surgical drainage)		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
	26 Other		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Medical complications	27 Pulmonary embolus		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Death	36		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Other	37		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	

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**Section E: In Patient post-operation and prior to Discharge***(refers to events whilst still an in-patient prior to discharge and details of discharge)***C36. Pain management post operation (tick and give details of all relevant)**

	<i>Pain management- Medication</i>	<i>Tick<sub>a</sub></i>	<i>Details<sub>b</sub></i>	<i>Total Dose<sub>c</sub></i>
2	Non-PCA narcotics			
3	PCA narcotics			
6	NSAID			
7	Other			

**In hospital events:**

**C37.** Were there any complications after the operation and prior to discharge?  *(tick if yes and complete the table)*

	<i>Complication</i>	<i>Yes</i>	<i>Date</i>	<i>Details</i>
Operative sequelae	20 Ureteric damage		<input type="text"/>	
	21 Ovarian damage		<input type="text"/>	
	22 Bowel damage		<input type="text"/>	
	23 Bladder damage		<input type="text"/>	
	24 Haemorrhage (req. Transfusion)		<input type="text"/>	
	25 Haematoma (req. surgical drainage)		<input type="text"/>	
	26 Other		<input type="text"/>	
Medical complications	27 Pulmonary embolus		<input type="text"/>	
	28 Deep vein thrombosis		<input type="text"/>	
	32 Other		<input type="text"/>	
Adverse drug reaction	33 Sedative		<input type="text"/>	
	34 Analgesia		<input type="text"/>	
	35 Other		<input type="text"/>	
Death	36		<input type="text"/>	
Other	37 <i>Specify:</i>		<input type="text"/>	



**C38.** Was there any infection present prior to discharge:  (tick yes if positive culture documented, and then complete the following table)

	<i>Infection</i>	<i>Yes<sub>a</sub></i>	<i>Date<sub>b</sub></i>	<i>Details<sub>c</sub></i>
1	Systemic		<input type="text"/>	
2	Urinary tract		<input type="text"/>	
3	Pelvic		<input type="text"/>	
4	Wound		<input type="text"/>	
5	Chest		<input type="text"/>	
6	Other		<input type="text"/>	

**C39. a)** Pyrexia (>38.0°C on at least one occasion)  *a*  (tick if yes)

**b)** If yes, please give details.....

**C40.** Was further treatment required prior to discharge?  (tick if yes and complete the following)

	<i>Further treatment<sub>a</sub></i>	<i>Details<sub>b</sub></i>	<i>Date<sub>c</sub></i>	<i>Outcome<sub>d</sub></i>
1			<input type="text"/>	
2			<input type="text"/>	
3			<input type="text"/>	
4			<input type="text"/>	
5			<input type="text"/>	

**C41.** Date of discharge:  (dd/mm/yy)

**HOPEFUL Hysterectomy Follow up Form**Patient ID: 

(One form to be completed for each follow up occasion including scheduled outpatient appointments related to the hysterectomy index treatment or any associated hospital readmissions)

F1. Date of follow up:  (dd/mm/yy)

F2. Was the follow up an outpatient appointment  <sub>1</sub> or a readmission?  <sub>2</sub> (tick one only)

F10. Were there any of the following complications since the last follow up?  <sub>a</sub> (tick if yes and complete the following)

Complication		Yes	Date	Details	Readmission (tick if yes)
Infection	1 Systemic		<input type="text"/>		
	2 Urinary tract		<input type="text"/>		
	3 Pelvic		<input type="text"/>		
	4 Wound		<input type="text"/>		
	5 Chest		<input type="text"/>		
	6 Other		<input type="text"/>		
Operative sequelae	20 Ureteric damage		<input type="text"/>		
	21 Ovarian damage		<input type="text"/>		
	22 Bowel damage		<input type="text"/>		
	23 Bladder damage		<input type="text"/>		
	24 Haemorrhage (req. Transfusion)		<input type="text"/>		
	25 Haematoma (req. surgical drainage)		<input type="text"/>		
	26 Other		<input type="text"/>		
Medical complications	27 Pulmonary embolus		<input type="text"/>		
	28 Deep vein thrombosis		<input type="text"/>		
	29 Myocardial infarction		<input type="text"/>		
	30 Cerebrovascular accident		<input type="text"/>		
	31 Renal failure		<input type="text"/>		
		32 Other		<input type="text"/>	
Death	36		<input type="text"/>		
Other	37		<input type="text"/>		

**F11.** Comments *(Please include the question number and subset number next to any comments to enable us to relate them)*

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**HOPEFUL Hysterectomy Follow up Form**Patient ID: 

(One form to be completed for each follow up occasion including scheduled outpatient appointments related to the hysterectomy index treatment or any associated hospital readmissions)

F1. Date of follow up:  (dd/mm/yy)

F2. Was the follow up an outpatient appointment  or a readmission?  (tick one only)

F10. Were there any of the following complications since the last follow up?  (tick if yes and complete the following)

Complication		Yes	Date	Details	Readmission (tick if yes)
Infection	1 Systemic		<input type="text"/>		
	2 Urinary tract		<input type="text"/>		
	3 Pelvic		<input type="text"/>		
	4 Wound		<input type="text"/>		
	5 Chest		<input type="text"/>		
	6 Other		<input type="text"/>		
Operative sequelae	20 Ureteric damage		<input type="text"/>		
	21 Ovarian damage		<input type="text"/>		
	22 Bowel damage		<input type="text"/>		
	23 Bladder damage		<input type="text"/>		
	24 Haemorrhage (req. Transfusion)		<input type="text"/>		
	25 Haematoma (req. surgical drainage)		<input type="text"/>		
	26 Other		<input type="text"/>		
Medical complications	27 Pulmonary embolus		<input type="text"/>		
	28 Deep vein thrombosis		<input type="text"/>		
	29 Myocardial infarction		<input type="text"/>		
	30 Cerebrovascular accident		<input type="text"/>		
	31 Renal failure		<input type="text"/>		
	32 Other		<input type="text"/>		
Death	36		<input type="text"/>		
Other	37 Specify:		<input type="text"/>		

**F11.** Comments *(Please include the question number and subset number next to any comments to enable us to relate them)*

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**HOPEFUL Hysterectomy Follow up Form**Patient ID: 

(One form to be completed for each follow up occasion including scheduled outpatient appointments related to the hysterectomy index treatment or any associated hospital readmissions)

F1. Date of follow up:  (dd/mm/yy)

F2. Was the follow up an outpatient appointment  or a readmission?  (tick one only)

F10. Were there any of the following complications since the last follow up?  (tick if yes and complete the following)

Complication		Yes	Date	Details	Readmission (tick if yes)
Infection	1 Systemic		<input type="text"/>		
	2 Urinary tract		<input type="text"/>		
	3 Pelvic		<input type="text"/>		
	4 Wound		<input type="text"/>		
	5 Chest		<input type="text"/>		
	6 Other		<input type="text"/>		
Operative sequelae	20 Ureteric damage		<input type="text"/>		
	21 Ovarian damage		<input type="text"/>		
	22 Bowel damage		<input type="text"/>		
	23 Bladder damage		<input type="text"/>		
	24 Haemorrhage (req. Transfusion)		<input type="text"/>		
	25 Haematoma (req. surgical drainage)		<input type="text"/>		
	26 Other		<input type="text"/>		
Medical complications	27 Pulmonary embolus		<input type="text"/>		
	28 Deep vein thrombosis		<input type="text"/>		
	29 Myocardial infarction		<input type="text"/>		
	30 Cerebrovascular accident		<input type="text"/>		
	31 Renal failure		<input type="text"/>		
	32 Other		<input type="text"/>		
Death	36		<input type="text"/>		
Other	37 Specify:		<input type="text"/>		

**F11.** Comments *(Please include the question number and subset number next to any comments to enable us to relate them)*

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**HOPEFUL Data Collection Form for Deceased Patients**

Patient ID:

D1. Date of birth:  (dd/mm/yy)

D2. Date of death:  (dd/mm/yy)

D3. Cause of death: .....

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D4. a) Was death related to the fibroid treatment? Yes <sub>1</sub>  No <sub>2</sub>  Not sure <sub>3</sub>  (please tick. If "Not sure" please refer to Principal Investigator)

b) If yes, give details: .....

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## **Instruction Sheet for HOPEFUL Clinical Data Forms – Hysterectomy**

*We have prepared these notes to assist you in completing the data forms but please call us if you have any queries whilst collating the patient data.*

*Many thanks*

*Allison (01865) 225209*

*Sue (01865) 225830*

*Or Freephone (0800) 0283202*

### **General comments:**

- Always ensure Patient ID code is completed.
- If information is unavailable please leave the box blank and write N/R (not recorded) next to the box. This will be treated as a missing value in our data analysis.
- If there is not enough space please \* and add the information at the side or on the blank back page, recording question and part clearly.
- Some question numbers appear to be missing. These questions are found on the UAE clinical data form. The numbers have been kept consistent across the 2 forms to help us with data inputting and analysis.
- The numbers appearing in some of the tables are for ease of data manipulation after collection, please ignore (unless adding extra information when this can be used as part of the labelling).
- We have structured the data form within sections ordered chronologically so this should assist in your locating the information in the patient's notes.
- A lot of this form will be blank because very few people have complications (~4%), so only record information that is readily available.

### **Question Specific comments:**

- C1: Please compile a list of the gynaecologists in your department at the time of the VALUE hysterectomies and allocate each a simple number code e.g. Joe Bloggs 1, Harry Clark 2  
Include all gynaecologists, even if they have left. The list does not need to be complete at the start as more may be added as you discover them in the notes.  
Please insert the code of the most senior doctor present at the patient's operation, their status is asked for in question C22.b.  
Please retain a copy of this list with your HOPEFUL files but do not send to us. We should not be able to identify them individually.
- C6: If height and weight are available please complete these and our computer will calculate body mass index (BMI). Or, if Ht and Wt are not given, but BMI is please fill it in. You have the option to fill in Ht in cm or feet/inches, and Wt in kg or stones/lbs. You don't need to fill in both.
- C15: This question is on the UAE clinical data form.
- C16-C19: Information on MR Imaging can usually be found in the radiology department, although this may vary from one hospital to another.
- C16: If more than one imaging is carried out, please give details from the imaging providing the best information.

- C18: These details are not always available depending on the type of imaging carried out.
- C18.1: If the number of fibroids (regardless of size) is stated please record as 1, 2, 3 or >3. Please ignore the >2 cm.
- C18.2: Sometimes the dimensions are given and sometimes only the estimated volume. You do not need to fill in both. If dimensions are available complete these and our computer will calculate the volume.
- C19: Again you don't need to give both dimensions and volume if dimensions are given. Alternatively, sometimes the uterus size is given as equivalent to number of weeks pregnant, particularly if a scan has not been carried out. The latter may be available from the pre-op assessment or during the operation.
- C20: Please record any medical conditions and associated medications, mentioned in the notes at the time of admission for treatment.
- C22: The status of the senior operator present during the operation, not necessarily carrying out the operation.
- C23-C26: These questions are found on the UAE clinical data form.
- C28: Please tick both the planned (intended) and actual method of hysterectomy. These will be the same if there was no change to the plan in surgery.
- C33: Details should include number of drug doses, but drug names or manufacturer not necessary (These can usually be found on the drug sheets).
- C34/C36: Please note there are two tables dealing with pain management, one for during the operation and one for post operation. Post operative suppositories should be filled in C36.
- C35/C37: Please ignore numbering within these tables – this is for our future data manipulation and analysis. If in doubt about the complication, please ask your consultant (PI) or phone us for advice.
- C40: This refers to further treatment given prior to discharge, and may be related to one of the complications ticked in C37 or C38. This includes return to theatre.
- C41: Date of discharge is important as it enables us to compare length of stay in hospital for the two groups.

### **Follow Up Forms (F)**

- A follow up form should be completed for each scheduled outpatient appointment following the hysterectomy, and for each hospital readmission for treatment related to the original operation or complications caused by the operation or later gynaecological events or investigations.
- Three follow up forms are included in each booklet. Please complete as required. Further copies are available on request if needed.
- F1: It is very important to include this as it enables us to differentiate between follow up events.
- F3-F9: These questions are on the UAE follow up forms.
- F10: If there is not sufficient room to fill in all the details reported, please use F11, and label the comments according to the number in the 2<sup>nd</sup> column of the table.
- Any additional comments can also be added in F11.

We hope these have been helpful. If there are any problems, please call us.

## Appendix 12

### Patient questionnaire

# University of Oxford

Nuffield Department of Obstetrics & Gynaecology  
Research Institute,  
Churchill Hospital,  
Headington,  
Oxford OX3 7LJ



### The HOPEFUL Study

### Hysterectomy Or Percutaneous Embolisation For Uterine Leiomyomata?

## QUESTIONNAIRE

### CONFIDENTIAL

Thank you for taking the time to complete this confidential form. Please answer each question by ticking the box/es that best describes your situation. We would be grateful if you could answer as many questions as you are able but please note your response is voluntary and you are not obliged to reply to every question if you prefer not to.

Please ignore any numbers near tick boxes: they are codes for our computer use only.

Please keep a copy of your questionnaire if you wish.

**Please freephone 0800 0283202 (answering machine out of normal office hours) if you need any assistance in the completion of this form.**

**Please return your questionnaire in the FREEPOST envelope provided to:**

HOPEFUL Study, Nuffield Department of Obstetrics and Gynaecology,  
Research Institute, Churchill Hospital, Old Rd, Headington, Oxford, OX3 7LJ.

**Thank you for contributing to our research.**

Patient ID:     

## The HOPEFUL Study

### Hysterectomy Or Percutaneous Embolisation For Uterine Leiomyomata?

**Please note that the index treatment referred to in this questionnaire is your first uterine artery embolisation (UAE) or your hysterectomy (if this was without a prior UAE).**

#### **SECTION 1: GENERAL INFORMATION**

1. Today's date:       (dd/mm/yy)
2. Please confirm your date of birth.       (dd/mm/yy)
3. Please give us your initials. (This helps us to cross reference for our database without breaching your confidentiality)    <sub>1</sub> First name initial     <sub>2</sub> Surname initial
4. What best describes your highest level of education? (Please tick one box)
   
<sub>1</sub> No formal exams taken     <sub>2</sub> O Level/CSE/GCSE     <sub>3</sub> A level/AS/A2 
  
<sub>4</sub> First degree     <sub>5</sub> Postgraduate Degree     <sub>6</sub> Professional Qualifications
5. What best describes your ethnic origin: (please tick **one** box only)
   
 (These categories are based on those used in the 2001 census of the UK population)
 

<b>White</b> <sub>1</sub> British <input type="checkbox"/> <sub>2</sub> Irish <input type="checkbox"/> <sub>3</sub> Other white? <input type="checkbox"/> <sub>3b</sub> (specify) .....	<b>Black or Black British</b> <sub>4</sub> Caribbean <input type="checkbox"/> <sub>5</sub> African <input type="checkbox"/> <sub>6</sub> Other black? <input type="checkbox"/> <sub>6b</sub> (specify) .....	<b>Chinese</b> <sub>7</sub> Chinese <input type="checkbox"/>
<b>Mixed</b> <sub>8</sub> White and Black Caribbean <input type="checkbox"/> <sub>9</sub> White and Black African <input type="checkbox"/> <sub>10</sub> White and Asian <input type="checkbox"/> <sub>11</sub> Other mixed? <input type="checkbox"/> <sub>11b</sub> (specify) .....	<b>Asian or Asian British</b> <sub>12</sub> Indian <input type="checkbox"/> <sub>13</sub> Pakistani <input type="checkbox"/> <sub>14</sub> Bangladeshi <input type="checkbox"/> <sub>15</sub> Other Asian? <input type="checkbox"/> <sub>15b</sub> (specify) .....	<b>Other ethnic group</b> <sub>16</sub> Any other <input type="checkbox"/> <sub>16b</sub> (specify).....
6. What is your height? <sub>a</sub>   / <sub>b</sub>   (Feet/inches) **or** <sub>c</sub>    (cm)
7. What is your weight now? <sub>a</sub>   / <sub>b</sub>   (Stones/lbs) **or** <sub>c</sub>   .  (kg)

8. Please tick the box that you feel best describes your cigarette smoking:

- <sub>1</sub> never smoked  *If you have never smoked please go straight on to question 10.*  
<sub>2</sub> current smoker   
<sub>3</sub> ex-smoker  <sub>3b</sub> smoked regularly in the past but stopped   years ago

9. a) Have you smoked any cigarettes at all **during the last 12 months**? <sub>1</sub> yes  <sub>2</sub> no

b) If yes, approximately how many cigarettes per day?

10. What was your age at menarche (first menstrual period)?   years

11. a) How many children have you had?

b) If you have had children, how many were born by caesarean section?

12. a) Have you been through the menopause?

- <sub>1</sub> yes-naturally  <sub>2</sub> yes-surgically  <sub>3</sub> no  <sub>4</sub> not sure

b) If yes, year of menopause: <sub>b1</sub>     (yyyy), **or** your age at menopause: <sub>b2</sub>   years old

c) If no or not sure, please tell us **approximately** when was your last period?

Date: <sub>c1</sub>   / <sub>c2</sub>   (mm/yy) **or** age: <sub>c3</sub>   years.

13. a) Have any of your family members been diagnosed with uterine fibroids?

- <sub>1</sub> yes  <sub>2</sub> no  <sub>3</sub> not sure

b) If yes, please complete the following:

	<sub>1</sub> Relationship to you	<sub>2</sub> Age at diagnosis	<sub>3</sub> Side of family (m=mother, f=father)
i)			
ii)			
iii)			

14. a) Have any of your family members been diagnosed with breast cancer?

- <sub>1</sub> yes  <sub>2</sub> no  <sub>3</sub> not sure

b) If yes, please complete the following:

	<sub>1</sub> Relationship to you	<sub>2</sub> Age at diagnosis	<sub>3</sub> Side of family (m=mother, f=father)
i)			
ii)			
iii)			

## SECTION 2: PRE TREATMENT

This section is about both your general health and about your health related to your fibroids, before your index treatment (either your first UAE or your hysterectomy).

### Part A – General health before index treatment

15. a) Before your index treatment were you ever diagnosed with any of the following gynaecological conditions? (please tick if yes and give relevant dates and details)

	<b>Gynaecological conditions</b>	<b>Yes<sub>a</sub></b>	<b>Date<sub>b</sub></b>	<b>Details<sub>c</sub></b>
i)	Pelvic inflammatory disease		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
ii)	Urinary tract infection/s		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
iii)	Endometriosis		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
iv)	Adenomyosis		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
v)	Other (Specify <sub>vd</sub> .....)		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	

b) Before your index treatment were you ever diagnosed with any of the following other medical conditions? (please tick if yes and give relevant dates and details)

	<b>Medical conditions</b>	<b>Yes<sub>a</sub></b>	<b>Date<sub>b</sub></b>	<b>Details<sub>c</sub></b>
i)	Diabetes		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
ii)	Stroke		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
iii)	Pulmonary embolism (blood clot in the lung)		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
iv)	Deep vein thrombosis (blood clot elsewhere)		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
v)	A benign (non-cancerous) breast lump		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
vi)	Osteoporosis (brittle bone disease)		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
vii)	Ovarian cancer		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
viii)	Other (Specify <sub>d</sub> .....)		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	

16. a) Before your index treatment did you have major surgery?

1 yes  2 no  3 not sure  If no or not sure, please go to question 17.

b) If yes, please fill in the table below (please tick if yes and give dates and details)

	<b>Prior surgery</b>	<b>Yes<sub>a</sub></b>	<b>Date<sub>b</sub></b>	<b>Details<sub>c</sub></b>
i)	Were you sterilised (tubes tied/clipped/removed)?		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
ii)	Did you have surgery for bowel problems?		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
iii)	Did you have surgery for bladder problems?		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
iv)	Did you have surgery for endometriosis?		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
v)	Did you have a myomectomy?		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
vi)	Other surgery? (Specify.....)		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	

17. a) Before your index treatment, were you on hormone replacement therapy (HRT)?  
 1 yes  2 no  3 not sure  *If no or not sure, please go to question 18.*

b) If yes,  
 i) Approximately how long **in total** did you have HRT prior to your index treatment?  
 yrs  months

ii) Please tell us which type of HRT you had prior to your index treatment (*tick 1 or more boxes*)  
 1 implant  (approximate date of **last** implant: ii1a  / ii1b  (*mm/yy*)  
 2 tablets  3 patches  4 other  (Please specify: ii4a.....)  
 5 not sure

**Part B – Fibroid specific health before your index treatment**

18. a) Before your index treatment did you receive any other treatment for fibroids?  
 1 yes  2 no  3 not sure  *If no or not sure, please go to question 19.*

b) If yes, please fill in the table below (*tick and give dates and details where relevant*):

	<b>Treatment</b>	<b>Yes<sub>a</sub></b>	<b>Date<sub>b</sub></b>	<b>Details<sub>c</sub></b>
i)	Medical therapy – Gonadotropin-releasing hormone (Gn-RH) agonists	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	
ii)	Medical therapy – Androgens	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	
iii)	Medical therapy – Other medication	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	
iv)	Myomectomy	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	
v)	Endometrial ablation	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	
vi)	Myolysis (electrical current treatment)	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	
vii)	Cryomyolysis (Freezing treatment)	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	
viii)	Other	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	

19. We would like to know what the principal symptoms of your fibroids were like prior to your index treatment and whether your treatment changed these symptoms.

a) (i) Before your treatment were you troubled by heavy menstrual bleeding (with or without anaemia)?

1 yes  2 no  3 not sure

(ii) If yes, since your treatment has this; 1 improved  2 stayed the same  3 worsened

b) (i) Before your treatment were you troubled by painful periods? 1 yes  2 no  3 not sure

(ii) If yes, since your treatment has this; 1 improved  2 stayed the same  3 worsened

c) (i) Before your treatment were you troubled by bulk-related symptoms, for example abdominal mass causing pain, pressure on the bladder or bowel, or other?

1 yes  2 no  3 not sure

(ii) If yes, since your treatment has this; 1 improved  2 stayed the same  3 worsened

**20.** At the time of your index treatment for your fibroids which of the following best describes your feelings about your family size? (please tick **one** box)

- <sub>1</sub> I definitely did not want any/any more children
- <sub>2</sub> I had hoped I might be able to have children/more children in the future
- <sub>3</sub> Not sure
- <sub>4</sub> Other  <sub>4b</sub> (Specify .....) )

*We would like to know more about the decisions that led to your index treatment for fibroids.*

**21. a)** Were you offered a choice of treatment for your fibroids at your hospital consultation?

- <sub>1</sub> yes  <sub>2</sub> no  <sub>3</sub> not sure  *If no or not sure, please go to question 22.*

*If yes, please complete the following.*

**b)** What treatments were you offered?

- <sub>1</sub> hysterectomy  <sub>2</sub> myomectomy  <sub>3</sub> uterine artery embolisation UAE
- <sub>4</sub> Other  (<sub>4b</sub>specify.....)

**c)** Which treatment did you choose?

- <sub>1</sub> hysterectomy  <sub>2</sub> myomectomy  <sub>3</sub> uterine artery embolisation UAE
- <sub>4</sub> Other  (<sub>4b</sub>specify.....)

**d)** Please could you tell us about what major factors influenced your choice of treatment?

- 1) .....
- 2) .....
- 3) .....
- 4) .....
- 5) .....
- 6) .....
- 7) .....
- 8) .....



**SECTION 3: POST TREATMENT**

This section asks you about your health since your index treatment.

**Part A**

22. In general, would you say your health is:

- 1 excellent  2 very good  3 good  4 fair  5 poor

23. How would you rate your health since receiving your fibroid treatment compared with before?

- 1 much better  2 better  3 about the same  4 worse  5 much worse

24. It is a few years since your treatment for fibroids, and we would like to know what your feelings are now about your treatment. *(Please tick)*

a) My expectations about my treatment have now been fulfilled 1 yes  2 no

If no, please tell us why: a2.....

