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Uterine artery embolization or myomectomy for women with uterine fibroids wishing to avoid hysterectomy: a cost-utility analysis of the FEMME trial

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Running title: Cost-effectiveness of UAE compared with myomectomy

Abstract

Objectives

To assess the cost-effectiveness of uterine artery embolization (UAE) and myomectomy for women with symptomatic uterine fibroids wishing to avoid hysterectomy.

Design

Economic evaluation alongside the FEMME randomised controlled trial.

Setting

29 UK hospitals.

Population

Premenopausal women who had symptomatic uterine fibroids amenable to UAE or myomectomy wishing to avoid hysterectomy. 254 women were randomised to UAE (127) and myomectomy (127).

Methods

A within trial cost-utility analysis was conducted from the perspective of the UK NHS.

Main outcome measures

Quality-adjusted life years measured using the EuroQoL 3L, combined with costs to estimate cost-effectiveness over two and four years of follow-up.

Results

Over a two-year time horizon, UAE was associated with higher mean costs (difference £645; 95% CI -1,381 to 2,580) and lower QALYs (difference -0.09; 95% CI -0.11 to -0.04) when compared with myomectomy. Similar results were observed over the four-year time horizon. Thus, UAE was dominated by myomectomy. Results of the sensitivity analyses were consistent with the basecase results for both years. Over two years, UAE was

associated with higher costs (difference £456; 95% CI -1,823; 3,164) and lower QALYs (difference -0.06; 95% CI (-0.11; -0.02).

Conclusions

Myomectomy is a cost-effective option for the treatment of uterine fibroids. The differences in costs and quality-adjusted life years are small. Women should be fully informed and have the option to choose between the two procedures.

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Keywords: uterine fibroids; uterine artery embolization; myomectomy; economic evaluation; cost-effectiveness

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Tweetable abstract: Fully informed women with uterine fibroids should have a choice between uterine artery embolization or myomectomy.

Introduction

The current UK guidance from the National Institute for Health and Clinical Excellence (NICE) on treatment for uterine fibroids recommends uterine artery embolization (UAE) as a non-surgical alternative option for women who do not wish to have surgery and/or who wish to preserve their fertility. Conventionally, the main approach is to recommend surgical treatments (hysterectomy and myomectomy), of which, the latter conserves the uterus. Another non-invasive option is high-intensity transcutaneous focused ultrasound (MRgHIFU) – NICE notes that there is adequate evidence of short-term efficacy, but it is only used in the UK with special arrangements or research purposes [1].

Few studies have evaluated the cost-effectiveness of treatments available for symptomatic fibroids. These studies focused on pre-menopausal women over 25 years old until menopause. In these studies, UAE [2-10] was compared with MRgHIFU [2, 4, 5, 7, 10], myomectomy [2, 4, 6, 7, 9, 10], hysterectomy [2, 3, 5-10], and pharmacotherapy [7]. Cost-effectiveness analyses typically comprised of model-based approaches, evaluating costs and quality-adjusted life years (QALYs). Time horizons of five years [4, 6, 9], eleven years ending at menopause [2, 3, 5, 8] and lifetime [7] were considered. Four [3-5, 7] evaluations were performed in the US with a societal perspective, three [6, 8, 10] in the UK from NHS perspective, one[9] in Hong Kong from a societal perspective, and one [3] evaluation in Canada with a public-payer perspective. The results from the economic literature vary, given differences in settings, populations, and perspectives. Economic evaluations which compared MRgHIFU to other treatments considered it to be the most cost-effective treatment for treating fibroids [2, 4, 5, 7, 10]. Of the evaluations that did not consider MRgHIFU, all remaining treatments led to an improvement in the quality of life of women. UAE was found to dominate (be less costly and provide better outcomes), than hysterectomy[3, 6, 8] over a short time horizon. However, over a longer-term time horizon, this was no longer the case. It was not cost-effective when compared with hysterectomy [6, 8]. Hysterectomy was favoured compared to myomectomy as well [9].

Given the lack of conclusive evidence comparing UAE and myomectomy, the FEMME trial was