.....

b) The treatment has relieved my symptoms 1 yes  2 no

c) I feel much better since I had the treatment 1 yes  2 no

d) If I needed to have treatment for fibroids I would undergo the same treatment

- 1 yes  2 no

e) I would recommend this treatment to a friend 1 yes  2 no

f) I have suffered from problems caused by the treatment 1 yes  2 no

If yes, please give details about the problems:

f2.....

.....

.....

25. We would like to know what your bladder function is like now compared with **before** your **index** treatment.

a) (i) Before your treatment were you troubled by a frequent need to urinate during the day?  
1 yes  2 no  3 not sure

(ii) Since your treatment has this; 1 improved  2 stayed the same  3 worsened

b) (i) Before your treatment were you troubled by a frequent need to urinate during the night?  
1 yes  2 no  3 not sure

(ii) Since your treatment has this; 1 improved  2 stayed the same  3 worsened

c) (i) Before your treatment did you lose urine unexpectedly (e.g. when sneezing)?  
1 yes  2 no  3 not sure

(ii) Since your treatment has this; 1 improved  2 stayed the same  3 worsened

**26. a)** Since your index treatment have you been diagnosed with any of the following gynaecological conditions? (please tick if yes and give relevant dates and details)

	<b>Gynaecological conditions</b>	<b>Yes<sub>a</sub></b>	<b>Date<sub>b</sub></b>	<b>Details<sub>c</sub></b>
i)	Pelvic inflammatory disease		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
ii)	Urinary tract infection/s		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
iii)	Endometriosis		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
iv)	Adenomyosis		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
v)	Other (Specify <sub>vd</sub> .....)		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	

**b)** Since your index treatment have you been diagnosed with any of the following other medical conditions? (please tick if yes and give relevant dates and details)

	<b>Medical conditions</b>	<b>Yes<sub>a</sub></b>	<b>Date<sub>b</sub></b>	<b>Details<sub>c</sub></b>
i)	Diabetes		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
ii)	Stroke		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
iii)	Pulmonary embolism (blood clot in the lung)		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
iv)	Deep vein thrombosis (blood clot elsewhere)		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
v)	A benign (non-cancerous) breast lump		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
vi)	Osteoporosis (brittle bone disease)		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
vii)	Ovarian cancer		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
viii)	Other (Specify <sub>d</sub> .....)		<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	

**27. a)** Since your index treatment, have you been admitted to hospital for any reason? This includes day case **or** overnight stays. <sub>1</sub> yes  <sub>0</sub> no  If no, please go straight on to question 28.

**b)** If yes, for each admission please tell us the approximate date, the reason for your admission and the investigation/treatment you received (if relevant). In addition please indicate number of **nights** you spent in hospital **or** tick the box if you were a day case.

	<b>Date<sub>a</sub></b> <i>mm/yy</i>	<b>Reason/investigation/treatment<sub>b</sub></b>	<b>No. of nights in hospital<sub>c</sub></b>	<b>Day case?<sub>d</sub></b> <input type="checkbox"/> if yes
i)	<input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/>			
ii)	<input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/>			
iii)	<input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/>			
iv)	<input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/>			
v)	<input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/>			

28. a) Since your index treatment, have you had hormone replacement therapy (HRT) at any time?  
 1 yes  2 no  3 not sure  *If no or not sure, please go to question 29.*

b) *If yes, please complete the following:*

i) Approximately how long **in total** have you had HRT since your index treatment?

yrs  months

ii) Which type of HRT you have had since your index treatment (*tick 1 or more boxes*)

1 implant  (approximate date of **last** implant: ii1a  / ii1b  (mm/yy))

2 tablets  3 patches  4 other  (Please specify: ii4a.....)

5 not sure

iii) Are you still having HRT? 1 yes  2 no  3 not sure

iii b If yes, please tell us the name of the HRT you are taking now:.....

29. a) We would like to know whether you still have your ovaries or whether they have been removed. Please tick **one** of the boxes below that best describes your case.

1 both ovaries remain  2 one ovary remains  3 both ovaries removed  4 not sure

b) If you now have **no** ovaries, when was the last one removed?  (dd/mm/yy)

## Part B – Treatment specific health post index treatment

*If you had a hysterectomy but NO previous UAE treatment, please go straight on to Section 4. Answer questions 30 to 34 only if you have ever had UAE treatment for your fibroids.*

30. a) Some women may be able to become pregnant after having undergone UAE treatment. Have you been pregnant since your UAE treatment? (*Please tick one box*)

1 yes  2 no  3 not sure

b) Please tell us the outcome of your pregnancy: b1.....

.....  
 .....  
 .....  
 .....

31. a) Since your first UAE treatment, have you had further UAE treatment?

1 yes  2 no  3 not sure  *If no or not sure, please go to question 32.*

b) If yes, please tell us when you had these further treatments (month/year);

i) first subsequent treatment  /

ii) second subsequent treatment  /

iii) third subsequent treatment  /

32. a) After your UAE treatment(s) did you also have a hysterectomy?

1 yes  2 no  3 not sure  *If no or not sure, please go to question 33.*

b) If yes, please could you answer the following if you are able to do so.

i) What was the date of your hysterectomy?  (ddmmyy)

ii) What do you think were the reasons for your hysterectomy? (you may tick more than one box)

1 excessive bleeding  2 pelvic pain  3 pelvic pressure  4 urinary problems

5 abnormal cells/CIN2/CIN3  6 not sure  7 other  7a Please specify .....

33. a) After your UAE treatment(s) did you also have a myomectomy (surgical removal of fibroids only, keeping your uterus (womb))?

1 yes  2 no  3 not sure  *If no or not sure, please go to question 34.*

b) If yes, please could you answer the following if you are able to do so.

i) What was the date of your myomectomy?  (ddmmyy)

ii) What do you think were the reasons for your myomectomy? (you may tick more than one box)

1 excessive bleeding  2 pelvic pain  3 pelvic pressure  4 urinary problems

5 abnormal cells/CIN2/CIN3  6 not sure  7 other  7a Please specify .....

34. We would like to know what your periods were like **after treatment**, compared with **before** your **first** UAE treatment.

a) Compared with before your first UAE treatment, how often did your periods come after your first UAE treatment?

1 have no periods  2 less often  3 about the same as before  4 more often

*If you have no periods go straight on to Section 4, question 35*

b) Compared with before your first UAE treatment, for how long did your menstrual bleeding last after your first UAE treatment?

1 far fewer days  2 fewer days  3 about the same  4 more days  5 many more days

c) Compared with before your first UAE treatment, how heavy were your periods after your first UAE treatment?

1 very much lighter  2 lighter  3 unchanged  4 heavier  5 very much heavier

d) Before your first UAE treatment did you suffer from period pains?

1 no pains  2 mild pains  3 moderate pains  4 severe pains

e) Compared with before your UAE treatment what was your experience of period pains after your first UAE treatment? 1 better  2 about the same  3 worse

**SECTION 4: OTHER INFORMATION**

*Everyone, please fill in the following section*

**35.** If there is anything else about your treatment/s for fibroids and your health which is important to you, please tell us in the space below: (for example this might include your feelings about your fertility, your uterus or ovaries)

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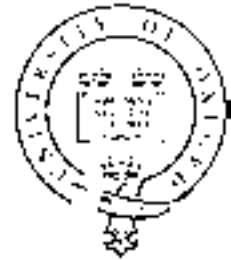
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**Thank you very much for your help.**



## Appendix 13

### Patient questionnaire 4-week reminder letter



#### The HOPEFUL Study: Hysterectomy Or Percutaneous Embolisation For Uterine Leiomyomata?

Dear

You may recall we sent you a questionnaire 4 weeks ago asking about (insert appropriate intervention), which also included some general questions about your health.

As the Study Coordinator of this project, I am sending you another questionnaire and Patient Information Sheet because we have not yet had a response from you. It would be very much appreciated if you could complete the questionnaire and return it as soon as possible in the FREEPOST envelope provided. Thank you.

It may be that you are uncertain about completing the questionnaire. I would like to reassure you that our work and your participation are absolutely confidential, and nobody involved in your care will see your completed questionnaire. The more women who help us the better our study results will be. Your contribution to our work is therefore extremely important to us. We understand however, if you prefer not to complete the questionnaire.

Please do not hesitate to contact me on 0800 0283202 if you would like further information regarding our study.

Thank you very much for your help in contributing to our research.

Yours sincerely

Allison Hirst  
HOPEFUL Project Coordinator





## Appendix 14

### Primary outcome analyses – details of logistic regression and coefficients

Note that the respective ORs and their CIs can be found by exponentiating the coefficients and their CIs in the following tables.

#### Primary outcome [1] analysis

Comparison of complications versus no complications.

##### Crude model adjusted for clustering by centre

Outcome [1]: severe/major/minor vs none	Coefficient	Standard error	z	p >  z	95% CI
Treatment	-0.5076	0.3293	-1.54	0.123	-1.1529 to 0.1378
Constant	-1.0385	0.1870	-5.55	0.000	-1.4051 to -0.6719

##### Full model adjusted for clustering by centre

Outcome [1]: severe/major/minor vs none	Coefficient	Standard error	z	p >  z	95% CI
Treatment	-0.8711	0.3163	-2.75	0.006	-1.4911 to -0.2512
Age at procedure	-0.0192	0.0168	-1.14	0.252	-0.0521 to 0.0137
Educational group 2 vs 1	0.1261	0.2173	0.58	0.562	-0.2998 to 0.5520
Educational group 3 vs 1	0.1371	0.1813	0.76	0.450	-0.2182 to 0.4924
Educational group 2 vs 1	-0.1580	0.4340	-0.36	0.716	-1.0087 to 0.6926
Educational group 3 vs 1	1.4454	0.4034	3.58	0.000	0.6548 to 2.2360
Parity	-0.0397	0.1829	-0.22	0.828	-0.3982 to 0.3189
Smoking	-0.1310	0.2470	-0.53	0.596	-0.6150 to 0.3531
Medical co-morbidity	0.6077	0.2317	2.62	0.009	0.1536 to 1.0617
Gynaecological co-morbidity	-0.0616	0.2497	-0.25	0.805	-0.5510 to 0.4279
Prior pelvic surgery	0.4632	0.2214	2.09	0.036	0.0293 to 0.8971
High BP	-0.3500	0.1680	-2.08	0.037	-0.6792 to -0.0208
Obesity	0.4350	0.1890	2.30	0.021	0.0645 to 0.8056
Antibiotics	-0.7804	0.1662	-4.70	0.000	-1.1062 to -0.4546
Q-Symptom 2 vs 1	0.0168	0.1542	0.11	0.913	-0.2854 to 0.3189
Q-Symptom 3 vs 1	0.0115	0.2575	0.04	0.964	-0.4933 to 0.5162
C-Symptom 2 vs 1	0.1814	0.1491	1.22	0.224	-0.1108 to 0.4737
C-Symptom 3 vs 1	-0.0988	0.2409	-0.41	0.682	-0.5709 to 0.3734
Menopause	0.6158	0.3449	1.79	0.074	-0.0602 to 1.2917
Age at menarche	0.1446	0.0472	3.06	0.002	0.0521 to 0.2370
Constant	-1.5672	1.1730	-1.34	0.182	-3.8662 to 0.7317

**Minimum model adjusted for clustering by centre**

Outcome [1]: severe/major/minor vs none	Coefficient	Standard error	z	p >  z	95% CI
Treatment	-0.7268	0.3125	-2.33	0.020	-1.3394 to -0.1142
Ethnic group 2 vs 1	-0.0574	0.4145	-0.14	0.890	-0.8697 to 0.7550
Ethnic group 3 vs 1	1.5582	0.3900	4.00	0.000	0.7937 to 2.3226
Medical co-morbidity	0.6260	0.2338	2.68	0.007	0.1677 to 1.0844
Prior pelvic surgery	0.4710	0.2152	2.19	0.029	0.0491 to 0.8929
High BP	-0.3809	0.1770	-2.15	0.031	-0.7278 to -0.0341
Obesity	0.4050	0.1969	2.06	0.040	0.0191 to 0.7909
Antibiotics	-0.7926	0.1565	-5.07	0.000	-1.0992 to -0.4859
Age at menarche	0.1349	0.0471	2.86	0.004	0.0425 to 0.2273
Constant	-2.2661	0.5920	-3.83	0.000	-3.4265 to -1.1057

**Primary outcome [2] analysis: severe/major versus minor/no complications**

Comparison of severe/major complications versus minor or no complications.

**Crude model adjusted for clustering by centre**

Outcome [2]: severe/major vs minor/none	Coefficient	Standard error	z	p >  z	95% CI
Treatment	-1.159705	0.3821862	-3.03	0.002	-1.908776 to -0.4106339
Constant	-2.057569	0.1727598	-11.91	0.000	-2.396172 to -1.718966

**Full model adjusted for clustering by centre**

Outcome [2]: severe/major vs minor/none	Coefficient	Standard error	z	p >  z	95% CI
Treatment	-1.5710	0.3739	-4.20	0.000	-2.3038 to -0.8382
Age at procedure	-0.0236	0.0183	-1.29	0.197	-0.0595 to 0.0123
Educational group 2 vs 1	-0.1240	0.3026	-0.41	0.682	-0.7171 to 0.4692
Educational group 3 vs 1	0.0264	0.3163	0.08	0.934	-0.5935 to 0.6463
Ethnic group 2 vs 1	-0.3176	0.6017	-0.53	0.598	-1.4969 to 0.8617
Ethnic group 3 vs 1	0.5824	0.7077	0.82	0.411	-0.8048 to 1.9695
Parity group	-0.1013	0.2815	-0.36	0.719	-0.6530 to 0.4504
Smoking group	-0.1294	0.3299	-0.39	0.695	-0.7760 to 0.5172
Medical co-morbidity	0.8720	0.2168	4.02	0.000	0.4471 to 1.2968
Gynaecological co-morbidity	-0.1132	0.3238	-0.35	0.727	-0.7478 to 0.5214
Surgery	0.2772	0.3537	0.78	0.433	-0.4160 to 0.9705
High BP	-0.5125	0.3261	-1.57	0.116	-1.1517 to 0.1266
Obesity	0.5996	0.2493	2.40	0.016	0.1109 to 1.0884
Antibiotics	-0.9291	0.4638	-2.00	0.045	-1.8381 to -0.0200
Q-Symptom 2 vs 1	0.2071	0.3463	0.60	0.550	-0.4717 to 0.8860
Q-Symptom 3 vs 1	0.1588	0.4107	0.39	0.699	-0.6460 to 0.9637
C-Symptom 2 vs 1	0.1508	0.2464	0.61	0.541	-0.3321 to 0.6337
C-Symptom 3 vs 1	0.0013	0.5191	0.00	0.998	-1.0161 to 1.0186
Menopause	0.8160	0.5420	1.51	0.132	-0.2462 to 1.8782
Age at menarche	0.1456	0.0874	1.67	0.096	-0.0258 to 0.3169
Constant	-2.3220	1.4906	-1.56	0.119	-5.2436 to 0.5995

**Minimum model adjusted for clustering by centre**

Outcome [2]: severe/major vs minor/none	Coefficient	Standard error	z	p >  z	95% CI
Treatment	-1.3881	0.3323	-4.18	0.000	-2.0395 to -0.7367
Medical co-morbidity	0.8759	0.2203	3.98	0.000	0.4440 to 1.3076
High BP	-0.5462	0.3133	-1.74	0.081	-1.1602 to 0.0678
Obesity	0.5839	0.2456	2.38	0.017	0.1026 to 1.0652
Antibiotics	-0.9633	0.4417	-2.18	0.029	-1.8291 to -0.0976
Age at menarche	0.1519	0.0856	1.78	0.076	-0.0158 to 0.3196
Constant	-3.3701	1.2321	-2.74	0.006	-5.7849 to -0.9552

**General side-effect analysis**

GSE/not GSE treated as outcome variable, severity of outcome as a covariate (coded none, minor or major/severe as per health economics)

**Crude model adjusted for clustering by centre**

Outcome: GSE/not GSE	Coefficient	Standard error	z	p > z	95% CI
Severe/major vs none	1.0635	0.3557	2.99	0.003	0.3663 to 1.7606
Minor vs none	0.5004	0.2895	1.73	0.084	-0.0671 to 1.0679
Constant	-0.9059	0.4564	-1.98	0.047	-1.8004 to -0.0113

**GSE/not GSE – full model, adjusted for clustering by centre**

Outcome: GSE/not GSE	Coefficient	Standard error	z	p > z	95% CI
Severe/major vs none	1.0998	0.3400	3.23	0.001	0.4334 to 1.7662
Minor vs none	0.0552	0.4235	0.13	0.896	-0.7749 to 0.8853
Age at procedure	-0.0030	0.0166	-0.18	0.856	-0.0355 to 0.0295
Educational group 2 vs 1	-0.0332	0.3424	-0.1	0.923	-0.7044 to 0.6380
Educational group 3 vs 1	0.0648	0.3870	0.17	0.867	-0.6937 to 0.8234
Ethnic group 2 vs 1	-0.7463	0.3239	-2.3	0.021	-1.3812 to -0.1114
Ethnic group 3 vs 1	-0.3209	0.7053	-0.46	0.649	-1.7032 to 1.0614
Parity	-0.3197	0.2393	-1.34	0.182	-0.7888 to 0.1494
Smoking	0.1769	0.1769	1	0.317	-0.1697 to 0.5236
Medical co-morbidity	0.4674	0.3141	1.49	0.137	-0.1482 to 1.0830
Gynaecological co-morbidity	-0.2141	0.2894	-0.74	0.459	-0.7813 to 0.3531
Prior pelvic surgery	-0.1601	0.2847	-0.56	0.574	-0.7181 to 0.3978
High BP	0.1332	0.3159	0.42	0.673	-0.4859 to 0.7522
Obesity	-0.0713	0.4043	-0.18	0.86	-0.8637 to 0.7210
Antibiotics	-1.1309	0.2481	-4.56	0	-1.6171 to -0.6447
Q-symptom 2 vs 1	0.1150	0.2642	0.44	0.663	-0.4029 to 0.6329
Q-symptom 3 vs 1	0.1713	0.5120	0.33	0.738	-0.8321 to 1.1748
C-symptom 2 vs 1	0.6170	0.3755	1.64	0.1	-0.1189 to 1.3530
C-symptom 3 vs 1	-0.0003	0.3359	0	0.999	-0.6588 to 0.6581
Menopause	-0.5539	0.4406	-1.26	0.209	-1.4174 to 0.3096
Age at menarche	-0.0241	0.0481	-0.5	0.617	-0.1184 to 0.0703
Constant	0.0539	0.8954	0.06	0.952	-1.7011 to 1.8089

**Minimum model adjusted for clustering by centre**

<b>Outcome: GSE/not GSE</b>	<b>Coefficient</b>	<b>Standard error</b>	<b>z</b>	<b>p &gt; z</b>	<b>95% CI</b>
Severe/major vs none	1.0486	0.3422	3.06	0.002	0.3779 to 1.7194
Minor vs none	0.0796	0.3747	0.21	0.832	-0.6547 to 0.8140
Ethnic group 2 vs 1	-0.6824	0.2864	-2.38	0.017	-1.2437 to -0.1212
Ethnic group 3 vs 1	-0.1509	0.6430	-0.23	0.814	-1.4112 to 1.1094
Parity	-0.3861	0.2268	-1.70	0.089	-0.8307 to 0.0585
Antibiotics	-1.0785	0.2686	-4.02	0	-1.6049 to -0.5521
Constant	0.1497	0.3456	0.43	0.665	-0.5276 to 0.8271

# Appendix 15

## Health economics

### Search strategy for the literature review of cost-effectiveness of UAE and hysterectomy

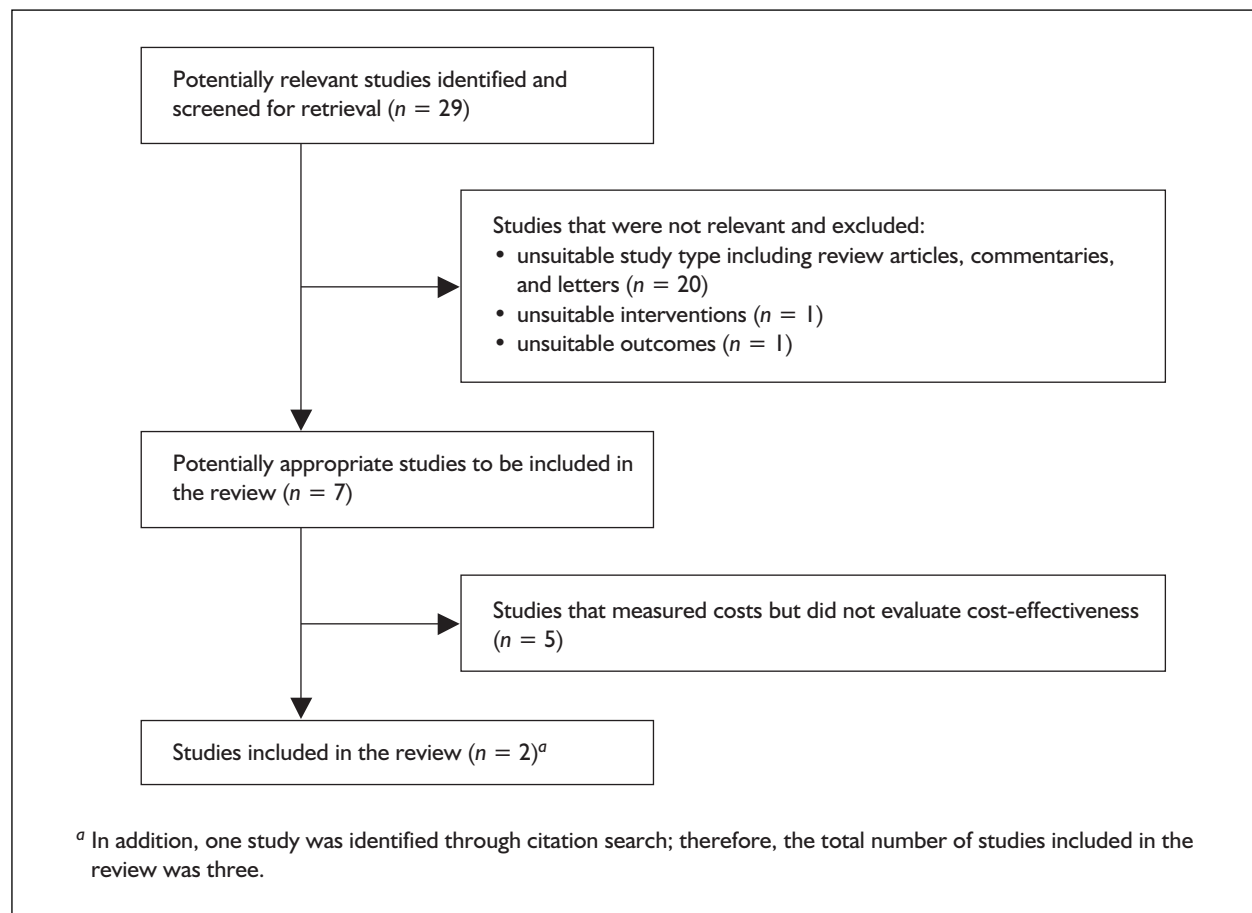
#### Search filters used in the MEDLINE search

1. Uterine artery emboli?ation.tw
2. Uterine fibroid emboli?aton.tw
3. UAE.tw
4. Fibroid adj5 emboli?ation.tw
5. Uter\$ adj5 emboli?ation.tw
6. Or/1-5
7. Economics/
8. "costs and cost analysis"/
9. Cost allocation/
10. Cost-benefit analysis/
11. Cost control/
12. Cost savings/
13. Cost of illness/
14. Cost sharing/
15. "deductibles and coinsurance"/
16. Medical savings accounts/
17. Health care costs/
18. Direct service costs/
19. Drug costs/
20. Employer health costs/
21. Hospital costs/
22. Health expenditures/
23. Capital expenditures/
24. Value of life/
25. Exp economics, hospital/
26. Exp economics, medical/
27. Economics, nursing/
28. Economics, pharmaceutical/
29. Exp "fees and charges"/
30. Exp budgets/
31. (low adj cost).mp.
32. (high adj cost).mp.
33. (health?care adj cost\$).mp.
34. (fiscal or funding or financial or finance).tw.
35. (cost adj estimate\$).mp.
36. (cost adj variable).mp.
37. (unit adj cost\$).mp.
38. (economic\$ or pharmacoeconomic\$ or price\$ or pricing).tw.
39. or/7-38
40. 6 and 39

#### Search filters used in the EMBASE search

1. Uterine artery emboli?ation.tw
2. Uterine fibroid emboli?aton.tw
3. UAE.tw
4. Fibroid adj5 emboli?ation.tw
5. Uter\$ adj5 emboli?ation.tw
6. Or/1-5
7. Socioeconomics/
8. Cost benefit analysis/
9. Cost effectiveness analysis/
10. Cost of illness/
11. Cost control/
12. Economic aspect/
13. Financial management/
14. Health care cost/
15. Health care financing/
16. Health economics/
17. Hospital cost/
18. (fiscal or financial or finance or funding).tw.
19. Cost minimization analysis/
20. (cost adj estimate\$).mp.
21. (cost adj variable\$).mp.
22. (unit adj cost\$).mp.
23. or/7-22
24. 6 and 23

## Flow of studies through the review process



## Kaplan–Meier analysis

Time	Begin total	Fail	Net lost	Survivor function	Standard error	95% CI
1	649	48	27	0.9260	0.0103	0.9031 to 0.9437
2	574	27	18	0.8825	0.0128	0.8549 to 0.9051
3	529	19	82	0.8508	0.0142	0.8204 to 0.8764
4	428	11	96	0.8289	0.0153	0.7965 to 0.8567
5	321	9	66	0.8057	0.0167	0.7704 to 0.8361
6	246	4	100	0.7926	0.0177	0.7553 to 0.8248
7	142	1	84	0.7870	0.0184	0.7482 to 0.8206
8	57	0	47	0.7870	0.0184	0.7482 to 0.8206
9	10	0	9	0.7870	0.0184	0.7482 to 0.8206
10	1	0	1	0.7870	0.0184	0.7482 to 0.8206

## Cox proportional hazard analysis

_t	Coefficient	Robust standard error	z	p > z	95% CI
ageatop	-0.035729	0.0143398	-2.49	0.013	-0.0638345 to -0.0076235

## Parametric model using Weibull distribution

_t	Coefficient	Robust standard error	z	p > z	95% CI
age at operation	-0.0331	0.0151	-2.19	0.029	-0.0628 to -0.0035
constant	-1.8053	0.6804	-2.65	0.008	-3.1388 to -0.4718
ln(p)	0.0102	0.0551	0.19	0.853	-0.0978 to 0.1182
p	1.0103	0.0557			0.9069 to 1.1255
1/p	0.9898	0.0545			0.8885 to 1.1027

## Parametric model using exponential distribution

_t	Coefficient	Robust standard error	z	p > z	95% CI
age at operation	-0.0332	0.0152	-2.18	0.029	-0.0630 to -0.0034
constant	-1.7864	0.7072	-2.53	0.012	-3.1725 to -0.4004

## Using generalised ordered logit models

Few severe complications were recorded in both groups (UAE  $n = 1$ , Hyst  $n = 3$ ). Therefore, for the purpose of analysis, the categories for severe and major complications were collapsed into one category to give three categories that have a clear ordering (severe/major, minor and none).

The generalised ordered logit model can be written as

$$p(Y_i > j) = g(X\beta_j) = \frac{\exp(\alpha_j + X_i\beta_j)}{1 + \exp(\alpha_j + X_i\beta_j)}, j = 1, \dots, M - 1$$

where  $M$  is the number of categories,  $\alpha_j$  are intercept terms for the model and  $\beta_j$  are the coefficients for the explanatory variables  $X_i$ . Writing the generalised ordered logit model in this way facilitates comparison with the standard ordered logit and standard logit models. Clearly, the expression above equates to a standard logit for each potential dichotomous split across the  $M$  categories and the term on the right-hand side is the standard inverse logit transformation. The standard ordered logit model is often termed the 'parallel lines' model and corresponds to restricting the  $\beta$  coefficients in the above equation

to be the same across categories with only the  $\alpha_j$ s allowed to vary. The generalised ordered logit model relaxes this assumption – at its most saturated it corresponds to fitting separate logistic regressions. However, its flexibility and efficiency stem from being able to test and specify the appropriate restrictions, allowing some of the coefficients to vary while constraining the others.

In terms of the current example, it is worth noting that, based on pooling severe/major complications to a single category, the split already presented for the two primary outcomes corresponds to a fully saturated generalised ordered logit. This means that it is possible to use the models, as presented in Appendix 14, to estimate the probability of falling into each of the three categories. In terms of the three-category model above, we can specify the probabilities of complications in each of the three categories in terms of the logistic regressions for each of the primary outcomes reported above:

$$\begin{aligned} p(Y_i = \text{no complications}) &= 1 - g(X_i\beta_1) \\ p(Y_i = \text{minor complications}) &= g(X_i\beta_1) - g(X_i\beta_2) \\ p(Y_i = \text{major/severe complications}) &= g(X_i\beta_2) \end{aligned}$$

where the subscript 1 relates to the coefficients for primary outcome [1] (Appendix 14) and the subscript 2 relates to the coefficients for primary outcome [2] (Appendix 14).





## Appendix I6

### Q24a and f – expectations not fulfilled and why and problems caused by the treatment

#### Q24a Expectations not fulfilled and why

##### Expectations and feelings prior to procedure

- “Did not expect to still have numbness of the stomach.” (H, 43 years)
- “Not entirely – expected to have flatter abdomen, it remained much the same – also inclined to put on weight.” (H, 64 years)
- “No follow-up treatment offered and did not take HRT – suffer from head hair loss and other male symptoms.” (H, 63 years)
- “I did not have any expectations.” (H, 39 years)
- “Treatment stopped the bleeding, but didn’t feel the NEW WOMAN a hysterectomy and HRT was reputed to make me.” (H, 64 years)
- “Did not expect to have hot flushes.” (H, 57 years)
- “I did not expect a prolapse. I did not expect to lose ovaries and Fallopian tubes.” (H, 60 years)
- “I was led to believe fibroid would shrink to negligible size not just 50%.” (U, 39 years)
- “Fibroid did not shrink as much as expected.” (U, 49 years)
- “Although there has been improvement my uterus is still very bulky.” (U, 53 years)
- “Wanted to be completely free of fibroids with fully functioning uterus.” (U, 42 years)
- “Would have liked total disappearance, not just shrinkage.” (U, 52 years)
- “The fibroids took much longer to shrink than I expected and returned within 18 months of the operation.” (U, 39 years)
- “I still have masses of fibroids in my womb, even though lots were discharged after treatment.” (U, 52 years)
- “The fibroids were reduced in size to some extent, but not as much as I had hoped.” (U, 45 years)
- “I don’t feel much better than before my treatment – fibroid hasn’t decreased in size as much as I thought it would, and my weight has increased.” (U, 44 years)
- “Promised MRI scan after treatment to check shrinkage – it didn’t happen.” (U, 56 years)
- “I am disappointed by the lack of reduction in size and little reduction in symptoms.” (U, 43 years)

- “I anticipated fibroids shrinking and being absorbed back into body, as explained prior to treatment. This was not the case.” (U, 38 years)
- “I had anticipated a complete reversal of the fibroid growth – the treatment appears to have slowed the growth of the fibroid, the symptoms have returned.” (U, 46 years)
- “I was hoping my periods would stop all together.” (U, 46 years)
- “Really didn’t have any expectations, it all happened so quick.” (U, 35 years)
- “The fibroid only shrank less than 50%.” (U, 52 years)
- “... I was assured my fertility would remain intact ... I should have been informed of the risks to my fertility at the time ...” (U, 46 years)
- “I hoped the volume and bulkiness would be reduced further.” (U, 35 years)
- “Fibroids were not reduced by expected amount.” (U, 46 years)
- “I was hoping the fibroids would have shrunk much more.” (U, 56 years)
- “Generally satisfied, but I had hoped the fibroid would shrink more than the 40% it did.” (U, 49 years)
- “My fibroids did not shrink as much as I was hoping they would do.” (U, 51 years)
- “My intermural fibroid shrunk only by 23%. Expected as much as 60%.” (U, 39 years)
- “Lost less fibroid mass than I had hoped and no affect on bladder, although I admit I was not promised more.” (U, 49 years)

##### Damage related to the procedure itself

- “The fibroid did not go away, and the treatment was very painful.” (U, 41 years)
- “Because it took 2 years to recover from treatment and fibroids have grown back.” (U, 50 years)
- “At operation unable to find blood sources – only half done. Very painful. Still bleed a lot.” (U, 53 years)
- “Emergency surgery after treatment.” (U, 30 years)
- “I became very poorly after op for UAE ending with a hysterectomy which cured me.” (U, 49 years)
- “Taken very ill 2 weeks after op with blocked bowel.” (U, 60 years)

- “Severe pain, unable to walk and readmitted to hospital for pain management whilst the fibroid shrank. Still needed an operation to remove fibroid.” (U, 42 years)
- “UAE unsuccessful and caused severe symptoms which resulted in urgent surgery 4.75 months later.” (U, 58 years)
- “Treatment could not be completed successfully, fibroids returned, conception proved unlikely – eventual hysterectomy.” (U, 40 years)
- “Not removed.” (U, 59 years)
- “I was in far worse pain after UAE and had a hysterectomy within a few months of UAE.” (U, 55 years)
- “I didn’t know how painful the treatment was going to be.” (U, 57 years)

### **Continue to get the same problems**

- “Still get urine infections and stomach pain and thrush”(H, 47 years)
- “I believe fibroid still large and will require treatment in future.” (U, 53 years)
- “Fibroids still grew, haemorrhaging more frequently, required alternative surgical treatment – hysterectomy.” (U, 46 years)
- “Feel the fibroids still there. Uterus still big and never had any children.” (U, 50 years)
- “Although there has been improvement my uterus is still very bulky.” (U, 59 years)
- “Heavy bleeding only slightly improved afterwards.” (U, 58 years)
- “The fibroid did not go away and the treatment was very painful.” (U, 41 years)
- “Due to continuation of symptoms had to undergo a hysterectomy after 2 years.” (U, 51 years)
- “Pain not reduced, still unable to carry a child.” (U, 40 years)
- “I still have menstrual pains and severe constipation. I strongly believe my fibroids have come back and are even bigger.” (U, 42 years)
- “Still got heavy periods and bulk symptoms.” (U, 53 years)
- “I did not experience any benefits.” (U, 50 years)
- “I had to have 2 treatments, did not have another child, fibroid still very large.” (U, 44 years)
- “Because the heavy bleeding and pain continue and was worse.” (U, 48 years)
- “I don’t feel much better than before my treatment – fibroid hasn’t decreased in size as much as I thought it would, and my weight has increased.” (U, 44 years)
- “My periods are still the same, sometimes pain is worse. I wish I had opted for a hysterectomy.” (U, 46 years)
- “I am disappointed by the lack of reduction in size and little reduction in symptoms.” (U, 43 years)
- “I have more small fibroids.” (U, 42 years)

- “Fibroids continued to grow.” (U, 51 years)
- “Still got heavy periods.” (U, 42 years)
- “I don’t think the treatment worked for me. I still have fibroids and the symptoms associated with them.” (U, 44 years)
- “Periods remain heavy and other symptoms unresolved.” (U, 49 years)
- “The treatment did not reduce the fibroids...heavy bleeding and pain only stopped as my periods lessened and stopped.” (U, 57 years)
- “Still have pains, especially on some mornings, having been laying down for >4–5 hours, pressure on bladder, some pains down legs/groin, often relieved by period, which is now less painful.” (U, 38 years)
- “I still suffer from heavy bleeding though not as bad as before.” (U, 38 years)
- “My menstrual bleeding still heavy. I can’t live without mefenamic and tranexamic acid.” (U, 45 years)
- “Although growth had been halted, the fibroid has not reduced in size sufficiently.” (U, 45 years)
- “Flatter tummy, but worsened pain and continual heavy periods.” (U, 45 years)
- “Still bleeding every day.” (U, 41 years)
- “Still have large mass, size only slightly smaller”(U, 51 years)
- “I still have large fibroids.” (U, 55 years)
- “Still troublesome periods – longer, stopping and starting.” (U, 46 years)
- “Only partly fulfilled i.e. bleeding improved.” (U, 45 years)
- “I still have severe pelvic pain.” (U, 42 years)
- “The fibroids were still growing, I was still bleeding heavily”(U, 49 years)

### **For a while it seemed OK but things have gone wrong again now**

- “A year after treatment I had heavier periods. I was alright for 1 year.” (U, 56 years)
- “Recently I felt the fibroids have increased, although initially happy with treatment.” (U, 50 years)
- “Treatment did not work in long term.” (U, 34 years)
- “My fibroid has come back and am at present awaiting further treatment.” (U, 46 years)
- “I was alright for 4 years, then the symptoms returned and I had to have a hysterectomy in 2003.” (U, 54 years)
- “At the time, yes, but the fibroid regrew after a couple of years.” (U, 55 years)
- “Periods stayed same, fibroid in later years grew again and had to have a myomectomy.” (U, 40 years)
- “The fibroids took much longer to shrink than I expected and returned within 18 months of the operation.” (U, 39 years)

“I still have menstrual pains and severe constipation. I strongly believe my fibroids have come back are even bigger.” (U, 42 years)

“Because it took 2 years to recover from treatment and fibroids have grown back.” (U, 50 years)

“Unfortunately original symptoms have been gradually returning over last year.” (U, 51 years)

“Fibroids recurred 9–12 months later – until this I was better.” (U, 50 years)

“My relief was short-lived and I have since had a hysterectomy.” (U, 30 years)

“Good for a while, but symptoms soon returned.” (U, 51 years)

“Fibroids back.” (U, 38 years)

“Still have clotting and pain has become quite severe again, though it did improve for a while.” (U, 45 years)

“Have recently started to have heavy periods again.” (U, 52 years)

“The treatment was successful for approximately 2 years. The symptoms returned and I had a hysterectomy.” (U, 40 years)

“The symptoms I experience before treatment have gradually returned.” (U, 47 years)

“Fibroids grew back and a hysterectomy was necessary, but results were good to begin with.” (U, 58 years)

“Successful for 4 years – now regrowing and experiencing problems again.” (U, 47 years)

“Fibroids have returned and I received no follow-up treatment.” (U, 43 years)

“Three more fibroids have occurred.” (U, 48 years)

“Fibroids returned and bigger, needed a hysterectomy.” (U, 65 years)

“After 2 years I started discharging which went on for weeks.” (U, 50 years)

“Starting in the last year to experience problems again.” (U, 35 years)

### **New unpleasant symptoms have come**

“Since operation I have developed IBS symptoms, severe wind pains and increase in weight.” (H, 53 years)

“I am now suffering aching joints, premature sexual feelings diminished from onset.” (H, 56 years)

“Side effects which I assume are UAE-related.” (U, 39 years)

“I have not had regular periods since treatment.” (U, 43 years)

“My symptoms changed from heavy bleeding to severe painful periods.” (U, 53 years)

### **Bowel problems**

“Since operation I have developed IBS symptoms, severe wind pains and increase in weight.” (H, 53 years)

“It seems to have caused bowel problems.” (H, 58 years)

“Taken very ill 2 weeks after op with blocked bowel.” (U, 60 years)

### **Energy, lack of**

“Emotionally and physically felt drained – affected sexual relationship and partner climatically.” (H, 53 years)

“Left me exhausted and took about a year to recover.” (H, 60 years)

### **Fertility, specifically concerning**

“I might have liked to be able to have another child maybe!” (H, 47 years)

“Would have liked to have more children.” (H, 50 years)

“Feel the fibroids still there. Uterus still big and never had any children.” (U, 50 years)

“Pain not reduced, still unable to carry a child.” (U, 40 years)

“Although fibroid mass has reduced, I have not become pregnant.” (U, 50 years)

“I am still childless and have gone through the menopause early.” (U, 45 years)

“I had to have 2 treatments, did not have another child, fibroid still very large.” (U, 44 years)

“Because the myomectomy was not possible I still have fibroids and have not been able to have children.” (U, 39 years)

“I was hoping the fibroids would reduce enough for a pregnancy.” (U, 48 years)

“Can’t get pregnant.” (U, 43 years)

“The fibroids did not shrink enough to allow conception.” (U, 46 years)

“I did not get pregnant.” (U, 49 years)

“I was told my fertility would not be affected post-treatment, this has not been the case.” (U, 46 years)

“Treatment could not be completed successfully, fibroids returned, conception proved unlikely – eventual hysterectomy.” (U, 40 years)

“I was unable to conceive and after 2 years suffered degeneration of the ‘dead’ fibroids, leading to a hysterectomy.” (U, 50 years)

“Had undertaken treatment to improve fertility prospects with no success.” (U, 47 years)

“Still trying to become pregnant.” (U, 31 years)

“It created more scar tissue internally than I expected, it reduced my chances of pregnancy more than expected.” (U, 46 years)

“I hoped fertility/chance to have children would have been improved – but possibly fibroid has too much of a hold and distorted womb.” (U, 54 years)

“Because I did not conceive.” (U, 53 years)

**Menopause + its symptoms/HRT**

- “No follow-up treatment offered and did not take HRT – suffer from head hair loss and other male symptoms.” (H, 63 years)
- “Ovaries removed resulting in never-ending hot flushes.” (H, 59 years)
- “I didn’t know I wouldn’t have to go for smear test anymore.” (H, 42 years)
- “Treatment stopped the bleeding, but didn’t feel the NEW WOMAN a hysterectomy and HRT was reputed to make me.” (H, 64 years)
- “Did not expect to have hot flushes.” (H, 57 years)
- “If I could have had some other treatment I would as I went into early menopause.” (H, 47 years)
- “I am still childless and have gone through the menopause early.” (U, 45 years)

**Prolapse**

- “I did not expect a prolapse. I did not expect to lose ovaries and Fallopian tubes.” (H, 60 years)

**Sexual problems**

- “Emotionally and physically felt drained – affected sexual relationship and partner climatically.” (H, 53 years)
- “I am now suffering aching joints, premature sexual feelings diminished from onset.” (H, 56 years)

**Urinary problems**

- “Still bleed heavily sometimes and urinate all the time.” (U, 48 years)
- “Lost less fibroid mass than I had hoped and no effect on bladder, although I admit I was not promised more.” (U, 49 years)

**Weight gain**

- “Since operation I have developed IBS symptoms, severe wind pains and increase in weight.” (H, 53 years)
- “Not entirely – expected to have flatter abdomen, it remained much the same – also inclined to put on weight.” (H, 64 years)
- “Unexpected weight gain and glandular problems.” (H, 56 years)
- “I don’t feel much better than before my treatment – fibroid hasn’t decreased in size as much as I thought it would, and my weight has increased.” (U, 44 years)
- “The fibroids have lessened but I’ve put on a lot of weight and don’t feel good about myself.” (U, 39 years)

**Further treatment needed**

- “I believe fibroid still large and will require treatment in future.” (U, 53 years)

- “UAE did not work for me, had a myomectomy.” (U, 46 years)
- “Subsequently underwent a hysterectomy.” (U, 48 years)
- “Fibroids still grew, haemorrhaging more frequently, required alternative surgical treatment – hysterectomy.” (U, 46 years)
- “It was not entirely successful, I still had a myomectomy a couple of years later.” (U, 46 years)
- “My fibroid has come back and am at present awaiting further treatment.” (U, 46 years)
- “I was alright for 4 years, then the symptoms returned, and I had to have a hysterectomy in 2003.” (U, 54 years)
- “Due to continuation of symptoms had to undergo a hysterectomy after 2 years.” (U, 51 years)
- “Ended up having a hysterectomy.” (U, 44 years)
- “Periods stayed same, fibroid in later years grew again and had to have a myomectomy.” (U, 40 years)
- “I’ve had to have a hysterectomy.” (U, 48 years)
- “I had to have 2 treatments, did not have another child, fibroid still very large.” (U, 44 years)
- “Treatment didn’t work, so I had a hysterectomy – another fibroid appeared.” (U, 52 years)
- “My relief was short-lived, and I have since had a hysterectomy.” (U, 30 years)
- “I became very poorly after op for UAE ending with a hysterectomy which cured me.” (U, 49 years)
- “No major improvements so underwent a hysterectomy in 2002.” (U, 45 years)
- “I have since had a hysterectomy.” (U, 45 years)
- “Condition did not improve so went on to have hysterectomy.” (U, 52 years)
- “A fibroid has grown large and has solidified. I now need a hysterectomy – May 2005.” (U, 59 years)
- “Nothing changed, instead I had worse period pains and heavy period until I had a myomectomy.” (U, 36 years)
- “Unfortunately treatment did not work – had to have part hysterectomy.” (U, 47 years)
- “Fibroid did not shrink – had to have a hysterectomy.” (U, 53 years)
- “Severe pain, unable to walk and readmitted to hospital for pain management whilst the fibroid shrank. Still needed an operation to remove fibroid.” (U, 42 years)
- “I still had to have a myomectomy a year later, and I still have 1 fibroid.” (U, 35 years)
- “UAE was not successful – I needed a partial hysterectomy Dec 2002.” (U, 50 years)
- “UAE unsuccessful and caused severe symptoms which resulted in urgent surgery 4.75 months later” (U, 58 years)

- “In my case I was unlucky – they grew back and I had to have a hysterectomy.”  
(U, 43 years)
- “Because I still had to go and have a hysterectomy.” (U, 44 years)
- “I think I was unlucky. I had it done twice and it didn’t work for me.” (U, 34 years)
- “Treatment could not be completed successfully, fibroids returned, conception proved unlikely – eventual hysterectomy.” (U, 40 years)
- “The treatment was successful for approximately 2 years. The symptoms returned and I had a hysterectomy.” (U, 40 years)
- “I was unable to conceive and after 2 years suffered degeneration of the ‘dead’ fibroids, leading to a hysterectomy.” (U, 49 years)
- “Fibroids grew back and a hysterectomy was necessary, but results were good to begin with.”  
(U, 58 years)
- “After second UAE they were fulfilled.”  
(U, 40 years)
- “I had to have a hysterectomy.” (U, 38 years)
- “Fibroid reduced to 1/2 its original size – subsequently had a successful myomectomy.”  
(U, 50 years)
- “Fibroids became necrotic, had years of bad infections. Then had to have a hysterectomy.”  
(U, 48 years)
- “Fibroids returned and bigger, needed a hysterectomy.” (U, 65 years)
- “I was in far worse pain after UAE and had a hysterectomy within a few months of UAE.”  
(U, 55 years)

### Not knowing/post-treatment beliefs and speculations

- “I was diagnosed with low thyroid and high cholesterol 4 years ago. I think it might be because my right ovary was removed.”  
(H, 54 years)
- “Did not know what was happening and what they done.” (H, 38 years)
- “I still have menstrual pains and severe constipation. I strongly believe my fibroids have come back are even bigger.”  
(U, 42 years)
- “Have not had any follow-up so don’t know if fibroids were got rid of.” (U, 46 years)
- “Almost completely – but I suspect some regrowth as sometimes bleed quite heavily again – but nothing like the haemorrhage prior to UAE.”  
(U, 47 years)
- “Never told results of MRI scans – if improvement or not.” (U, 48 years)
- “I am not sure if the fibroids have regrown as I am now suffering similar swellings as before.”  
(U, 53 years)

### Negative emotions

- “Emotionally and physically felt drained – affected sexual relationship and partner climatically.”  
(H, 53 years)

### Simply ‘unsuccessful’

- “Hysterectomy as treatment unsuccessful.”  
(U, 51 years)
- “Uterine embolisation was unsuccessful in my case.” (U, 46 years)
- “UAE did not work for me, had a myomectomy.”  
(U, 46 years)
- “It was not entirely successful, I still had a myomectomy a couple of years later.”  
(U, 46 years)
- “It was unsuccessful for me.” (U, 45 years)
- “Didn’t appear to work.” (U, 50 years)
- “I did not experience any benefits.” (U, 50 years)
- “Treatment did not work for me.” (U, 55 years)
- “Did not work.” (U, 49 years)
- “Fibroids did not appear to shrink from day one.”  
(U, 45 years)
- “I think I was unlucky. I had it done twice and it didn’t work for me.” (U, 34 years)
- “I experienced no improvement in symptoms.”  
(U, 61 years)
- “Had undertaken treatment to improve fertility prospects with no success.” (U, 47 years)
- “Didn’t work.” (U, 55 years)

### Q24f: Problems caused by the treatment

#### Expectations and feelings prior to procedure

- “... I was not told about the side effects of the treatment and I still suffered from very bad stomach and back pains.” (H, 49 years)
- “The bleeding continued for a lot longer than usual, resulting in several visits to day clinics and incurring quite a lot of discomfort.”  
(H, 53 years)
- “I still have trouble with my tummy...very bad pains, bloatedness and cannot lose weight easily.” (H, 38 years)
- “I have struggled for many years to come to terms with not being able to have children. This has severely affected my mental health at times.”  
(H, 44 years)
- “Unnecessary surgery, referral was for ovarian cyst when fibroids were discovered.” (H, 61 years)
- “Back pains. Surgeon tried to remove my uterus; I told the surgeon before operation to remove womb only.” (H, 54 years)
- “Sudden earlier menopause requiring HRT instead of gradual natural one.” (H, 56 years)

“Initially had pelvic infection which extended recovery period. Probably up to 3 months following treatment before back to good health.” (U, 51 years)

“I was much more ill in the week after treatment than I expected.” (U, 53 years)

“The protracted period of painful suffering I endured for 2 years after being told that it would last a few weeks.” (U, 50 years)

“I feel it was the 2nd angiogram to check my fibroid being fed again by other vessels that caused a little tenderness when lifting. I did not need a second embolisation as it shrunk within next 2 years as predicted.” (U, 61 years)

“I had a chronic discharge and pain after 1.5 years and 2 exploratory ops told that fibroids did not shrivel but died off and broke up causing very bad injections and I am sure that some of the ‘white goo’ was the ‘glue’ ”(U, 53 years)

“Only found out about fibroid because it blocked my bladder. First operation laparotomy couldn’t remove, embolisation, then myomectomy stomach lining falling apart, had hernia op, but still have problems now.” (U, 35 years)

“The recovery period was much longer than expected – about 10 weeks.” (U, 57 years)

“Discharge for year after treatment – very distressing. Pain after op much greater than I expected.” (U, 50 years)

“I was unwell prior to the treatment and after the treatment I was diagnosed with coeliac disease. I’m not sure whether the total intolerance of gluten was triggered by the treatment.” (U, 56 years)

“I was in far worse pain after UAE and had a hysterectomy within a few months of UAE.” (U, 55 years)

### **Damage related to the procedure itself**

“They damaged my kidney during surgery.” (H, 54 years)

“Because of negligence during my hysterectomy I suffered 6 months of extreme bladder discomfort and had to undergo a second major operation to repair a fistula.” (H, 63 years)

“Emergency return to theatre for suture as artery damaged during procedure, suffered to a certain extent due to the trauma of the operation, although symptoms relieved.” (H, 58 years)

“Hysterectomy led to 3 further operations in following 5 weeks (one which led to stomach being cut open at right angles to initial incision for approx 6 inches and left open for about 2.5 weeks!). I could probably write a book about this.” (H, 53 years)

“My bladder was cut causing me painful problems. I even had to be sent home and self-catheterising for 3 months (H, 71 years)

“I had problems after my hysterectomy and had further treatment ... to repair my bladder which turned out to be far worse than original surgery.” (H, 56 years)

“Irregular lower right abdominal pain, at times severe, possible scar tissue, eventually requiring emergency surgery for strangulated inguinal hernia – Sept 2000 – Possible connection?.” (H, 58 years)

“... discomfort when bladder was full, and sometimes still get this discomfort – investigated.” (H, 64 years)

“The doctor perforated my bowel. Lungs collapsed, kidneys failed and I went on dialysis. I was in Hospital for 3 months.” (H, 68 years)

“Unnecessary surgery – referral was for ovarian cyst when fibroids were discovered.” (H, 61 years)

“Only initially as I got an infection within a couple of days and had to be re-admitted as blood suddenly started pouring down my legs when I was walking outside.” (H, 58 years)

“A hernia on operation site. Operated on a year after my hysterectomy, but in last few years has come back again.” (H, 61 years)

“Contracted hospital infection after treatment, now fully recovered.” (U, 56 years)

“Initially had pelvic infection which extended recovery period. Probably up to 3 months following treatment before back to good health.” (U, 51 years)

“Too much morphine during treatment. It completely blocked me up and put me in hospital for 2 weeks.” (U, 54 years)

“I was much more ill in the week after treatment than I expected.” (U, 53 years)

“I spent 3 months out of work – I had complications, during this time I was admitted to hospital twice.” (U, 54 years)

“My womb went septic 2 weeks after the UAE. I had to have an emergency hysterectomy ... was on life-support, then intensive care ....” (U, 44 years)

“Heavy discharge and infection almost continuously for 2 years following treatment (treated by GP only).” (U, 50 years)

“I was bleeding heavily after one month of treatment, admitted to hospital. I got infections and I became very anaemic. I had to be given 2 pints of blood.” (U, 51 years)

“The pain from the embolisation went on for several months where the lesser fibroids were expelled.” (U, 50 years)

“Leg pain high in right leg, a trapped nerve feeling (groin).” (U, 53 years)

“... the 2nd angiogram to check my fibroid being fed again by other vessels that caused a little tenderness when lifting ....” (U, 61 years)

“I had a fibroid measuring 37 cm in the end which I nearly died. I underwent surgery to remove it along with a hysterectomy and the fibroid was ready to burst.” (U, 48 years)

“Seven months after treatment fragments of the fibroid became infected. I spent time in hospital having antibiotic treatment.” (U, 42 years)

“Severe +++ pain post-operatively.” (U, 58 years)

“Tired ache in right thigh which radiates into groin after walking. This may or may not be related.” (U, 46 years)

“Only issue was during procedure – lots of pain, sedation seemed to wear off during procedure. Very constipated after treatment, caused bad cramps relieved with strong painkillers (morphine), longer in hospital because of this.” (U, 38 years)

“Complications after surgery – severe pain with large clots, readmitted to hospital and told by consultant that fibroid was very hot, which was causing pain, could only wait for fibroids to cool and reduce, took months before I could return to work.” (U, 53 years)

“Big fibroid was killed and became a big problem at home. After operation had problems with stomach, first 12 days didn’t function at all, then sent home, 2 days later ended up in emergency where given proper antibiotic.” (U, 43 years)

“No problems caused by treatment but aftercare in hospital was not a good experience – the nurses were neglectful as pain relief did not work.” (U, 52 years)

“The recovery period was much longer than expected about 10 weeks.” (U, 57 years)

“The treatment caused my genitals and vagina to shrink and lose a lot of feeling. This made me feel angry and depressed.” (U, 52 years)

“I felt very unwell after the UAE. It was very painful. I felt it was worse than when I had my hysterectomy.” (U, 44 years)

“I lost the use of my left leg for two months and suffered unimaginable pain and no one cared.” (U, 55 years)

“Discharge for year after treatment – very distressing. Pain after op much greater than I expected.” (U, 50 years)

“Septicaemia following procedure, which necessitated 6 nights in hospital for IV antibiotics and other treatment.” (U, 61 years)

“Fibroids became necrotic, suffered years of infections and subsequently had a hysterectomy....” (U, 48 years)

“I suffered a vaginal infection, which was very unpleasant and resulted in a full anaesthetic to have my coil removed.” (U, 51 years)

“I suffered a bit with a nasty discharge for some time after the treatment which has now cleared. It was very painful after the actual treatment.” (U, 52 years)

“I was unwell prior to the treatment and after the treatment I was diagnosed with coeliac disease – I’m not sure whether the total intolerance of gluten was triggered by the treatment.” (U, 56 years)

“I was in far worse pain after UAE and had a hysterectomy within a few months of UAE.” (U, 55 years)

### **New unpleasant symptoms have come Abdomen**

“Irregular lower right *abdominal* pain, at times severe, possible scar tissue, eventually requiring emergency surgery for strangulated inguinal hernia – Sept 2000 – Possible connection?.” (H, 58 years)

“I still have trouble with my *tummy* ... very bad pains – bloatedness ...” (H, 38 years)

“A hernia on *operation site*. Operated on a year after my hysterectomy, but in last few years has come back again.” (H, 61 years)

“Cannot put any pressure on *abdomen*, cannot lie on *tummy* at all.” (U, 40 years)

“Heavy period and pain on the lower *abdomen* for no apparent reason.” (U, 49 years)

“*Abdominal* adhesion.” (U, 40 years)

“Severe *abdominal* pain some time after treatment – several months lasting for several weeks, so much so that consultant referred me for bowel examination – nothing found.” (U, 55 years)

### **Adhesions**

“At least two minor ops to relieve *adhesions* and sometimes still cause concern.” (H, 49 years)

“*Abdominal adhesion*.” (U, 40 years)

### **Anaemia**

“I was bleeding heavily after one month of treatment, admitted to hospital. I got infections and I became very *anaemic*. I had to be given 2 pints of blood.” (U, 51 years)

“... several days after treatment I bled very badly and was bedridden for 2 weeks, becoming very *anaemic*.” (U, 51 years)

“After UAE I had persistent daily bleeding and/or foul discharge for 4.75 months plus increasing pain and tenderness over the fibroids, increasing tiredness and exhaustion and fever and eventually could hardly work when I was found to have become very *anaemic* and with

very high white cell count indicating sepsis.”  
(U, 58 years)

### Artery

“Emergency return to theatre for suture as *artery* damaged during procedure, suffered to a certain extent due to the trauma of the operation, although symptoms relieved.” (H, 58 years)  
“Slight pain in left-hand *artery* of leg.” (U, 51 years)

### Back

“... I still suffered from very bad ... back pains.”  
(H, 49 years)  
“*Back* pains. Surgeon tried to remove my uterus; I told the surgeon before operation to remove womb only.” (H, 54 years)  
“Since the treatment I have suffered SEVERE *BACK* ACHE and right leg in PAIN.” (U, 44 years)

### Bleeding post-hysterectomy

“Granulation of scar; several episodes of light *bleeding* on intercourse.” (H, 54 years)  
“The *bleeding* continued for a lot longer than usual, resulting in several visits to day clinics and incurring quite a lot of discomfort.”  
(H, 53 years)  
“Only initially as I got an infection within a couple of days and had to be re-admitted as *blood suddenly started pouring down my legs* when I was walking outside.” (H, 58 years)

### Bloating

“I still have trouble with my tummy – I don’t have any bleeding, but I do have very bad pains – *bloatedness* and cannot lose weight easily.”  
(H, 38 years)  
“I have fibromyalgia and IBS – weight gain (but I can’t say if it’s from the fibroid). *Bloating*.”  
(H, 53 years)

### Cancer

“I now have *non-Hodgkins lymphoma* as a result of the treatment.” (U, 57 years)  
“I felt better and bleeding stopped. Last August/September bleeding started again. It was recommended I had a hysterectomy. Dec 10 bleeding stopped, *cancer* found in womb.”  
(U, 60 years)

### Discharge/fibroid changes after UAE

“*Discharge* around menstrual cycle – I understand relates to *fibroid discharge*. Weaker bladder. Diagnosed with cystocele. Assumed *fibroid growth*. Increasingly painful..” (U, 39 years)  
“Heavy *discharge* and infection almost continuously for 2 years following treatment (treated by GP only).” (U, 50 years)

“The pain from the embolisation went on for several months – where the lesser *fibroids were expelled*.” (U, 50 years)

“I feel it was the 2nd angiogram to check my fibroid being fed again by other vessels that caused a little tenderness when lifting. I did not need a second embolisation as *it shrunk within next 2 years* as predicted.” (U, 61 years)  
“I had a *fibroid measuring 37 cm* in the end which I nearly died. I underwent surgery to remove it along with a hysterectomy and the *fibroid was ready to burst*.” (U, 48 years)  
“The *fibroid is growing back*, although not as large as before (so far).” (U, 50 years)  
“*Necrotic fibroid extracted* vaginally and hysteroscopically.” (U, 50 years)  
“7 months after treatment *fragments of the fibroid became infected*. I spent time in hospital having antibiotic treatment.” (U, 42 years)  
“*Fibroids stayed same size but became necrotic*. It was also attached to an ovary causing much discomfort and nausea.” (U, 49 years)  
“*Fibroids continued to grow*. Several days after treatment I bled very badly and was bedridden for 2 weeks, becoming very anaemic.”  
(U, 51 years)  
“Since menopause, continued bleeding and *discharge* caused by *disintegration of fibroids* resulting in hysteroscopy ....” (U, 58 years)  
“I had a chronic *discharge* and pain after 1.5 years and 2 exploratory ops told that *fibroids did not shrivel but died off and broke up* causing very bad injections and I am sure that some of the ‘white goo’ was the ‘glue’ .” (U, 53 years)  
“Complications after surgery – severe pain with *large clots*, readmitted to hospital and told by consultant that *fibroid was very hot, which was causing pain, could only wait for fibroids to cool and reduce*, took months before I could return to work.” (U, 53 years)  
“*Degenerating fibroids* causing discharge.”  
(U, 55 years)  
“*Big fibroid was killed and became a big problem at home* ....” (U, 43 years)  
“After UAE I had persistent daily bleeding and/or foul *discharge* for 4.75 months plus increasing *pain and tenderness over the fibroids*, increasing tiredness and exhaustion and fever and eventually could hardly work when I was found to have become very anaemic and with very high white cell count indicating sepsis.” (U, 58 years)  
“I was unable to conceive and after 2 years suffered *degeneration of the ‘dead’ fibroids*, leading to a hysterectomy, which revealed advanced endometriosis which had not been previously diagnosed (this could have caused the infertility not the fibroids).” (U, 50 years)



“Discharge due to fibroid ‘melting’.” (U, 55 years)

“I have had a continuous heavy discharge for the past 3 years, which I am told by my gynaecologist is common after embolisation.” (U, 47 years)

“Bleeding and discharge from fibroid rubbing the wall of my womb.” (U, 53 years)

“All short-term and now resolved – (1) expulsion of 3 fibroids – 2 needed surgical help. (2) Infection with first fibroid expulsion. (3) Discharge for a few months.” (U, 48 years)

“Fibroid not reduced enough. Due to cervical prolapse and difficult position of fibroid – safest option was to have a hysterectomy – sadly.” (U, 38 years)

“Discharge for year after treatment – very distressing. Pain after op much greater than I expected.” (U, 50 years)

“Fibroids became necrotic, suffered years of infections and subsequently had a hysterectomy ....” (U, 48 years)

“Initially satisfied after UAE in 1995, in 2001 developed persistent cough and a nasty vaginal discharge, which antibiotics did not relieve. Contacted Dr X who identified rotting fibroid, but failed to remove successfully. Developed septicaemia and admitted for 4 days. Fibroid eventually moved out of uterus and was removed by forceps. Recovered well.” (U, 60 years)

“Been left with fibroid, giving pain and causing problems to bladder/bowel: no solution has been offered medically.” (U, 59 years)

“I had a necrotised fibroid which made me very unwell, high temperature etc. I had been unaware of the symptoms of this complication and did not know what was wrong.” (U, 51 years)

“I suffered a bit with a nasty discharge for some time after the treatment which has now cleared. It was very painful after the actual treatment.” (U, 52 years)

“Until 6 months ago I had regular mid-term liquid seepage for 4–5 days and prolonged periods (almost 12 days) so was almost constantly ‘seeping’ or ‘bleeding’.” (U, 46 years)

“Only that fibroids have returned and discovered this when I had laparoscopy which caused infection lasting several months (U, 43 years)

“Vaginal discharge.” (U, 51 years)

“... intolerance symptoms to wheat and dairy. Symptoms were discharge after eating (sometimes heavy flow).” (U, 38 years)

“After 2 years I started discharging dark brown blood, for weeks – I was then referred to a consultant – ended up having a hysterectomy.” (U, 50 years)

#### Food intolerances

“Food intolerances which has now largely resolved itself.” (U, 49 years)

“I was unwell prior to the treatment and after the treatment I was diagnosed with coeliac disease – I’m not sure whether the total intolerance of gluten was triggered by the treatment.” (U, 56 years)

“Not sure but may have caused intolerance symptoms to wheat and dairy. Symptoms were discharge after eating (sometimes heavy flow).” (U, 38 years)

#### Groin/leg

“Trapped nerve causing pain down outside of left thigh to knee, gets worse when standing or carrying even light loads.” (H, 56 years)

“Leg pain high in right leg, a trapped nerve feeling (groin).” (U, 53 years)

“Since the treatment I have suffered SEVERE BACK ACHE and right leg in PAIN.” (U, 44 years)

“Pain in my groin where the catheter was inserted.” (U, 31 years)

“Tired ache in right thigh which radiates into groin after walking. This may or may not be related.” (U, 46 years)

“I lost the use of my left leg for two months and suffered unimaginable pain and no one cared.” (U, 55 years)

“Painful periods, slight ache in groin when period is due.” (U, 49 years)

“... pain near right groin/pubis bone ... saw surgeon ... who said it was similar to ‘tennis elbow’. Approx 1 year post UAE.” (U, 59 years)

“Slight pain in left-hand artery of leg.” (U, 51 years)

#### Hair growth problems

“Thinning and loss of hair. Constipation at times.” (U, 62 years)

“Loss of body/head hair. Increase in facial hair and bad skin.” (H, 63 years)

#### Hernia

“Irregular lower right abdominal pain, at times severe, possible scar tissue, eventually requiring emergency surgery for strangulated inguinal hernia – Sept 2000 – Possible connection?.” (H, 58 years)

“A hernia on operation site. Operated on a year after my hysterectomy, but in last few years has come back again.” (H, 61 years)

“Only found out about fibroid because it blocked my bladder. First operation – laparotomy couldn’t remove, embolisation, then myomectomy – stomach lining falling apart, had hernia op, but still have problems now.” (U, 35 years)

#### Infections

“Very little muscle control – painful sex (due to infections).” (H, 56 years)

- “Only initially as I got an *infection* within a couple of days and had to be re-admitted as blood suddenly started pouring down my legs when I was walking outside.” (H, 58 years)
- “Kidney *infection* following operation.” (H, 54 years)
- “Contracted hospital *infection* after treatment, now fully recovered.” (U, 56 years)
- “Initially had pelvic *infection* which extended recovery period ...” (U, 51 years)
- “My womb went *septic* 2 weeks after the UAE. I had to have an emergency hysterectomy ... was on life-support, then intensive care ...” (U, 44 years)
- “Heavy discharge and *infection* almost continuously for 2 years following treatment (treated by GP only).” (U, 50 years)
- “I was bleeding heavily after one month of treatment, admitted to hospital. I got *infections* and I became very anaemic. I had to be given 2 pints of blood.” (U, 51 years)
- “It could be a coincidence but I have repeated attacks of vaginal *thrush* which I never had before the operation.” (U, 42 years)
- “*Necrotic* fibroid extracted vaginally and hysteroscopically.” (U, 30 years)
- “I had an *infection* 6 weeks after the procedure.” (U, 30 years)
- “7 months after treatment fragments of the fibroid became *infected*. I spent time in hospital having antibiotic treatment.” (U, 42 years)
- “I had a chronic discharge and pain after 1.5 years and 2 exploratory ops told that fibroids did not shrivel but died off and broke up causing very bad *infections* and I am sure that some of the ‘white goo’ was the ‘glue’ .” (U, 53 years)
- “Complications after surgery – severe pain with large clots, readmitted to hospital and told by consultant that fibroid was very *hot*, which was causing pain, could only wait for fibroids to cool and reduce, took months before I could return to work.” (U, 53 years)
- “Big fibroid was killed and became a big problem at home. After operation had problems with stomach, first 12 days didn’t function at all, then sent home, 2 days later ended up in emergency where given proper *antibiotic*.” (U, 43 years)
- “After UAE I had persistent daily bleeding and/or foul discharge for 4.75 months plus increasing pain and tenderness over the fibroids, increasing tiredness and exhaustion and *fever* and eventually could hardly work when I was found to have become very anaemic and with *very high white cell count indicating sepsis*.” (U, 58 years)
- “My womb is now *inflamed* due to fibroid.” (U, 46 years)
- “*Septicaemia* following procedure, which necessitated 6 nights in hospital for IV antibiotics and other treatment.” (U, 61 years)
- “All short-term and now resolved – (1) expulsion of 3 fibroids – 2 needed surgical help. (2) *Infection* with first fibroid expulsion. (3) Discharge for a few months.” (U, 48 years)
- “Caught an *infection* after treatment – painful, rest at home and prescribed tablets. Better after a few days.” (U, 53 years)
- “Fibroids became necrotic, suffered years of *infections* ... had a hysterectomy. Still suffering recurrent *infections*.” (U, 48 years)
- “I suffered a vaginal *infection*, which was very unpleasant and resulted in a full anaesthetic to have my coil removed.” (U, 51 years)
- “Initially satisfied after UAE in 1995, in 2001 developed persistent cough and a nasty vaginal discharge, which *antibiotics* did not relieve. Contacted Dr X who identified rotting fibroid, but failed to remove successfully. Developed *septicaemia* and admitted for 4 days. Fibroid eventually moved out of uterus and was removed by forceps. Recovered well.” (U, 60 years)
- “Pain and *fever* leading to an emergency hysterectomy.” (U, 46 years)
- “I had a *necrotised* fibroid which made me very unwell, *high temperature* etc. I had been unaware of the symptoms of this complication and did not know what was wrong.” (U, 51 years)
- “Only that fibroids have returned and discovered this when I had laparoscopy which caused *infection* lasting several months.” (U, 43 years)
- Menstrual period/bleeding post-UAE**
- “*Heavy and clotting periods* – slightly weak bladder/social embarrassment/less self esteem.” (U, 42 years)
- “*Discharge around menstrual cycle* – I understand relates to fibroid discharge ... fibroid growth. Increasingly painful.” (U, 39 years)
- “I was *bleeding heavily* after one month of treatment, admitted to hospital. I got infections and I became very anaemic. I had to be given 2 pints of blood.” (U, 51 years)
- “Extreme pain on-going at time of treatment – *continual bleeding* since treatment.” (U, 55 years)
- “Fibroids continued to grow. Several days after treatment I *bled very badly* and was bedridden for 2 weeks, becoming very anaemic.” (U, 51 years)
- “I have *not had regular periods* since this treatment.” (U, 43 years)
- “Since menopause, *continued bleeding* and discharge caused by disintegration of fibroids resulting in hysteroscopy ...” (U, 58 years)
- “Early menopause?? *Periods very light* only 4–5 periods in last 3 years.” (U, 46 years)

- “Complications after surgery – severe pain with *large clots*, readmitted to hospital ....” (U, 53 years)
- “*Periods* have completely stopped – not sure if this is related to UAE.” (U, 42 years)
- “*Heavy period* and pain on the lower abdomen for no apparent reason.” (U, 49 years)
- “After UAE I had *persistent daily bleeding* and/or foul discharge for 4.75 months plus increasing pain and tenderness over the fibroids, increasing tiredness and exhaustion and fever and eventually could hardly work when I was found to have become very anaemic ....” (U, 58 years)
- “After the treatment I experienced severe pain. Also the symptoms (*heavy bleeding*) returned after 1 year ....” (U, 46 years)
- “Although not as *heavy*, *now longer stopping/starting 10–12 days*.” (U, 46 years)
- “*Bleeding* and discharge from fibroid rubbing the wall of my womb.” (U, 53 years)
- “*Painful periods*, slight ache in groin when period is due.” (U, 49 years)
- “I felt better and *bleeding stopped*. Last August/September *bleeding started again* ... Dec 10 *bleeding stopped*, cancer found in womb.” (U, 60 years)
- “Until 6 months ago I had regular mid-term liquid seepage for 4–5 days and *prolonged periods (almost 12 days)* so was almost constantly ‘seeping’ or ‘bleeding’.” (U, 46 years)
- “... intolerance symptoms to wheat and dairy. Symptoms were discharge after eating (*sometimes heavy flow*).” (U, 38 years)
- “After 2 years I started discharging dark brown blood, for weeks ....” (U, 50 years)
- “I started *bleeding continuously (slightly)* and my Gynae suggested I have something done as my cells were leaking ....” (U, 61 years)

### **Mental health/emotions**

- “*Emotional* – but only for a few weeks.” (H, 63 years)
- “Loss of libido, dryness, *emotional loss of feeling feminine*. HRT helped but never found right one.” (H, 53 years)
- “I have *suffered* very bad ... I am *very stressed* ....” (H, 49 years)
- “I have *struggled for many years to come to terms* with not being able to have children. This has *severely affected my mental health at times*.” (H, 44 years)
- “Unexplained weight gain. Skin irritation, *migraines, irritable*.” (H, 56 years)
- “Heavy and clotting periods – slightly weak bladder/*social embarrassment/less self esteem*.” (U, 42 years)

- “The treatment caused my genitals and vagina to shrink and lose a lot of feeling. This made me feel *angry and depressed*.” (U, 52 years)
- “Discharge for year after treatment – *very distressing*. Pain after op much greater than I expected.” (U, 50 years)

### **Migraines**

- “Unexplained weight gain. Skin irritation, *migraines, irritable*.” (H, 56 years)

### **Muscle problems**

- “*Very little muscle control* – painful sex (due to infections).” (H, 56 years)
- “*Collapsed pelvic floor muscles*.” (U, 65 years)

### **Osteoarthritis**

- “Prolapse, *osteoarthritis* in both hips.” (H, 55 years)

### **Ovaries**

- “Unnecessary surgery – referral was for *ovarian* cyst when fibroids were discovered.” (H, 61 years)
- “Had accident, major trauma and went into menopause. Medical ‘...’ was ‘beads’ used in UAE moved cutting off *ovaries* – menopause but not immediately.” (U, 44 years)
- “Fibroids stayed same size but became necrotic. It was also attached to an *ovary* causing much discomfort and nausea.” (U, 49 years)

### **Pain/discomfort/ache/tenderness**

- “Because of negligence during my hysterectomy I suffered 6 months of extreme bladder *discomfort* and had to undergo a second major operation to repair a fistula.” (H, 63 years)
- “... I am now troubled ... with very occasional diarrhoea but regular constipation and *pain* ...” (H, 63 years)
- “Problem with sex – not easy, very dry and *painful* at times.” (H, 61 years)
- “... I still suffered from very bad stomach and back *pains*.” (H, 49 years)
- “The bleeding continued for a lot longer than usual ... incurring quite a lot of *discomfort*.” (H, 53 years)
- “My bladder was cut causing me *painful* problems. I even had to be sent home and self-catheterising for 3 months.” (H, 71 years)
- “Irregular lower right abdominal *pain*, at times severe, possible scar tissue, eventually requiring emergency surgery for strangulated inguinal hernia – Sept 2000 – Possible connection?.” (H, 58 years)
- “Early menopause – I am now suffering *aching joints*, premature sexual feelings diminished from onset and ongoing 10 years after treatment.” (H, 56 years)

- “Trapped nerve causing *pain* down outside of left thigh to knee, gets worse when standing or carrying even light loads.” (H, 56 years)
- “Not sure if the treatment was the cause of *discomfort* when bladder was full, and sometimes still get this discomfort – investigated.” (H, 64 years)
- “I still have trouble with my tummy ... very bad *pains* ....” (H, 38 years)
- “Very little muscle control – *painful* sex (due to infections).” (H, 56 years)
- “Back *pains*. Surgeon tried to remove my uterus; I told the surgeon before operation to remove womb only.” (H, 54 years)
- “... assumed fibroid growth. Increasingly *painful*.” (U, 39 years)
- “The protracted period of *painful* suffering I endured for 2 years after being told that it would last a few weeks.” (U, 50 years)
- “The *pain* from the embolisation went on for several months – where the lesser fibroids were expelled.” (U, 50 years)
- “Leg *pain* high in right leg, a trapped nerve feeling (groin).” (U, 53 years)
- “Since the treatment I have suffered SEVERE BACK ACHE and right leg in PAIN.” (U, 44 years)
- “I feel it was the 2nd angiogram to check my fibroid being fed again by other vessels that caused a little *tenderness* when lifting. I did not need a second embolisation as it shrunk within next 2 years as predicted.” (U, 61 years)
- “Cannot put any pressure on abdomen, cannot lie on tummy at all.” (U, 40 years)
- “Severe +++ *pain* post-operatively.” (U, 58 years)
- “*Pain* in my groin where the catheter was inserted.” (U, 31 years)
- “Fibroids stayed same size but became necrotic. It was also attached to an ovary causing much *discomfort* and nausea.” (U, 49 years)
- “Extreme *pain* on-going at time of treatment – continual bleeding since treatment (U, 55 years)
- “Still get *pain* – but much better Would still choose over hysterectomy.” (U, 39 years)
- “I had a chronic discharge and *pain* after 1.5 years ....” (U, 53 years)
- “Tired *ache* in right thigh which radiates into groin after walking. This may or may not be related.” (U, 46 years)
- “Only issue was during procedure – lots of *pain*, sedation seemed to wear off during procedure. Very constipated after treatment, caused bad cramps relieved with strong painkillers (morphine), longer in hospital because of this.” (U, 38 years)
- “Complications after surgery – severe *pain* with large clots, readmitted to hospital and told by consultant that fibroid was very hot, which was causing *pain*, could only wait for fibroids to cool and reduce, took months before I could return to work.” (U, 53 years)
- “No problems caused by treatment but aftercare in hospital was not a good experience – the nurses were neglectful as *pain* relief did not work.” (U, 52 years)
- “Heavy period and *pain* on the lower abdomen for no apparent reason.” (U, 49 years)
- “After UAE I had persistent daily bleeding and/or foul discharge for 4.75 months plus increasing *pain and tenderness* over the fibroids ....” (U, 58 years)
- “After the treatment I experienced severe *pain*. Also the symptoms (heavy bleeding) returned after 1 year – I was offered a hysterectomy but chose homeopathic treatment which worked.” (U, 46 years)
- “I felt very unwell after the UAE. It was very *painful*. I felt it was worse than when I had my hysterectomy.” (U, 44 years)
- “One night of severe *pain* a couple of months after the operation.” (U, 43 years)
- “I lost the use of my left leg for two months and suffered unimaginable *pain* and no one cared.” (U, 55 years)
- “*Painful* periods, slight ache in groin when period is due.” (U, 49 years)
- “Caught an infection after treatment – *painful*, rest at home and prescribed tablets. Better after a few days.” (U, 53 years)
- “Discharge for year after treatment – very distressing. *Pain* after op much greater than I expected.” (U, 50 years)
- “I suffered with *pain* near right groin/pubis bone – eventually saw surgeon ... who said it was similar to ‘tennis elbow’. Approx 1 year post UAE.” (U, 59 years)
- “I had *pain* for a number of months after the treatment but I was able to carry on with everyday life.” (U, 51 years)
- “Been left with fibroid, giving *pain* and causing problems to bladder/bowel: no solution has been offered medically.” (U, 59 years)
- “*Pain* and fever leading to an emergency hysterectomy.” (U, 46 years)
- “Some *pain* on intercourse, whereas never had any before the UAE.” (U, 49 years)
- “... It was very *painful* after the actual treatment.” (U, 52 years)
- “I was in far worse *pain* after UAE and had a hysterectomy within a few months of UAE.” (U, 55 years)
- “Severe abdominal *pain* some time after treatment – several months lasting for several weeks, so much so that consultant referred me for bowel examination – nothing found.” (U, 55 years)

“Slight *pain* in left-hand artery of leg.” (U, 51 years)

### **Pelvic**

“Recently found that I have a weakness in the vagina (partial prolapse). *Pelvic* floor exercised ... recommended by consultant (H, 49 years)

“Initially had *pelvic* infection which extended recovery period ....” (U, 51 years)

“Collapsed *pelvic* floor muscles.” (U, 65 years)

### **Respiratory problems**

“Weight gain, *heavy breathing*.” (H, 59 years)

“The doctor perforated my bowel. *Lungs collapsed*, kidneys failed and I went on dialysis. I was in hospital for 3 months.” (H, 68 years)

“Initially satisfied after UAE in 1995. In 2001, developed *persistent cough* and a nasty vaginal discharge, which antibiotics did not relieve. Contacted Dr X who identified rotting fibroid, but failed to remove successfully. Developed septicaemia and admitted for 4 days. Fibroid eventually moved out of uterus and was removed by forceps. Recovered well.” (U, 60 years)

### **Scar/skin-related**

“*Granulation* of scar several episodes on light bleeding on intercourse.” (H, 54 years)

“Irregular lower right abdominal pain, at times severe, possible *scar tissue*, eventually requiring emergency surgery for strangulated inguinal hernia – Sept 2000 – Possible connection?.” (H, 58 years)

“Loss of body/head hair. Increase in facial hair and *bad skin*.” (U, 63 years)

“Unexplained weight gain. *Skin irritation*, migraines, irritable.” (H, 56 years)

“After having hysterectomy I seemed to develop *dermatitis herpetiformis* not having any symptoms of this beforehand.” (H, 46 years)

### **Sleep problems**

“Frequent hot flushes, excessive sweating. *Unable to sleep because of the heat my body is generating*.” (U, 53 years)

### **Stomach/tummy/nausea**

“... I still suffered from very bad *stomach* ... pains.” (H, 49 years)

“Hysterectomy led to 3 further operations in following 5 weeks (one which led to *stomach* being cut open at right angles to initial incision for approx 6 inches and left open for about 2.5 weeks!). I could probably write a book about this.” (H, 53 years)

“I still have trouble with my *tummy* ... very bad pains – bloatedness and cannot lose weight easily.” (H, 38 years)

“Fibroids stayed same size but became necrotic ... attached to ... ovary causing much discomfort and *nausea*.” (U, 49 years)

“Only found out about fibroid because it blocked my bladder. First operation, laparotomy, couldn't remove, embolisation, then myomectomy – *stomach* lining falling apart, had hernia op, but still have problems now.” (U, 35 years)

“Big fibroid was killed and became a big problem at home. After operation had problems with *stomach*, first 12 days didn't function at all, then sent home, 2 days later ended up in emergency where given proper antibiotic.” (U, 43 years)

### **Uterus/womb**

“Back pains – surgeon tried to remove my *uterus*. I told the surgeon before operation to remove *womb* only.” (H, 54 years)

“My *womb* went septic 2 weeks after the UAE. I had to have an emergency hysterectomy ... was on life-support, then intensive care ....” (U, 44 years)

“My *womb* is now inflamed due to fibroid.” (U, 46 years)

“Bleeding and discharge from fibroid rubbing the wall of my *womb*.” (U, 53 years)

“I felt better and bleeding stopped. Last August/September bleeding started again. It was recommended I had a hysterectomy. Dec 10 bleeding stopped, cancer found in *womb*.” (U, 60 years)

“... Fibroid eventually moved out of *uterus* and was removed by forceps. Recovered well.” (U, 60 years)

### **Vagina**

“Recently found that I have a weakness in the *vagina* (partial prolapse) ...” (H, 49 years)

“Dryness in *vaginal* area.” (H, 62 years)

“It could be a coincidence but I have repeated attacks of *vaginal* thrush which I never had before the operation.” (U, 42 years)

“Necrotic fibroid extracted *vaginally* and hysteroscopically.” (U, 30 years)

“The treatment caused my genitals and *vagina* to shrink and lose a lot of feeling. This made me feel angry and depressed.” (U, 52 years)

“I suffered a *vaginal* infection, which was very unpleasant and resulted in a full anaesthetic to have my coil removed.” (U, 51 years)

“Initially satisfied after UAE in 1995. In 2001 developed persistent cough and a nasty *vaginal* discharge, which antibiotics did not relieve ....” (U, 60 years)

“*Vaginal* discharge.” (U, 51 years)

**Veins on legs**

“Veins on my legs.” (U, 45 years)

**Bowel problems**

“*Prolapse of bowel* – moves down if constipation have to push back then OK.” (H, 47 years)

“IBS causing excessive diarrhoea for 9 years. I was taking HRT. I am now troubled with the opposite way with very occasional *diarrhoea* but regular *constipation and pain*.” (H, 63 years)

“It is thought that my *bowel problems* are relevant to the hysterectomy.” (H, 71 years)

“Minor only – *wind*, weaker bladder, weight gain.” (H, 51 years)

“Thinning and loss of hair. *Constipation* at times.” (U, 62 years)

“Possibly – more *urgency in bowel movements*.” (H, 62 years)

“After op my *bowel was twisted and then righted itself*, since then I have had *bowel problems* which I believe MAY be associated with this. I have not sought medical advice about these problems.” (H, 58 years)

“*Bowels don't open as regular*.” (H, 42 years)

“The *doctor perforated my bowel*. Lungs collapsed, kidneys failed and I went on dialysis. I was in hospital for 3 months.” (H, 68 years)

“I have fibromyalgia and *IBS* – weight gain (but I can't say if it's from the fibroid). *Bloating*.” (H, 53 years)

“*Prolapse onto bladder and bowel*.” (H, 60 years)

“Too much *morphine* during treatment. It completely *blocked me up* and put me *in hospital for 2 weeks*.” (U, 54 years)

“*Constipation*.” (U, 44 years)

“I have *piles*, weight gain and sluggish metabolism.” (U, 39 years)

“*Blocked bowel about 2 weeks after procedure*. Also still have problems with cystitis (every 6 weeks).” (U, 60 years)

“... *Very constipated after treatment, caused bad cramps* relieved with strong painkillers (morphine), longer in hospital because of this.” (U, 38 years)

“Been left with fibroid, giving pain and causing *problems to bladder/bowel*: no solution has been offered medically.” (U, 59 years)

“Severe abdominal pain some time after treatment – several months lasting for several weeks, so much so that consultant referred me for *bowel examination* – *nothing found*.” (U, 55 years)

**Energy, lack of**

“Weight gain, *lack of energy*.” (H, 43 years)

“*Tired ache* in right thigh which radiates into groin after walking. This may or may not be related.” (U, 46 years)

“After UAE I had persistent daily bleeding and/or foul discharge for 4.75 months plus increasing pain and tenderness over the fibroids, increasing tiredness and *exhaustion* and fever and eventually could hardly work when I was found to have become very anaemic and with very high white cell count indicating sepsis.” (U, 58 years)

**Fertility, specifically regarding**

“*Not being able to have more children*.” (H, 43 years)

“I have struggled for many years to come to terms with *not being able to have children*. This has severely affected my mental health at times.” (H, 44 years)

“I was unable to *conceive* and after 2 years suffered degeneration of the ‘dead’ fibroids, leading to a hysterectomy, which revealed advanced endometriosis which had not been previously diagnosed (this could have caused the *infertility* not the fibroids.” (U, 50 years)

**Menopause**

“Lack of sexual desire, on-going *menopausal problems*.” (H, 56 years)

“*Early menopause* – I am now suffering aching joints, premature sexual feelings diminished from onset and ongoing 10 years after treatment.” (H, 56 years)

“Instant *menopause* and ‘its’ problems.” (H, 57 years)

“I became *menopausal* 2 weeks after surgery.” (H, 54 years)

“*Menopausal*.” (U, 54 years)

“Had accident, major trauma and went into *menopause*. Medical ‘...’ was ‘beads’ used in UAE moved cutting off ovaries – *menopause* but not immediately.” (U, 44 years)

“Since *menopause*, continued bleeding and discharge caused by disintegration of fibroids resulting in hysteroscopy ...” (U, 58 years)

“*Early menopause??* Periods very light only 4–5 periods in last 3 years.” (U, 46 years)

**Hot flushes/night sweats/excessive sweating**

“Problem is easy to put up with but I have had *hot flushes for 10 years in various cycles and intensity*. None during the night.” (H, 54 years)

“Weakness of bladder leaking when sneezing etc. weight gain, uncontrollable *hot flushes/night sweats*.” (H, 59 years)

“*Hot flushes* sometimes difficult to cope with especially in summer – still persistent after surgical menopause.” (H, 60 years)

“Still suffering from *hot flushes*.” (H, 61 years)

“*Hot sweats* all the time.” (H, 54 years)

“Frequent *hot flushes, excessive sweating*. Unable to sleep because of the heat my body is generating.” (U, 53 years)

### HRT/hormonal changes

“IBS causing excessive diarrhoea for 9 years.

I was taking *HRT*. I am now troubled with the opposite way with very occasional diarrhoea but regular constipation and pain.”

(H, 63 years)

“Loss of libido, dryness, emotional loss of feeling feminine. *HRT* helped but never found right one.” (H, 53 years)

“Early menopause, necessity for *HRT* long-term.” (H, 57 years)

“Finding suitable *HRT*. Had implant at time of op – that worked well. Patches not very good, tablets better, but I was not really sure they were the right strength – I probably erred on side of caution.” (H, 52 years)

“I have further health problems including weight gain, *no HRT*, eating disorder since 1985 and vitamin deficiency.” (H, 61 years)

“Early menopause. Need to take *HRT* now.” (H, 47 years)

“Sudden earlier menopause requiring *HRT* instead of gradual natural one.” (H, 56 years)

### Prolapse

“Recently found that I have a weakness in the *vagina (partial prolapse)*. Pelvic floor exercised have been recommended by consultant.” (H, 49 years)

“*Prolapse of bowel* – moves down if constipation have to push back then OK.” (H, 47 years)

“*Prolapsed bladder and posterial wall*.” (H, 58 years)

“*Prolapse*, osteoarthritis in both hips.” (H, 55 years)

“*Prolapse onto bladder and bowel*.” (H, 60 years)

“... *cervical prolapse* and difficult position of fibroid – safest option was to have a hysterectomy – sadly.” (U, 38 years)

### Sexual problems

“*Complete lack of libido*.” (H, 64 years)

“Problem with *sex – not easy, very dry and painful at times*.” (H, 61 years)

“*Loss of libido, dryness, emotional loss of feeling feminine*. *HRT* helped but never found right one.” (H, 53 years)

“... This has had an *effect on my sex life. I am very stressed by this and my body has changed very badly* ...” (H, 49 years)

“Granulation of scar; several episodes on *light bleeding on intercourse*.” (H, 54 years)

“Lack of sexual desire, on-going menopausal problems.” (H, 56 years)

“Early menopause – I am now suffering aching joints, *premature sexual feelings diminished from onset and ongoing 10 years after treatment*.”

(H, 56 years)

“*Loss of libido*.” (H, 55 years)

“*Lack of sex drive*.” (H, 58 years)

“*Very little muscle control – painful sex (due to infections)*.” (H, 56 years)

“The treatment caused my *genitals and vagina to shrink and lose a lot of feeling*. This made me feel angry and depressed.” (U, 52 years)

“*Loss of sexual appetite* (could be my age of course! – but it was quite noticeable).” (U, 48 years)

“Some *pain on intercourse*, whereas never had any before the UAE.” (U, 49 years)

### Urinary/bladder/kidney problems

“They *damaged my kidney* during surgery.” (H, 54 years)

“Because of negligence during my hysterectomy I suffered 6 months of extreme *bladder discomfort* and had to undergo a second major operation to repair a fistula.” (H, 63 years)

“*Urine problems, not serious*.” (H, 51 years)

“Minor only – wind, *weaker bladder*, weight gain.” (H, 51 years)

“My *bladder was cut causing me painful problems*. I even had to be sent home and self-catheterising for 3 months.” (H, 53 years)

“I had problems after my hysterectomy and had *further treatment ... to repair my bladder which turned out to be far worse than original surgery*.” (H, 56 years)

“*Bladder weakness*.” (H, 65 years)

“*Bladder*.” (H, 56 years)

“*Prolapsed bladder and posterial wall*.” (H, 58 years)

“*Stress incontinence*.” (H, 55 years)

“*Weakness of bladder, leaking when sneezing etc., weight gain, uncontrollable hot flushes/night sweats*.” (H, 59 years)

“Not sure if the treatment was the cause of *discomfort when bladder was full, and sometimes still get this discomfort – investigated*.” (H, 64 years)

“*Bladder problems*.” (H, 57 years)

“*Bladder weakness, weight gain*.” (H, 52 years)

“The doctor perforated my bowel. Lungs collapsed, *kidneys failed* and I went on dialysis. I was in hospital for 3 months.” (H, 68 years)

“*Prolapse onto bladder and bowel*.” (H, 60 years)

“*Kidney infection* following operation.” (H, 54 years)

“Heavy and clotting periods – *slightly weak bladder/social embarrassment/less self esteem*.” (U, 42 years)

“... *weaker bladder*. Diagnosed with cystocele. Assumed fibroid growth. Increasingly painful.” (U, 39 years)

- “Blocked bowel about 2 weeks after procedure. Also still have problems with *cystitis (every 6 weeks)*.” (U, 60 years)
- “Only found out about *fibroid because it blocked my bladder*. First operation, aparotomy couldn’t remove, embolisation, then myomectomy – stomach lining falling apart, had hernia op, but still have problems now.” (U, 35 years)
- “I have had a *few bladder problems* since my treatment for fibroids – *more prone to cystitis and stress incontinence*.” (U, 56 years)
- “Been left with *fibroid, giving pain and causing problems to bladder/bowel*: no solution has been offered medically.” (U, 59 years)

### Weight gain

- “*Weight gain, lack of energy*.” (H, 43 years)
- “*Weight gain*.” (H, 58 years)
- “Minor only – wind, weaker bladder, *weight gain*.” (H, 51 years)
- “*Weight gain*.” (H, 58 years)
- “*Weight gain*.” (H, 56 years)
- “*Weight gain, heavy breathing*.” (H, 59 years)
- “Weakness of bladder leaking when sneezing etc, *weight gain, uncontrollable hot flushes/night sweats*.” (H, 59 years)
- “I have further health problems including *weight gain, no HRT eating disorder since 1985 and vitamin deficiency*.” (H, 61 years)
- “Bladder weakness, *weight gain*.” (H, 52 years)
- “I still have trouble with my tummy ... *cannot lose weight easily*.” (H, 38 years)
- “*Unexplained weight gain. Skin irritation, migraines, irritable*.” (H, 56 years)
- “I have fibromyalgia and IBS – *weight gain (but I can’t say if its from the fibroid)*. Bloating.” (H, 53 years)
- “In the 2 days I was in hospital, my *weight increased (and stayed) by 0.5 stone – mainly the top of my legs*.” (U, 53 years)
- “I have piles, *weight gain* and sluggish metabolism.” (U, 39 years)

### Further treatment needed

- “*At least two minor ops to relieve adhesions and sometimes still cause concern*.” (H, 49 years)
- “... *discomfort when bladder was full, and sometimes still get this discomfort – investigated*.” (H, 64 years)
- “The treatment did not work so I ended up having a *myomectomy*. But I was given the best treatment by staff.” (U, 38 years)
- “7 months after treatment fragments of the fibroid became infected. I spent time *in hospital having antibiotic treatment*.” (U, 42 years)
- “Since menopause, continued bleeding and discharge caused by disintegration of fibroids resulting in *hysteroscopy ...*” (U, 58 years)

- “Only found out about fibroid because it blocked my bladder. First operation, laparotomy couldn’t remove, embolisation, then *myomectomy* – stomach lining falling apart, had *hernia op*, but still have problems now.” (U, 35 years)
- “Big fibroid was killed and became a big problem at home. After operation had problems with stomach, first 12 days didn’t function at all, then sent home, 2 days later *ended up in emergency where given proper antibiotic*.” (U, 43 years)
- “After UAE I had persistent daily bleeding and/or foul discharge for 4.75 months plus increasing pain and tenderness over the fibroids, increasing tiredness and exhaustion and fever and eventually could hardly work when I was found to have become *very anaemic and with very high white cell count indicating sepsis*.” (U, 58 years)
- “I had to have a *hysterectomy* as it didn’t work for me.” (U, 34 years)
- “I was unable to conceive and after 2 years suffered degeneration of the ‘dead’ fibroids, leading to a *hysterectomy*, which revealed advanced endometriosis which had not been previously diagnosed (this could have caused the infertility not the fibroids).” (U, 50 years)
- “Fibroid not reduced enough. Due to cervical prolapse and difficult position of fibroid – safest option was to have a *hysterectomy* – sadly.” (U, 38 years)
- “Less than a year after the embolisation I needed a *hysterectomy*.” (U, 57 years)
- “Fibroids became necrotic, suffered years of infections and subsequently had a *hysterectomy ...*” (U, 48 years)
- “Initially satisfied after UAE in 1995. In 2001 developed persistent cough and a nasty vaginal discharge, which *antibiotics* did not relieve. Contacted Dr X who identified *rotting fibroid, but failed to remove successfully*. Developed *septicaemia and admitted for 4 days*. Fibroid eventually moved out of uterus and was *removed by forceps*. Recovered well.” (U, 60 years)
- “Pain and fever leading to an *emergency hysterectomy*.” (U, 46 years)
- “Only that fibroids have returned and discovered this when I had *laparoscopy which caused infection lasting several months*.” (U, 43 years)
- “After 2 years I started discharging dark brown blood, for weeks – I was then referred to a consultant – *ended up having a hysterectomy*.” (U, 50 years)
- “I was in far worse pain after UAE and had a *hysterectomy within a few months of UAE*.” (U, 55 years)
- “I started bleeding continuously (slightly) and my Gynae suggested I have something done as my cells were leaking. *Had small op and fine now*.” (U, 61 years)



### Not knowing/post treatment beliefs and speculations

- “Irregular lower right abdominal pain, at times severe, possible scar tissue, eventually requiring emergency surgery for strangulated inguinal hernia – Sept 2000 – *Possible connection?*.” (H, 58 years)
- “*Finding suitable HRT. Had implant at time of op – that worked well. Patches not very good, tablets better, but I was not really sure they were the right strength – I probably erred on side of caution.*” (H, 52 years)
- “After op my bowel was twisted and then righted itself, since then I have had *bowel problems which I believe MAY be associated with this. I have not sought medical advice about these problems.*” (H, 58 years)
- “*Not sure if the treatment was the cause of discomfort when bladder was full ... still get this ... investigated.*” (H, 64 years)
- “*Unexplained weight gain. Skin irritation, migraines, irritable.*” (H, 56 years)
- “*I have fibromyalgia and IBS – weight gain (but I can't say if it's from the fibroid). Bloating.*” (H, 53 years)
- “*Not sure.*” (U, 49 years)
- “*I feel it was the 2nd angiogram to check my fibroid being fed again by other vessels that caused a little tenderness when lifting. I did not need a second embolisation as it shrunk within next 2 years as predicted.*” (U, 61 years)
- “*It could be a coincidence but I have repeated attacks of vaginal thrush which I never had before the operation.*” (U, 42 years)
- “*Tired ache in right thigh which radiates into groin after walking. This may or may not be related.*” (U, 46 years)
- “*I now have non-Hodgkins lymphoma as a result of the treatment.*” (U, 57 years)
- “*Periods have completely stopped – not sure if this is related to UAE.*” (U, 42 years)
- “*Heavy period and pain on the lower abdomen for no apparent reason.*” (U, 49 years)
- “*I was unwell prior to the treatment and after the treatment I was diagnosed with coeliac disease – I'm not sure whether the total intolerance of gluten was triggered by the treatment.*” (U, 56 years)
- “*Not sure but may have caused intolerance symptoms to wheat and dairy. Symptoms were discharge after eating (sometimes heavy flow).*” (U, 38 years)

### Positive comments

- “*Problem is easy to put up with ... hot flushes for 10 years in various cycles and intensity. None during the night.*” (H, 54 years)

- “*Emotional – but only for a few weeks.*” (H, 63 years)
- “*Urine problems, not serious.*” (H, 51 years)
- “*Finding suitable HRT. Had implant at time of op – that worked well. Patches not very good, tablets better, but I was not really sure they were the right strength – I probably erred on side of caution.*” (H, 52 years)
- “*Only initially as I got an infection within a couple of days and had to be re-admitted ....*” (H, 58 years)
- “*Contracted hospital infection after treatment, now fully recovered.*” (U, 56 years)
- “*Initially had pelvic infection which extended recovery period. Probably up to 3 months following treatment before back to good health.*” (U, 51 years)
- “*... I did not need a second embolisation as it shrunk within next 2 years as predicted.*” (U, 61 years)
- “*The treatment did not work so I ended up having a myomectomy. But I was given the best treatment by staff.*” (U, 38 years)
- “*Still get pain – but much better Would still choose over hysterectomy.*” (U, 39 years)
- “*Although not as heavy, now longer stopping/starting 10–12 days.*” (U, 46 years)
- “*All short-term and now resolved – (1) Expulsion of 3 fibroids – 2 needed surgical help. (2) Infection with first fibroid expulsion. (3) Discharge for a few months.*” (U, 48 years)
- “*Caught an infection after treatment – painful, rest at home and prescribed tablets. Better after a few days.*” (U, 53 years)
- “*I had pain for a number of months after the treatment but I was able to carry on with everyday life.*” (U, 51 years)
- “*Initially satisfied after UAE in 1995. In 2001 developed persistent cough and a nasty vaginal discharge, which antibiotics did not relieve. Contacted Dr C who identified rotting fibroid, but failed to remove successfully. Developed septicaemia and admitted for 4 days. Fibroid eventually moved out of uterus and was removed by forceps. Recovered well.*” (U, 60 years)
- “*Food intolerances which has now largely resolved itself.*” (U, 49 years)
- “*I started bleeding continuously (slightly) and my Gynae suggested I have something done as my cells were leaking. Had small op and fine now.*” (U, 61 years)





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By Sculpher MJ, Petticrew M, Kelland JL, Elliott RA, Holdright DR, Buxton MJ.

### No. 11

Detection, adherence and control of hypertension for the prevention of stroke: a systematic review.

By Ebrahim S.

### No. 12

Postoperative analgesia and vomiting, with special reference to day-case surgery: a systematic review.

By McQuay HJ, Moore RA.

### No. 13

Choosing between randomised and nonrandomised studies: a systematic review.

By Britton A, McKee M, Black N, McPherson K, Sanderson C, Bain C.

### No. 14

Evaluating patient-based outcome measures for use in clinical trials.

A review by Fitzpatrick R, Davey C, Buxton MJ, Jones DR.

**No. 15**

Ethical issues in the design and conduct of randomised controlled trials.

A review by Edwards SJL, Lilford RJ, Brauholtz DA, Jackson JC, Hewison J, Thornton J.

**No. 16**

Qualitative research methods in health technology assessment: a review of the literature.

By Murphy E, Dingwall R, Greatbatch D, Parker S, Watson P.

**No. 17**

The costs and benefits of paramedic skills in pre-hospital trauma care.

By Nicholl J, Hughes S, Dixon S, Turner J, Yates D.

**No. 18**

Systematic review of endoscopic ultrasound in gastro-oesophageal cancer.

By Harris KM, Kelly S, Berry E, Hutton J, Roderick P, Cullingworth J, *et al.*

**No. 19**

Systematic reviews of trials and other studies.

By Sutton AJ, Abrams KR, Jones DR, Sheldon TA, Song F.

**No. 20**

Primary total hip replacement surgery: a systematic review of outcomes and modelling of cost-effectiveness associated with different prostheses.

A review by Fitzpatrick R, Shortall E, Sculpher M, Murray D, Morris R, Lodge M, *et al.*

**Volume 3, 1999**

**No. 1**

Informed decision making: an annotated bibliography and systematic review.

By Bekker H, Thornton JG, Airey CM, Connelly JB, Hewison J, Robinson MB, *et al.*

**No. 2**

Handling uncertainty when performing economic evaluation of healthcare interventions.

A review by Briggs AH, Gray AM.

**No. 3**

The role of expectancies in the placebo effect and their use in the delivery of health care: a systematic review.

By Crow R, Gage H, Hampson S, Hart J, Kimber A, Thomas H.

**No. 4**

A randomised controlled trial of different approaches to universal antenatal HIV testing: uptake and acceptability. Annex: Antenatal HIV testing – assessment of a routine voluntary approach.

By Simpson WM, Johnstone FD, Boyd FM, Goldberg DJ, Hart GJ, Gormley SM, *et al.*

**No. 5**

Methods for evaluating area-wide and organisation-based interventions in health and health care: a systematic review.

By Ukoumunne OC, Gulliford MC, Chinn S, Sterne JAC, Burney PGJ.

**No. 6**

Assessing the costs of healthcare technologies in clinical trials.

A review by Johnston K, Buxton MJ, Jones DR, Fitzpatrick R.

**No. 7**

Cooperatives and their primary care emergency centres: organisation and impact.

By Hallam L, Henthorne K.

**No. 8**

Screening for cystic fibrosis.

A review by Murray J, Cuckle H, Taylor G, Littlewood J, Hewison J.

**No. 9**

A review of the use of health status measures in economic evaluation.

By Brazier J, Deverill M, Green C, Harper R, Booth A.

**No. 10**

Methods for the analysis of quality-of-life and survival data in health technology assessment.

A review by Billingham LJ, Abrams KR, Jones DR.

**No. 11**

Antenatal and neonatal haemoglobinopathy screening in the UK: review and economic analysis.

By Zeuner D, Ades AE, Karnon J, Brown J, Dezateux C, Anionwu EN.

**No. 12**

Assessing the quality of reports of randomised trials: implications for the conduct of meta-analyses.

A review by Moher D, Cook DJ, Jadad AR, Tugwell P, Moher M, Jones A, *et al.*

**No. 13**

'Early warning systems' for identifying new healthcare technologies.

By Robert G, Stevens A, Gabbay J.

**No. 14**

A systematic review of the role of human papillomavirus testing within a cervical screening programme.

By Cuzick J, Sasieni P, Davies P, Adams J, Normand C, Frater A, *et al.*

**No. 15**

Near patient testing in diabetes clinics: appraising the costs and outcomes.

By Grieve R, Beech R, Vincent J, Mazurkiewicz J.

**No. 16**

Positron emission tomography: establishing priorities for health technology assessment.

A review by Robert G, Milne R.

**No. 17 (Pt 1)**

The debridement of chronic wounds: a systematic review.

By Bradley M, Cullum N, Sheldon T.

**No. 17 (Pt 2)**

Systematic reviews of wound care management: (2) Dressings and topical agents used in the healing of chronic wounds.

By Bradley M, Cullum N, Nelson EA, Petticrew M, Sheldon T, Torgerson D.

**No. 18**

A systematic literature review of spiral and electron beam computed tomography: with particular reference to clinical applications in hepatic lesions, pulmonary embolus and coronary artery disease.

By Berry E, Kelly S, Hutton J, Harris KM, Roderick P, Boyce JC, *et al.*

**No. 19**

What role for statins? A review and economic model.

By Ebrahim S, Davey Smith G, McCabe C, Payne N, Pickin M, Sheldon TA, *et al.*

**No. 20**

Factors that limit the quality, number and progress of randomised controlled trials.

A review by Prescott RJ, Counsell CE, Gillespie WJ, Grant AM, Russell IT, Kiauka S, *et al.*

**No. 21**

Antimicrobial prophylaxis in total hip replacement: a systematic review.

By Glenny AM, Song F.

**No. 22**

Health promoting schools and health promotion in schools: two systematic reviews.

By Lister-Sharp D, Chapman S, Stewart-Brown S, Sowden A.

**No. 23**

Economic evaluation of a primary care-based education programme for patients with osteoarthritis of the knee.

A review by Lord J, Victor C, Littlejohns P, Ross FM, Axford JS.

**Volume 4, 2000**

**No. 1**

The estimation of marginal time preference in a UK-wide sample (TEMPUS) project.

A review by Cairns JA, van der Pol MM.

**No. 2**

Geriatric rehabilitation following fractures in older people: a systematic review.

By Cameron I, Crotty M, Currie C, Finnegan T, Gillespie L, Gillespie W, *et al.*

**No. 3**

Screening for sickle cell disease and thalassaemia: a systematic review with supplementary research.

By Davies SC, Cronin E, Gill M, Greengross P, Hickman M, Normand C.

**No. 4**

Community provision of hearing aids and related audiology services.

A review by Reeves DJ, Alborz A, Hickson FS, Bamford JM.

**No. 5**

False-negative results in screening programmes: systematic review of impact and implications.

By Petticrew MP, Sowden AJ, Lister-Sharp D, Wright K.

**No. 6**

Costs and benefits of community postnatal support workers: a randomised controlled trial.

By Morrell CJ, Spiby H, Stewart P, Walters S, Morgan A.

**No. 7**

Implantable contraceptives (subdermal implants and hormonally impregnated intrauterine systems) versus other forms of reversible contraceptives: two systematic reviews to assess relative effectiveness, acceptability, tolerability and cost-effectiveness.

By French RS, Cowan FM, Mansour DJA, Morris S, Procter T, Hughes D, *et al.*

**No. 8**

An introduction to statistical methods for health technology assessment.

A review by White SJ, Ashby D, Brown PJ.

**No. 9**

Disease-modifying drugs for multiple sclerosis: a rapid and systematic review.

By Clegg A, Bryant J, Milne R.

**No. 10**

Publication and related biases.

A review by Song F, Eastwood AJ, Gilbody S, Duley L, Sutton AJ.

**No. 11**

Cost and outcome implications of the organisation of vascular services.

By Michaels J, Brazier J, Palfreyman S, Shackley P, Slack R.

**No. 12**

Monitoring blood glucose control in diabetes mellitus: a systematic review.

By Coster S, Gulliford MC, Seed PT, Powrie JK, Swaminathan R.

**No. 13**

The effectiveness of domiciliary health visiting: a systematic review of international studies and a selective review of the British literature.

By Elkan R, Kendrick D, Hewitt M, Robinson JJA, Tolley K, Blair M, *et al.*

**No. 14**

The determinants of screening uptake and interventions for increasing uptake: a systematic review.

By Jepson R, Clegg A, Forbes C, Lewis R, Sowden A, Kleijnen J.

**No. 15**

The effectiveness and cost-effectiveness of prophylactic removal of wisdom teeth.

A rapid review by Song F, O'Meara S, Wilson P, Golder S, Kleijnen J.

**No. 16**

Ultrasound screening in pregnancy: a systematic review of the clinical effectiveness, cost-effectiveness and women's views.

By Bricker L, Garcia J, Henderson J, Mugford M, Neilson J, Roberts T, *et al.*

**No. 17**

A rapid and systematic review of the effectiveness and cost-effectiveness of the taxanes used in the treatment of advanced breast and ovarian cancer.

By Lister-Sharp D, McDonagh MS, Khan KS, Kleijnen J.

**No. 18**

Liquid-based cytology in cervical screening: a rapid and systematic review.

By Payne N, Chilcott J, McGoogan E.

**No. 19**

Randomised controlled trial of non-directive counselling, cognitive-behaviour therapy and usual general practitioner care in the management of depression as well as mixed anxiety and depression in primary care.

By King M, Sibbald B, Ward E, Bower P, Lloyd M, Gabbay M, *et al.*

**No. 20**

Routine referral for radiography of patients presenting with low back pain: is patients' outcome influenced by GPs' referral for plain radiography?

By Kerry S, Hilton S, Patel S, Dundas D, Rink E, Lord J.

**No. 21**

Systematic reviews of wound care management: (3) antimicrobial agents for chronic wounds; (4) diabetic foot ulceration.

By O'Meara S, Cullum N, Majid M, Sheldon T.

**No. 22**

Using routine data to complement and enhance the results of randomised controlled trials.

By Lewsey JD, Leyland AH, Murray GD, Boddy FA.

**No. 23**

Coronary artery stents in the treatment of ischaemic heart disease: a rapid and systematic review.

By Meads C, Cummins C, Jolly K, Stevens A, Burls A, Hyde C.

**No. 24**

Outcome measures for adult critical care: a systematic review.

By Hayes JA, Black NA, Jenkinson C, Young JD, Rowan KM, Daly K, *et al.*

**No. 25**

A systematic review to evaluate the effectiveness of interventions to promote the initiation of breastfeeding.

By Fairbank L, O'Meara S, Renfrew MJ, Woolridge M, Sowden AJ, Lister-Sharp D.

**No. 26**

Implantable cardioverter defibrillators: arrhythmias. A rapid and systematic review.

By Parkes J, Bryant J, Milne R.

**No. 27**

Treatments for fatigue in multiple sclerosis: a rapid and systematic review.

By Brañas P, Jordan R, Fry-Smith A, Burls A, Hyde C.

**No. 28**

Early asthma prophylaxis, natural history, skeletal development and economy (EASE): a pilot randomised controlled trial.

By Baxter-Jones ADG, Helms PJ, Russell G, Grant A, Ross S, Cairns JA, *et al.*

**No. 29**

Screening for hypercholesterolaemia versus case finding for familial hypercholesterolaemia: a systematic review and cost-effectiveness analysis.

By Marks D, Wonderling D, Thorogood M, Lambert H, Humphries SE, Neil HAW.

**No. 30**

A rapid and systematic review of the clinical effectiveness and cost-effectiveness of glycoprotein IIb/IIIa antagonists in the medical management of unstable angina.

By McDonagh MS, Bachmann LM, Golder S, Kleijnen J, ter Riet G.

**No. 31**

A randomised controlled trial of prehospital intravenous fluid replacement therapy in serious trauma.

By Turner J, Nicholl J, Webber L, Cox H, Dixon S, Yates D.

**No. 32**

Intrathecal pumps for giving opioids in chronic pain: a systematic review.

By Williams JE, Louw G, Towler G.

**No. 33**

Combination therapy (interferon alfa and ribavirin) in the treatment of chronic hepatitis C: a rapid and systematic review.

By Shepherd J, Waugh N, Hewitson P.

**No. 34**

A systematic review of comparisons of effect sizes derived from randomised and non-randomised studies.

By MacLehose RR, Reeves BC, Harvey IM, Sheldon TA, Russell IT, Black AMS.

**No. 35**

Intravascular ultrasound-guided interventions in coronary artery disease: a systematic literature review, with decision-analytic modelling, of outcomes and cost-effectiveness.

By Berry E, Kelly S, Hutton J, Lindsay HSJ, Blaxill JM, Evans JA, *et al.*

**No. 36**

A randomised controlled trial to evaluate the effectiveness and cost-effectiveness of counselling patients with chronic depression.

By Simpson S, Corney R, Fitzgerald P, Beecham J.

**No. 37**

Systematic review of treatments for atopic eczema.

By Hoare C, Li Wan Po A, Williams H.

**No. 38**

Bayesian methods in health technology assessment: a review.

By Spiegelhalter DJ, Myles JP, Jones DR, Abrams KR.

**No. 39**

The management of dyspepsia: a systematic review.

By Delaney B, Moayyedi P, Deeks J, Innes M, Soo S, Barton P, *et al.*

**No. 40**

A systematic review of treatments for severe psoriasis.

By Griffiths CEM, Clark CM, Chalmers RJG, Li Wan Po A, Williams HC.

**Volume 5, 2001**

**No. 1**

Clinical and cost-effectiveness of donepezil, rivastigmine and galantamine for Alzheimer's disease: a rapid and systematic review.

By Clegg A, Bryant J, Nicholson T, McIntyre L, De Broe S, Gerard K, *et al.*

**No. 2**

The clinical effectiveness and cost-effectiveness of riluzole for motor neurone disease: a rapid and systematic review.

By Stewart A, Sandercock J, Bryan S, Hyde C, Barton PM, Fry-Smith A, *et al.*

**No. 3**

Equity and the economic evaluation of healthcare.

By Sassi F, Archard L, Le Grand J.

**No. 4**

Quality-of-life measures in chronic diseases of childhood.

By Eiser C, Morse R.

**No. 5**

Eliciting public preferences for healthcare: a systematic review of techniques.

By Ryan M, Scott DA, Reeves C, Bate A, van Teijlingen ER, Russell EM, *et al.*

**No. 6**

General health status measures for people with cognitive impairment: learning disability and acquired brain injury.

By Riemsma RP, Forbes CA, Glanville JM, Eastwood AJ, Kleijnen J.

**No. 7**

An assessment of screening strategies for fragile X syndrome in the UK.

By Pembrey ME, Barnicoat AJ, Carmichael B, Bobrow M, Turner G.

**No. 8**

Issues in methodological research: perspectives from researchers and commissioners.

By Lilford RJ, Richardson A, Stevens A, Fitzpatrick R, Edwards S, Rock F, *et al.*

**No. 9**

Systematic reviews of wound care management: (5) beds; (6) compression; (7) laser therapy, therapeutic ultrasound, electrotherapy and electromagnetic therapy.

By Cullum N, Nelson EA, Flemming K, Sheldon T.

**No. 10**

Effects of educational and psychosocial interventions for adolescents with diabetes mellitus: a systematic review.

By Hampson SE, Skinner TC, Hart J, Storey L, Gage H, Foxcroft D, *et al.*

**No. 11**

Effectiveness of autologous chondrocyte transplantation for hyaline cartilage defects in knees: a rapid and systematic review.

By Jobanputra P, Parry D, Fry-Smith A, Burls A.

**No. 12**

Statistical assessment of the learning curves of health technologies.

By Ramsay CR, Grant AM, Wallace SA, Garthwaite PH, Monk AF, Russell IT.

**No. 13**

The effectiveness and cost-effectiveness of temozolomide for the treatment of recurrent malignant glioma: a rapid and systematic review.

By Dinnes J, Cave C, Huang S, Major K, Milne R.

**No. 14**

A rapid and systematic review of the clinical effectiveness and cost-effectiveness of debriding agents in treating surgical wounds healing by secondary intention.

By Lewis R, Whiting P, ter Riet G, O'Meara S, Glanville J.

**No. 15**

Home treatment for mental health problems: a systematic review.

By Burns T, Knapp M, Catty J, Healey A, Henderson J, Watt H, *et al.*

**No. 16**

How to develop cost-conscious guidelines.

By Eccles M, Mason J.

**No. 17**

The role of specialist nurses in multiple sclerosis: a rapid and systematic review.

By De Broe S, Christopher F, Waugh N.

**No. 18**

A rapid and systematic review of the clinical effectiveness and cost-effectiveness of orlistat in the management of obesity.

By O'Meara S, Riemsma R, Shirran L, Mather L, ter Riet G.

**No. 19**

The clinical effectiveness and cost-effectiveness of pioglitazone for type 2 diabetes mellitus: a rapid and systematic review.

By Chilcott J, Wight J, Lloyd Jones M, Tappenden P.

**No. 20**

Extended scope of nursing practice: a multicentre randomised controlled trial of appropriately trained nurses and preregistration house officers in pre-operative assessment in elective general surgery.

By Kinley H, Czoski-Murray C, George S, McCabe C, Primrose J, Reilly C, *et al.*

**No. 21**

Systematic reviews of the effectiveness of day care for people with severe mental disorders: (1) Acute day hospital versus admission; (2) Vocational rehabilitation; (3) Day hospital versus outpatient care.

By Marshall M, Crowther R, Almaraz-Serrano A, Creed F, Sledge W, Kluiters H, *et al.*

**No. 22**

The measurement and monitoring of surgical adverse events.

By Bruce J, Russell EM, Mollison J, Krukowski ZH.

**No. 23**

Action research: a systematic review and guidance for assessment.

By Waterman H, Tillen D, Dickson R, de Koning K.

**No. 24**

A rapid and systematic review of the clinical effectiveness and cost-effectiveness of gemcitabine for the treatment of pancreatic cancer.

By Ward S, Morris E, Bansback N, Calvert N, Crellin A, Forman D, *et al.*

**No. 25**

A rapid and systematic review of the evidence for the clinical effectiveness and cost-effectiveness of irinotecan, oxaliplatin and raltitrexed for the treatment of advanced colorectal cancer.

By Lloyd Jones M, Hummel S, Bansback N, Orr B, Seymour M.

**No. 26**

Comparison of the effectiveness of inhaler devices in asthma and chronic obstructive airways disease: a systematic review of the literature.

By Brocklebank D, Ram F, Wright J, Barry P, Cates C, Davies L, *et al.*

**No. 27**

The cost-effectiveness of magnetic resonance imaging for investigation of the knee joint.

By Bryan S, Weatherburn G, Bungay H, Hatrick C, Salas C, Parry D, *et al.*

**No. 28**

A rapid and systematic review of the clinical effectiveness and cost-effectiveness of topotecan for ovarian cancer.

By Forbes C, Shirran L, Bagnall A-M, Duffy S, ter Riet G.

**No. 29**

Superseded by a report published in a later volume.

**No. 30**

The role of radiography in primary care patients with low back pain of at least 6 weeks duration: a randomised (unblinded) controlled trial.

By Kendrick D, Fielding K, Bentley E, Miller P, Kerslake R, Pringle M.

**No. 31**

Design and use of questionnaires: a review of best practice applicable to surveys of health service staff and patients.

By McColl E, Jacoby A, Thomas L, Soutter J, Bamford C, Steen N, *et al.*

**No. 32**

A rapid and systematic review of the clinical effectiveness and cost-effectiveness of paclitaxel, docetaxel, gemcitabine and vinorelbine in non-small-cell lung cancer.

By Clegg A, Scott DA, Sidhu M, Hewitson P, Waugh N.

**No. 33**

Subgroup analyses in randomised controlled trials: quantifying the risks of false-positives and false-negatives.

By Brookes ST, Whitley E, Peters TJ, Mulheran PA, Egger M, Davey Smith G.

**No. 34**

Depot antipsychotic medication in the treatment of patients with schizophrenia: (1) Meta-review; (2) Patient and nurse attitudes.

By David AS, Adams C.

**No. 35**

A systematic review of controlled trials of the effectiveness and cost-effectiveness of brief psychological treatments for depression.

By Churchill R, Hunot V, Corney R, Knapp M, McGuire H, Tylee A, *et al.*

**No. 36**

Cost analysis of child health surveillance.

By Sanderson D, Wright D, Acton C, Duree D.

**Volume 6, 2002****No. 1**

A study of the methods used to select review criteria for clinical audit.

By Hearnshaw H, Harker R, Cheater F, Baker R, Grimshaw G.

**No. 2**

Fludarabine as second-line therapy for B cell chronic lymphocytic leukaemia: a technology assessment.

By Hyde C, Wake B, Bryan S, Barton P, Fry-Smith A, Davenport C, *et al.*

**No. 3**

Rituximab as third-line treatment for refractory or recurrent Stage III or IV follicular non-Hodgkin's lymphoma: a systematic review and economic evaluation.

By Wake B, Hyde C, Bryan S, Barton P, Song F, Fry-Smith A, *et al.*

**No. 4**

A systematic review of discharge arrangements for older people.

By Parker SG, Peet SM, McPherson A, Cannaby AM, Baker R, Wilson A, *et al.*

**No. 5**

The clinical effectiveness and cost-effectiveness of inhaler devices used in the routine management of chronic asthma in older children: a systematic review and economic evaluation.

By Peters J, Stevenson M, Beverley C, Lim J, Smith S.

**No. 6**

The clinical effectiveness and cost-effectiveness of sibutramine in the management of obesity: a technology assessment.

By O'Meara S, Riemsma R, Shirran L, Mather L, ter Riet G.

**No. 7**

The cost-effectiveness of magnetic resonance angiography for carotid artery stenosis and peripheral vascular disease: a systematic review.

By Berry E, Kelly S, Westwood ME, Davies LM, Gough MJ, Bamford JM, *et al.*

**No. 8**

Promoting physical activity in South Asian Muslim women through 'exercise on prescription'.

By Carroll B, Ali N, Azam N.

**No. 9**

Zanamivir for the treatment of influenza in adults: a systematic review and economic evaluation.

By Burls A, Clark W, Stewart T, Preston C, Bryan S, Jefferson T, *et al.*

**No. 10**

A review of the natural history and epidemiology of multiple sclerosis: implications for resource allocation and health economic models.

By Richards RG, Sampson FC, Beard SM, Tappenden P.

**No. 11**

Screening for gestational diabetes: a systematic review and economic evaluation.

By Scott DA, Loveman E, McIntyre L, Waugh N.

**No. 12**

The clinical effectiveness and cost-effectiveness of surgery for people with morbid obesity: a systematic review and economic evaluation.

By Clegg AJ, Colquitt J, Sidhu MK, Royle P, Loveman E, Walker A.

**No. 13**

The clinical effectiveness of trastuzumab for breast cancer: a systematic review.

By Lewis R, Bagnall A-M, Forbes C, Shirran E, Duffy S, Kleijnen J, *et al.*

**No. 14**

The clinical effectiveness and cost-effectiveness of vinorelbine for breast cancer: a systematic review and economic evaluation.

By Lewis R, Bagnall A-M, King S, Woolcott N, Forbes C, Shirran L, *et al.*

**No. 15**

A systematic review of the effectiveness and cost-effectiveness of metal-on-metal hip resurfacing arthroplasty for treatment of hip disease.

By Vale L, Wyness L, McCormack K, McKenzie L, Brazzelli M, Stearns SC.

**No. 16**

The clinical effectiveness and cost-effectiveness of bupropion and nicotine replacement therapy for smoking cessation: a systematic review and economic evaluation.

By Woolcott NF, Jones L, Forbes CA, Mather LC, Sowden AJ, Song FJ, *et al.*

**No. 17**

A systematic review of effectiveness and economic evaluation of new drug treatments for juvenile idiopathic arthritis: etanercept.

By Cummins C, Connock M, Fry-Smith A, Burls A.

**No. 18**

Clinical effectiveness and cost-effectiveness of growth hormone in children: a systematic review and economic evaluation.

By Bryant J, Cave C, Mihaylova B, Chase D, McIntyre L, Gerard K, *et al.*

**No. 19**

Clinical effectiveness and cost-effectiveness of growth hormone in adults in relation to impact on quality of life: a systematic review and economic evaluation.

By Bryant J, Loveman E, Chase D, Mihaylova B, Cave C, Gerard K, *et al.*

**No. 20**

Clinical medication review by a pharmacist of patients on repeat prescriptions in general practice: a randomised controlled trial.

By Zermansky AG, Petty DR, Raynor DK, Lowe CJ, Frementle N, Vail A.

**No. 21**

The effectiveness of infliximab and etanercept for the treatment of rheumatoid arthritis: a systematic review and economic evaluation.

By Jobanputra P, Barton P, Bryan S, Burls A.

**No. 22**

A systematic review and economic evaluation of computerised cognitive behaviour therapy for depression and anxiety.

By Kaltenthaler E, Shackley P, Stevens K, Beverley C, Parry G, Chilcott J.

**No. 23**

A systematic review and economic evaluation of pegylated liposomal doxorubicin hydrochloride for ovarian cancer.

By Forbes C, Wilby J, Richardson G, Sculpher M, Mather L, Reimsma R.

**No. 24**

A systematic review of the effectiveness of interventions based on a stages-of-change approach to promote individual behaviour change.

By Riemsma RP, Pattenden J, Bridle C, Sowden AJ, Mather L, Watt IS, *et al.*

**No. 25**

A systematic review update of the clinical effectiveness and cost-effectiveness of glycoprotein IIb/IIIa antagonists.

By Robinson M, Ginnelly L, Sculpher M, Jones L, Riemsma R, Palmer S, *et al.*

**No. 26**

A systematic review of the effectiveness, cost-effectiveness and barriers to implementation of thrombolytic and neuroprotective therapy for acute ischaemic stroke in the NHS.

By Sandercock P, Berge E, Dennis M, Forbes J, Hand P, Kwan J, *et al.*

**No. 27**

A randomised controlled crossover trial of nurse practitioner versus doctor-led outpatient care in a bronchiectasis clinic.

By Caine N, Sharples LD, Hollingworth W, French J, Keogan M, Exley A, *et al.*

**No. 28**

Clinical effectiveness and cost – consequences of selective serotonin reuptake inhibitors in the treatment of sex offenders.

By Adi Y, Ashcroft D, Browne K, Beech A, Fry-Smith A, Hyde C.

**No. 29**

Treatment of established osteoporosis: a systematic review and cost-utility analysis.

By Kanis JA, Brazier JE, Stevenson M, Calvert NW, Lloyd Jones M.

**No. 30**

Which anaesthetic agents are cost-effective in day surgery? Literature review, national survey of practice and randomised controlled trial.

By Elliott RA Payne K, Moore JK, Davies LM, Harper NJN, St Leger AS, *et al.*

**No. 31**

Screening for hepatitis C among injecting drug users and in genitourinary medicine clinics: systematic reviews of effectiveness, modelling study and national survey of current practice.

By Stein K, Dalziel K, Walker A, McIntyre L, Jenkins B, Horne J, *et al.*

**No. 32**

The measurement of satisfaction with healthcare: implications for practice from a systematic review of the literature.

By Crow R, Gage H, Hampson S, Hart J, Kimber A, Storey L, *et al.*

**No. 33**

The effectiveness and cost-effectiveness of imatinib in chronic myeloid leukaemia: a systematic review.

By Garside R, Round A, Dalziel K, Stein K, Royle R.

**No. 34**

A comparative study of hypertonic saline, daily and alternate-day rhDNase in children with cystic fibrosis.

By Suri R, Wallis C, Bush A, Thompson S, Normand C, Flather M, *et al.*

**No. 35**

A systematic review of the costs and effectiveness of different models of paediatric home care.

By Parker G, Bhakta P, Lovett CA, Paisley S, Olsen R, Turner D, *et al.*

**Volume 7, 2003**

**No. 1**

How important are comprehensive literature searches and the assessment of trial quality in systematic reviews? Empirical study.

By Egger M, Jüni P, Bartlett C, Holenstein F, Sterne J.

**No. 2**

Systematic review of the effectiveness and cost-effectiveness, and economic evaluation, of home versus hospital or satellite unit haemodialysis for people with end-stage renal failure.

By Mowatt G, Vale L, Perez J, Wyness L, Fraser C, MacLeod A, *et al.*

**No. 3**

Systematic review and economic evaluation of the effectiveness of infliximab for the treatment of Crohn's disease.

By Clark W, Raftery J, Barton P, Song F, Fry-Smith A, Burls A.

**No. 4**

A review of the clinical effectiveness and cost-effectiveness of routine anti-D prophylaxis for pregnant women who are rhesus negative.

By Chilcott J, Lloyd Jones M, Wight J, Forman K, Wray J, Beverley C, *et al.*

**No. 5**

Systematic review and evaluation of the use of tumour markers in paediatric oncology: Ewing's sarcoma and neuroblastoma.

By Riley RD, Burchill SA, Abrams KR, Heney D, Lambert PC, Jones DR, *et al.*

**No. 6**

The cost-effectiveness of screening for *Helicobacter pylori* to reduce mortality and morbidity from gastric cancer and peptic ulcer disease: a discrete-event simulation model.

By Roderick P, Davies R, Raftery J, Crabbe D, Pearce R, Bhandari P, *et al.*

**No. 7**

The clinical effectiveness and cost-effectiveness of routine dental checks: a systematic review and economic evaluation.

By Davenport C, Elley K, Salas C, Taylor-Weetman CL, Fry-Smith A, Bryan S, *et al.*

**No. 8**

A multicentre randomised controlled trial assessing the costs and benefits of using structured information and analysis of women's preferences in the management of menorrhagia.

By Kennedy ADM, Sculpher MJ, Coulter A, Dwyer N, Rees M, Horsley S, *et al.*

**No. 9**

Clinical effectiveness and cost-utility of photodynamic therapy for wet age-related macular degeneration: a systematic review and economic evaluation.

By Meads C, Salas C, Roberts T, Moore D, Fry-Smith A, Hyde C.

**No. 10**

Evaluation of molecular tests for prenatal diagnosis of chromosome abnormalities.

By Grimshaw GM, Szczepura A, Hultén M, MacDonald F, Nevin NC, Sutton F, *et al.*



**No. 11**

First and second trimester antenatal screening for Down's syndrome: the results of the Serum, Urine and Ultrasound Screening Study (SURUSS).

By Wald NJ, Rodeck C, Hackshaw AK, Walters J, Chitty L, Mackinson AM.

**No. 12**

The effectiveness and cost-effectiveness of ultrasound locating devices for central venous access: a systematic review and economic evaluation.

By Calvert N, Hind D, McWilliams RG, Thomas SM, Beverley C, Davidson A.

**No. 13**

A systematic review of atypical antipsychotics in schizophrenia.

By Bagnall A-M, Jones L, Lewis R, Ginnelly L, Glanville J, Torgerson D, *et al.*

**No. 14**

Prostate Testing for Cancer and Treatment ( ProtecT) feasibility study.

By Donovan J, Hamdy F, Neal D, Peters T, Oliver S, Brindle L, *et al.*

**No. 15**

Early thrombolysis for the treatment of acute myocardial infarction: a systematic review and economic evaluation.

By Boland A, Dundar Y, Bagust A, Haycox A, Hill R, Mujica Mota R, *et al.*

**No. 16**

Screening for fragile X syndrome: a literature review and modelling.

By Song FJ, Barton P, Sleightholme V, Yao GL, Fry-Smith A.

**No. 17**

Systematic review of endoscopic sinus surgery for nasal polyps.

By Dalziel K, Stein K, Round A, Garside R, Royle P.

**No. 18**

Towards efficient guidelines: how to monitor guideline use in primary care.

By Hutchinson A, McIntosh A, Cox S, Gilbert C.

**No. 19**

Effectiveness and cost-effectiveness of acute hospital-based spinal cord injuries services: systematic review.

By Bagnall A-M, Jones L, Richardson G, Duffy S, Riemsma R.

**No. 20**

Prioritisation of health technology assessment. The PATHS model: methods and case studies.

By Townsend J, Buxton M, Harper G.

**No. 21**

Systematic review of the clinical effectiveness and cost-effectiveness of tension-free vaginal tape for treatment of urinary stress incontinence.

By Cody J, Wyness L, Wallace S, Glazener C, Kilonzo M, Stearns S, *et al.*

**No. 22**

The clinical and cost-effectiveness of patient education models for diabetes: a systematic review and economic evaluation.

By Loveman E, Cave C, Green C, Royle P, Dunn N, Waugh N.

**No. 23**

The role of modelling in prioritising and planning clinical trials.

By Chilcott J, Brennan A, Booth A, Karnon J, Tappenden P.

**No. 24**

Cost-benefit evaluation of routine influenza immunisation in people 65-74 years of age.

By Allsup S, Gosney M, Haycox A, Regan M.

**No. 25**

The clinical and cost-effectiveness of pulsatile machine perfusion versus cold storage of kidneys for transplantation retrieved from heart-beating and non-heart-beating donors.

By Wight J, Chilcott J, Holmes M, Brewer N.

**No. 26**

Can randomised trials rely on existing electronic data? A feasibility study to explore the value of routine data in health technology assessment.

By Williams JG, Cheung WY, Cohen DR, Hutchings HA, Longo MF, Russell IT.

**No. 27**

Evaluating non-randomised intervention studies.

By Deeks JJ, Dinnes J, D'Amico R, Sowden AJ, Sakarovich C, Song F, *et al.*

**No. 28**

A randomised controlled trial to assess the impact of a package comprising a patient-orientated, evidence-based self-help guidebook and patient-centred consultations on disease management and satisfaction in inflammatory bowel disease.

By Kennedy A, Nelson E, Reeves D, Richardson G, Roberts C, Robinson A, *et al.*

**No. 29**

The effectiveness of diagnostic tests for the assessment of shoulder pain due to soft tissue disorders: a systematic review.

By Dinnes J, Loveman E, McIntyre L, Waugh N.

**No. 30**

The value of digital imaging in diabetic retinopathy.

By Sharp PF, Olson J, Strachan F, Hipwell J, Ludbrook A, O'Donnell M, *et al.*

**No. 31**

Lowering blood pressure to prevent myocardial infarction and stroke: a new preventive strategy.

By Law M, Wald N, Morris J.

**No. 32**

Clinical and cost-effectiveness of capecitabine and tegafur with uracil for the treatment of metastatic colorectal cancer: systematic review and economic evaluation.

By Ward S, Kaltenthaler E, Cowan J, Brewer N.

**No. 33**

Clinical and cost-effectiveness of new and emerging technologies for early localised prostate cancer: a systematic review.

By Hummel S, Paisley S, Morgan A, Currie E, Brewer N.

**No. 34**

Literature searching for clinical and cost-effectiveness studies used in health technology assessment reports carried out for the National Institute for Clinical Excellence appraisal system.

By Royle P, Waugh N.

**No. 35**

Systematic review and economic decision modelling for the prevention and treatment of influenza A and B.

By Turner D, Wailoo A, Nicholson K, Cooper N, Sutton A, Abrams K.

**No. 36**

A randomised controlled trial to evaluate the clinical and cost-effectiveness of Hickman line insertions in adult cancer patients by nurses.

By Boland A, Haycox A, Bagust A, Fitzsimmons L.

**No. 37**

Redesigning postnatal care: a randomised controlled trial of protocol-based midwifery-led care focused on individual women's physical and psychological health needs.

By MacArthur C, Winter HR, Bick DE, Lilford RJ, Lancashire RJ, Knowles H, *et al.*

**No. 38**

Estimating implied rates of discount in healthcare decision-making.

By West RR, McNabb R, Thompson AGH, Sheldon TA, Grimley Evans J.

**No. 39**

Systematic review of isolation policies in the hospital management of methicillin-resistant *Staphylococcus aureus*: a review of the literature with epidemiological and economic modelling.

By Cooper BS, Stone SP, Kibbler CC, Cookson BD, Roberts JA, Medley GF, *et al.*

**No. 40**

Treatments for spasticity and pain in multiple sclerosis: a systematic review.

By Beard S, Hunn A, Wight J.

**No. 41**

The inclusion of reports of randomised trials published in languages other than English in systematic reviews.

By Moher D, Pham B, Lawson ML, Klassen TP.

**No. 42**

The impact of screening on future health-promoting behaviours and health beliefs: a systematic review.

By Bankhead CR, Brett J, Bukach C, Webster P, Stewart-Brown S, Munafa M, *et al.*

**Volume 8, 2004**

**No. 1**

What is the best imaging strategy for acute stroke?

By Wardlaw JM, Keir SL, Seymour J, Lewis S, Sandercock PAG, Dennis MS, *et al.*

**No. 2**

Systematic review and modelling of the investigation of acute and chronic chest pain presenting in primary care.

By Mant J, McManus RJ, Oakes RAL, Delaney BC, Barton PM, Deeks JJ, *et al.*

**No. 3**

The effectiveness and cost-effectiveness of microwave and thermal balloon endometrial ablation for heavy menstrual bleeding: a systematic review and economic modelling.

By Garside R, Stein K, Wyatt K, Round A, Price A.

**No. 4**

A systematic review of the role of bisphosphonates in metastatic disease.

By Ross JR, Saunders Y, Edmonds PM, Patel S, Wonderling D, Normand C, *et al.*

**No. 5**

Systematic review of the clinical effectiveness and cost-effectiveness of capecitabine (Xeloda®) for locally advanced and/or metastatic breast cancer.

By Jones L, Hawkins N, Westwood M, Wright K, Richardson G, Riemsma R.

**No. 6**

Effectiveness and efficiency of guideline dissemination and implementation strategies.

By Grimshaw JM, Thomas RE, MacLennan G, Fraser C, Ramsay CR, Vale L, *et al.*

**No. 7**

Clinical effectiveness and costs of the Sugarbaker procedure for the treatment of pseudomyxoma peritonei.

By Bryant J, Clegg AJ, Sidhu MK, Brodin H, Royle P, Davidson P.

**No. 8**

Psychological treatment for insomnia in the regulation of long-term hypnotic drug use.

By Morgan K, Dixon S, Mathers N, Thompson J, Tomeny M.

**No. 9**

Improving the evaluation of therapeutic interventions in multiple sclerosis: development of a patient-based measure of outcome.

By Hobart JC, Riazi A, Lamping DL, Fitzpatrick R, Thompson AJ.

**No. 10**

A systematic review and economic evaluation of magnetic resonance cholangiopancreatography compared with diagnostic endoscopic retrograde cholangiopancreatography.

By Kaltenthaler E, Bravo Vergel Y, Chilcott J, Thomas S, Blakeborough T, Walters SJ, *et al.*

**No. 11**

The use of modelling to evaluate new drugs for patients with a chronic condition: the case of antibodies against tumour necrosis factor in rheumatoid arthritis.

By Barton P, Jobanputra P, Wilson J, Bryan S, Burls A.

**No. 12**

Clinical effectiveness and cost-effectiveness of neonatal screening for inborn errors of metabolism using tandem mass spectrometry: a systematic review.

By Pandor A, Eastham J, Beverley C, Chilcott J, Paisley S.

**No. 13**

Clinical effectiveness and cost-effectiveness of pioglitazone and rosiglitazone in the treatment of type 2 diabetes: a systematic review and economic evaluation.

By Czoski-Murray C, Warren E, Chilcott J, Beverley C, Psyllaki MA, Cowan J.

**No. 14**

Routine examination of the newborn: the EMREN study. Evaluation of an extension of the midwife role including a randomised controlled trial of appropriately trained midwives and paediatric senior house officers.

By Townsend J, Wolke D, Hayes J, Davé S, Rogers C, Bloomfield L, *et al.*

**No. 15**

Involving consumers in research and development agenda setting for the NHS: developing an evidence-based approach.

By Oliver S, Clarke-Jones L, Rees R, Milne R, Buchanan P, Gabbay J, *et al.*

**No. 16**

A multi-centre randomised controlled trial of minimally invasive direct coronary bypass grafting versus percutaneous transluminal coronary angioplasty with stenting for proximal stenosis of the left anterior descending coronary artery.

By Reeves BC, Angelini GD, Bryan AJ, Taylor FC, Cripps T, Spyt TJ, *et al.*

**No. 17**

Does early magnetic resonance imaging influence management or improve outcome in patients referred to secondary care with low back pain? A pragmatic randomised controlled trial.

By Gilbert FJ, Grant AM, Gillan MGC, Vale L, Scott NW, Campbell MK, *et al.*

**No. 18**

The clinical and cost-effectiveness of anakinra for the treatment of rheumatoid arthritis in adults: a systematic review and economic analysis.

By Clark W, Jobanputra P, Barton P, Burls A.

**No. 19**

A rapid and systematic review and economic evaluation of the clinical and cost-effectiveness of newer drugs for treatment of mania associated with bipolar affective disorder.

By Bridle C, Palmer S, Bagnall A-M, Darba J, Duffy S, Sculpher M, *et al.*

**No. 20**

Liquid-based cytology in cervical screening: an updated rapid and systematic review and economic analysis.

By Karnon J, Peters J, Platt J, Chilcott J, McGoogan E, Brewer N.

**No. 21**

Systematic review of the long-term effects and economic consequences of treatments for obesity and implications for health improvement.

By Avenell A, Broom J, Brown TJ, Poobalan A, Aucott L, Stearns SC, *et al.*

**No. 22**

Autoantibody testing in children with newly diagnosed type 1 diabetes mellitus.

By Dretzke J, Cummins C, Sandercock J, Fry-Smith A, Barrett T, Burls A.

**No. 23**

Clinical effectiveness and cost-effectiveness of prehospital intravenous fluids in trauma patients.

By Dretzke J, Sandercock J, Bayliss S, Burls A.

**No. 24**

Newer hypnotic drugs for the short-term management of insomnia: a systematic review and economic evaluation.

By Dündar Y, Boland A, Strobl J, Dodd S, Haycox A, Bagust A, *et al.*

**No. 25**

Development and validation of methods for assessing the quality of diagnostic accuracy studies.

By Whiting P, Rutjes AWS, Dinnes J, Reitsma JB, Bossuyt PMM, Kleijnen J.

**No. 26**

EVALUATE hysterectomy trial: a multicentre randomised trial comparing abdominal, vaginal and laparoscopic methods of hysterectomy.

By Garry R, Fountain J, Brown J, Manca A, Mason S, Sculpher M, *et al.*

**No. 27**

Methods for expected value of information analysis in complex health economic models: developments on the health economics of interferon- $\beta$  and glatiramer acetate for multiple sclerosis.

By Tappenden P, Chilcott JB, Eggington S, Oakley J, McCabe C.

**No. 28**

Effectiveness and cost-effectiveness of imatinib for first-line treatment of chronic myeloid leukaemia in chronic phase: a systematic review and economic analysis.

By Dalziel K, Round A, Stein K, Garside R, Price A.

**No. 29**

VenUS I: a randomised controlled trial of two types of bandage for treating venous leg ulcers.

By Iglesias C, Nelson EA, Cullum NA, Torgerson DJ on behalf of the VenUS Team.

**No. 30**

Systematic review of the effectiveness and cost-effectiveness, and economic evaluation, of myocardial perfusion scintigraphy for the diagnosis and management of angina and myocardial infarction.

By Mowatt G, Vale L, Brazzelli M, Hernandez R, Murray A, Scott N, *et al.*

**No. 31**

A pilot study on the use of decision theory and value of information analysis as part of the NHS Health Technology Assessment programme.

By Claxton K, Ginnelly L, Sculpher M, Philips Z, Palmer S.

**No. 32**

The Social Support and Family Health Study: a randomised controlled trial and economic evaluation of two alternative forms of postnatal support for mothers living in disadvantaged inner-city areas.

By Wiggins M, Oakley A, Roberts I, Turner H, Rajan L, Austerberry H, *et al.*

**No. 33**

Psychosocial aspects of genetic screening of pregnant women and newborns: a systematic review.

By Green JM, Hewison J, Bekker HL, Bryant, Cuckle HS.

**No. 34**

Evaluation of abnormal uterine bleeding: comparison of three outpatient procedures within cohorts defined by age and menopausal status.

By Critchley HOD, Warner P, Lee AJ, Brechin S, Guise J, Graham B.

**No. 35**

Coronary artery stents: a rapid systematic review and economic evaluation.

By Hill R, Bagust A, Bakhai A, Dickson R, Dündar Y, Haycox A, *et al.*

**No. 36**

Review of guidelines for good practice in decision-analytic modelling in health technology assessment.

By Philips Z, Ginnelly L, Sculpher M, Claxton K, Golder S, Riemsma R, *et al.*

**No. 37**

Rituximab (MabThera<sup>®</sup>) for aggressive non-Hodgkin's lymphoma: systematic review and economic evaluation.

By Knight C, Hind D, Brewer N, Abbott V.

**No. 38**

Clinical effectiveness and cost-effectiveness of clopidogrel and modified-release dipyridamole in the secondary prevention of occlusive vascular events: a systematic review and economic evaluation.

By Jones L, Griffin S, Palmer S, Main C, Orton V, Sculpher M, *et al.*

**No. 39**

Pegylated interferon  $\alpha$ -2a and -2b in combination with ribavirin in the treatment of chronic hepatitis C: a systematic review and economic evaluation.

By Shepherd J, Brodin H, Cave C, Waugh N, Price A, Gabbay J.

**No. 40**

Clopidogrel used in combination with aspirin compared with aspirin alone in the treatment of non-ST-segment-elevation acute coronary syndromes: a systematic review and economic evaluation.

By Main C, Palmer S, Griffin S, Jones L, Orton V, Sculpher M, *et al.*

**No. 41**

Provision, uptake and cost of cardiac rehabilitation programmes: improving services to under-represented groups.

By Beswick AD, Rees K, Griebisch I, Taylor FC, Burke M, West RR, *et al.*

**No. 42**

Involving South Asian patients in clinical trials.

By Hussain-Gambles M, Leese B, Atkin K, Brown J, Mason S, Tovey P.

**No. 43**

Clinical and cost-effectiveness of continuous subcutaneous insulin infusion for diabetes.

By Colquitt JL, Green C, Sidhu MK, Hartwell D, Waugh N.

**No. 44**

Identification and assessment of ongoing trials in health technology assessment reviews.

By Song FJ, Fry-Smith A, Davenport C, Bayliss S, Adi Y, Wilson JS, *et al.*

**No. 45**

Systematic review and economic evaluation of a long-acting insulin analogue, insulin glargine

By Warren E, Weatherley-Jones E, Chilcott J, Beverley C.

**No. 46**

Supplementation of a home-based exercise programme with a class-based programme for people with osteoarthritis of the knees: a randomised controlled trial and health economic analysis.

By McCarthy CJ, Mills PM, Pullen R, Richardson G, Hawkins N, Roberts CR, *et al.*

**No. 47**

Clinical and cost-effectiveness of once-daily versus more frequent use of same potency topical corticosteroids for atopic eczema: a systematic review and economic evaluation.

By Green C, Colquitt JL, Kirby J, Davidson P, Payne E.

**No. 48**

Acupuncture of chronic headache disorders in primary care: randomised controlled trial and economic analysis.

By Vickers AJ, Rees RW, Zollman CE, McCarney R, Smith CM, Ellis N, *et al.*

**No. 49**

Generalisability in economic evaluation studies in healthcare: a review and case studies.

By Sculpher MJ, Pang FS, Manca A, Drummond MF, Golder S, Urdahl H, *et al.*

**No. 50**

Virtual outreach: a randomised controlled trial and economic evaluation of joint teleconferenced medical consultations.

By Wallace P, Barber J, Clayton W, Currell R, Fleming K, Garner P, *et al.*

**Volume 9, 2005**

**No. 1**

Randomised controlled multiple treatment comparison to provide a cost-effectiveness rationale for the selection of antimicrobial therapy in acne.

By Ozolins M, Eady EA, Avery A, Cunliffe WJ, O'Neill C, Simpson NB, *et al.*

**No. 2**

Do the findings of case series studies vary significantly according to methodological characteristics?

By Dalziel K, Round A, Stein K, Garside R, Castelnovo E, Payne L.

**No. 3**

Improving the referral process for familial breast cancer genetic counselling: findings of three randomised controlled trials of two interventions.

By Wilson BJ, Torrance N, Mollison J, Wordsworth S, Gray JR, Haites NE, *et al.*

**No. 4**

Randomised evaluation of alternative electrosurgical modalities to treat bladder outflow obstruction in men with benign prostatic hyperplasia.

By Fowler C, McAllister W, Plail R, Karim O, Yang Q.

**No. 5**

A pragmatic randomised controlled trial of the cost-effectiveness of palliative therapies for patients with inoperable oesophageal cancer.

By Shenfine J, McNamee P, Steen N, Bond J, Griffin SM.

**No. 6**

Impact of computer-aided detection prompts on the sensitivity and specificity of screening mammography.

By Taylor P, Champness J, Given-Wilson R, Johnston K, Potts H.

**No. 7**

Issues in data monitoring and interim analysis of trials.

By Grant AM, Altman DG, Babiker AB, Campbell MK, Clemens FJ, Darbyshire JH, *et al.*

**No. 8**

Lay public's understanding of equipoise and randomisation in randomised controlled trials.

By Robinson EJ, Kerr CEP, Stevens AJ, Lilford RJ, Brauholtz DA, Edwards SJ, *et al.*

**No. 9**

Clinical and cost-effectiveness of electroconvulsive therapy for depressive illness, schizophrenia, catatonia and mania: systematic reviews and economic modelling studies.

By Greenhalgh J, Knight C, Hind D, Beverley C, Walters S.

**No. 10**

Measurement of health-related quality of life for people with dementia: development of a new instrument (DEMQOL) and an evaluation of current methodology.

By Smith SC, Lamping DL, Banerjee S, Harwood R, Foley B, Smith P, *et al.*

**No. 11**

Clinical effectiveness and cost-effectiveness of drotrecogin alfa (activated) (Xigris<sup>®</sup>) for the treatment of severe sepsis in adults: a systematic review and economic evaluation.

By Green C, Dinnes J, Takeda A, Shepherd J, Hartwell D, Cave C, *et al.*

**No. 12**

A methodological review of how heterogeneity has been examined in systematic reviews of diagnostic test accuracy.

By Dinnes J, Deeks J, Kirby J, Roderick P.

**No. 13**

Cervical screening programmes: can automation help? Evidence from systematic reviews, an economic analysis and a simulation modelling exercise applied to the UK.

By Willis BH, Barton P, Pearmain P, Bryan S, Hyde C.

**No. 14**

Laparoscopic surgery for inguinal hernia repair: systematic review of effectiveness and economic evaluation.

By McCormack K, Wake B, Perez J, Fraser C, Cook J, McIntosh E, *et al.*

**No. 15**

Clinical effectiveness, tolerability and cost-effectiveness of newer drugs for epilepsy in adults: a systematic review and economic evaluation.

By Wilby J, Kainth A, Hawkins N, Epstein D, McIntosh H, McDaid C, *et al.*

**No. 16**

A randomised controlled trial to compare the cost-effectiveness of tricyclic antidepressants, selective serotonin reuptake inhibitors and lofepramine.

By Peveler R, Kendrick T, Buxton M, Longworth L, Baldwin D, Moore M, *et al.*

**No. 17**

Clinical effectiveness and cost-effectiveness of immediate angioplasty for acute myocardial infarction: systematic review and economic evaluation.

By Hartwell D, Colquitt J, Loveman E, Clegg AJ, Brodin H, Waugh N, *et al.*

**No. 18**

A randomised controlled comparison of alternative strategies in stroke care.

By Kalra L, Evans A, Perez I, Knapp M, Swift C, Donaldson N.

**No. 19**

The investigation and analysis of critical incidents and adverse events in healthcare.

By Woloshynowych M, Rogers S, Taylor-Adams S, Vincent C.

**No. 20**

Potential use of routine databases in health technology assessment.

By Raftery J, Roderick P, Stevens A.

**No. 21**

Clinical and cost-effectiveness of newer immunosuppressive regimens in renal transplantation: a systematic review and modelling study.

By Woodroffe R, Yao GL, Meads C, Bayliss S, Ready A, Raftery J, *et al.*

**No. 22**

A systematic review and economic evaluation of alendronate, etidronate, risedronate, raloxifene and teriparatide for the prevention and treatment of postmenopausal osteoporosis.

By Stevenson M, Lloyd Jones M, De Nigris E, Brewer N, Davis S, Oakley J.

**No. 23**

A systematic review to examine the impact of psycho-educational interventions on health outcomes and costs in adults and children with difficult asthma.

By Smith JR, Mugford M, Holland R, Candy B, Noble MJ, Harrison BDW, *et al.*

**No. 24**

An evaluation of the costs, effectiveness and quality of renal replacement therapy provision in renal satellite units in England and Wales.

By Roderick P, Nicholson T, Armitage A, Mehta R, Mullee M, Gerard K, *et al.*

**No. 25**

Imatinib for the treatment of patients with unresectable and/or metastatic gastrointestinal stromal tumours: systematic review and economic evaluation.

By Wilson J, Connock M, Song F, Yao G, Fry-Smith A, Raftery J, *et al.*

**No. 26**

Indirect comparisons of competing interventions.

By Glenny AM, Altman DG, Song F, Sakarovitch C, Deeks JJ, D'Amico R, *et al.*

**No. 27**

Cost-effectiveness of alternative strategies for the initial medical management of non-ST elevation acute coronary syndrome: systematic review and decision-analytical modelling.

By Robinson M, Palmer S, Sculpher M, Philips Z, Ginnelly L, Bowens A, *et al.*

**No. 28**

Outcomes of electrically stimulated gracilis neosphincter surgery.

By Tillin T, Chambers M, Feldman R.

**No. 29**

The effectiveness and cost-effectiveness of pimecrolimus and tacrolimus for atopic eczema: a systematic review and economic evaluation.

By Garside R, Stein K, Castelnovo E, Pitt M, Ashcroft D, Dimmock P, *et al.*

**No. 30**

Systematic review on urine albumin testing for early detection of diabetic complications.

By Newman DJ, Mattock MB, Dawney ABS, Kerry S, McGuire A, Yaqoob M, *et al.*

**No. 31**

Randomised controlled trial of the cost-effectiveness of water-based therapy for lower limb osteoarthritis.

By Cochrane T, Davey RC, Matthes Edwards SM.

**No. 32**

Longer term clinical and economic benefits of offering acupuncture care to patients with chronic low back pain.

By Thomas KJ, MacPherson H, Ratcliffe J, Thorpe L, Brazier J, Campbell M, *et al.*

**No. 33**

Cost-effectiveness and safety of epidural steroids in the management of sciatica.

By Price C, Arden N, Cogan L, Rogers P.

**No. 34**

The British Rheumatoid Outcome Study Group (BROSG) randomised controlled trial to compare the effectiveness and cost-effectiveness of aggressive versus symptomatic therapy in established rheumatoid arthritis.

By Symmons D, Tricker K, Roberts C, Davies L, Dawes P, Scott DL.

**No. 35**

Conceptual framework and systematic review of the effects of participants' and professionals' preferences in randomised controlled trials.

By King M, Nazareth I, Lampe F, Bower P, Chandler M, Morou M, *et al.*

**No. 36**

The clinical and cost-effectiveness of implantable cardioverter defibrillators: a systematic review.

By Bryant J, Brodin H, Loveman E, Payne E, Clegg A.

**No. 37**

A trial of problem-solving by community mental health nurses for anxiety, depression and life difficulties among general practice patients. The CPN-GP study.

By Kendrick T, Simons L, Mynors-Wallis L, Gray A, Lathlean J, Pickering R, *et al.*

**No. 38**

The causes and effects of socio-demographic exclusions from clinical trials.

By Bartlett C, Doyal L, Ebrahim S, Davey P, Bachmann M, Egger M, *et al.*

**No. 39**

Is hydrotherapy cost-effective? A randomised controlled trial of combined hydrotherapy programmes compared with physiotherapy land techniques in children with juvenile idiopathic arthritis.

By Epps H, Ginnelly L, Utley M, Southwood T, Gallivan S, Sculpher M, *et al.*

**No. 40**

A randomised controlled trial and cost-effectiveness study of systematic screening (targeted and total population screening) versus routine practice for the detection of atrial fibrillation in people aged 65 and over: The SAFE study.

By Hobbs FDR, Fitzmaurice DA, Mant J, Murray E, Jowett S, Bryan S, *et al.*

**No. 41**

Displaced intracapsular hip fractures in fit, older people: a randomised comparison of reduction and fixation, bipolar hemiarthroplasty and total hip arthroplasty.

By Keating JF, Grant A, Masson M, Scott NW, Forbes JF.

**No. 42**

Long-term outcome of cognitive behaviour therapy clinical trials in central Scotland.

By Durham RC, Chambers JA, Power KG, Sharp DM, Macdonald RR, Major KA, *et al.*

**No. 43**

The effectiveness and cost-effectiveness of dual-chamber pacemakers compared with single-chamber pacemakers for bradycardia due to atrioventricular block or sick sinus syndrome: systematic review and economic evaluation.

By Castelnovo E, Stein K, Pitt M, Garside R, Payne E.

**No. 44**

Newborn screening for congenital heart defects: a systematic review and cost-effectiveness analysis.

By Knowles R, Griesch I, Dezateux C, Brown J, Bull C, Wren C.

**No. 45**

The clinical and cost-effectiveness of left ventricular assist devices for end-stage heart failure: a systematic review and economic evaluation.

By Clegg AJ, Scott DA, Loveman E, Colquitt J, Hutchinson J, Royle P, *et al.*

**No. 46**

The effectiveness of the Heidelberg Retina Tomograph and laser diagnostic glaucoma scanning system (GDx) in detecting and monitoring glaucoma.

By Kwartz AJ, Henson DB, Harper RA, Spencer AF, McLeod D.

**No. 47**

Clinical and cost-effectiveness of autologous chondrocyte implantation for cartilage defects in knee joints: systematic review and economic evaluation.

By Clar C, Cummins E, McIntyre L, Thomas S, Lamb J, Bain L, *et al.*

**No. 48**

Systematic review of effectiveness of different treatments for childhood retinoblastoma.

By McDaid C, Hartley S, Bagnall A-M, Ritchie G, Light K, Riemsma R.

**No. 49**

Towards evidence-based guidelines for the prevention of venous thromboembolism: systematic reviews of mechanical methods, oral anticoagulation, dextran and regional anaesthesia as thromboprophylaxis.

By Roderick P, Ferris G, Wilson K, Halls H, Jackson D, Collins R, *et al.*

**No. 50**

The effectiveness and cost-effectiveness of parent training/education programmes for the treatment of conduct disorder, including oppositional defiant disorder, in children.

By Dretzke J, Frew E, Davenport C, Barlow J, Stewart-Brown S, Sandercock J, *et al.*

**Volume 10, 2006****No. 1**

The clinical and cost-effectiveness of donepezil, rivastigmine, galantamine and memantine for Alzheimer's disease.

By Loveman E, Green C, Kirby J, Takeda A, Picot J, Payne E, *et al.*

**No. 2**

FOOD: a multicentre randomised trial evaluating feeding policies in patients admitted to hospital with a recent stroke.

By Dennis M, Lewis S, Cranswick G, Forbes J.

**No. 3**

The clinical effectiveness and cost-effectiveness of computed tomography screening for lung cancer: systematic reviews.

By Black C, Bagust A, Boland A, Walker S, McLeod C, De Verteuil R, *et al.*

**No. 4**

A systematic review of the effectiveness and cost-effectiveness of neuroimaging assessments used to visualise the seizure focus in people with refractory epilepsy being considered for surgery.

By Whiting P, Gupta R, Burch J, Mujica Mota RE, Wright K, Marson A, *et al.*

**No. 5**

Comparison of conference abstracts and presentations with full-text articles in the health technology assessments of rapidly evolving technologies.

By Dundar Y, Dodd S, Dickson R, Walley T, Haycox A, Williamson PR.

**No. 6**

Systematic review and evaluation of methods of assessing urinary incontinence.

By Martin JL, Williams KS, Abrams KR, Turner DA, Sutton AJ, Chapple C, *et al.*

**No. 7**

The clinical effectiveness and cost-effectiveness of newer drugs for children with epilepsy. A systematic review.

By Connock M, Frew E, Evans B-W, Bryan S, Cummins C, Fry-Smith A, *et al.*

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Topotecan, pegylated liposomal doxorubicin hydrochloride and paclitaxel for second-line or subsequent treatment of advanced ovarian cancer: a systematic review and economic evaluation.

By Main C, Bojke L, Griffin S, Norman G, Barbieri M, Mather L, *et al.*

**No. 10**

Evaluation of molecular techniques in prediction and diagnosis of cytomegalovirus disease in immunocompromised patients.

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Screening for thrombophilia in high-risk situations: systematic review and cost-effectiveness analysis. The Thrombosis: Risk and Economic Assessment of Thrombophilia Screening (TREATS) study.

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Randomised clinical trial, observational study and assessment of cost-effectiveness of the treatment of varicose veins (REACTIV trial).

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The cost-effectiveness of screening for oral cancer in primary care.

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Measurement of the clinical and cost-effectiveness of non-invasive diagnostic testing strategies for deep vein thrombosis.

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Systematic review of the effectiveness and cost-effectiveness of HealOzone<sup>®</sup> for the treatment of occlusal pit/fissure caries and root caries.

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Randomised controlled trials of conventional antipsychotic versus new atypical drugs, and new atypical drugs versus clozapine, in people with schizophrenia responding poorly to, or intolerant of, current drug treatment.

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**No. 18**

Diagnostic tests and algorithms used in the investigation of haematuria: systematic reviews and economic evaluation.

By Rodgers M, Nixon J, Hempel S, Aho T, Kelly J, Neal D, *et al.*

**No. 19**

Cognitive behavioural therapy in addition to antispasmodic therapy for irritable bowel syndrome in primary care: randomised controlled trial.

By Kennedy TM, Chalder T, McCrone P, Darnley S, Knapp M, Jones RH, *et al.*

**No. 20**

A systematic review of the clinical effectiveness and cost-effectiveness of enzyme replacement therapies for Fabry's disease and mucopolysaccharidosis type 1.

By Connock M, Juarez-Garcia A, Frew E, Mans A, Dretzke J, Fry-Smith A, *et al.*

**No. 21**

Health benefits of antiviral therapy for mild chronic hepatitis C: randomised controlled trial and economic evaluation.

By Wright M, Grieve R, Roberts J, Main J, Thomas HC on behalf of the UK Mild Hepatitis C Trial Investigators.

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Pressure relieving support surfaces: a randomised evaluation.

By Nixon J, Nelson EA, Cranny G, Iglesias CP, Hawkins K, Cullum NA, *et al.*

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The clinical effectiveness and cost-effectiveness of enzyme replacement therapy for Gaucher's disease: a systematic review.

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Effectiveness and cost-effectiveness of salicylic acid and cryotherapy for cutaneous warts. An economic decision model.

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A systematic literature review of the effectiveness of non-pharmacological interventions to prevent wandering in dementia and evaluation of the ethical implications and acceptability of their use.

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A review of the evidence on the effects and costs of implantable cardioverter defibrillator therapy in different patient groups, and modelling of cost-effectiveness and cost-utility for these groups in a UK context.

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By Shepherd J, Jones J, Takeda A, Davidson P, Price A.

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Accurate, practical and cost-effective assessment of carotid stenosis in the UK.

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Etanercept and infliximab for the treatment of psoriatic arthritis: a systematic review and economic evaluation.

By Woolacott N, Bravo Vergel Y, Hawkins N, Kainth A, Khadjesari Z, Misso K, *et al.*

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The cost-effectiveness of testing for hepatitis C in former injecting drug users.

By Castelnuovo E, Thompson-Coon J, Pitt M, Cramp M, Siebert U, Price A, *et al.*

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Computerised cognitive behaviour therapy for depression and anxiety update: a systematic review and economic evaluation.

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Cost-effectiveness of using prognostic information to select women with breast cancer for adjuvant systemic therapy.

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Psychological therapies including dialectical behaviour therapy for borderline personality disorder: a systematic review and preliminary economic evaluation.

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Etanercept and efalizumab for the treatment of psoriasis: a systematic review.

By Woolacott N, Hawkins N, Mason A, Kainth A, Khadjesari Z, Bravo Vergel Y, *et al.*

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Systematic reviews of clinical decision tools for acute abdominal pain.

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**Volume 11, 2007****No. 1**

Pemetrexed disodium for the treatment of malignant pleural mesothelioma: a systematic review and economic evaluation.

By Dundar Y, Bagust A, Dickson R, Dodd S, Green J, Haycox A, *et al.*

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A randomised controlled trial of postoperative radiotherapy following breast-conserving surgery in a minimum-risk older population. The PRIME trial.

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Current practice, accuracy, effectiveness and cost-effectiveness of the school entry hearing screen.

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Recruitment to randomised trials: strategies for trial enrolment and participation study. The STEPS model.

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**No. 50**

Evaluation of diagnostic tests when there is no gold standard. A review of methods.

By Rutjes AWS, Reitsma JB, Coomarasamy A, Khan KS, Bossuyt PMM.

**No. 51**

Systematic reviews of the clinical effectiveness and cost-effectiveness of proton pump inhibitors in acute upper gastrointestinal bleeding.

By Leontiadis GI, Sreedharan A, Dorward S, Barton P, Delaney B, Howden CW, *et al.*

**No. 52**

A review and critique of modelling in prioritising and designing screening programmes.

By Karnon J, Goyder E, Tappenden P, McPhie S, Towers I, Brazier J, *et al.*

**No. 53**

An assessment of the impact of the NHS Health Technology Assessment Programme.

By Hanney S, Buxton M, Green C, Coulson D, Rafferty J.

**Volume 12, 2008****No. 1**

A systematic review and economic model of switching from non-glycopeptide to glycopeptide antibiotic prophylaxis for surgery.

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**No. 2**

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Dr Dennis Wright, Consultant Biochemist & Clinical Director, The North West London Hospitals NHS Trust, Middlesex

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Dr Yoon Loke, Senior Lecturer in Clinical Pharmacology, University of East Anglia

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Mrs Katrina Simister, Assistant Director New Medicines, National Prescribing Centre, Liverpool

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<p>Dr Mahmood Adil, Deputy Regional Director of Public Health, Department of Health, Manchester</p> <p>Dr Aileen Clarke, Consultant in Public Health, Public Health Resource Unit, Oxford</p>			

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<p>Mrs Sheila Clark, Chief Executive, St James's Hospital, Portsmouth</p> <p>Mr Richard Copeland, Lead Pharmacist: Clinical Economy/Interface, Wansbeck General Hospital, Northumberland</p>			

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### **Feedback**

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***We look forward to hearing from you.***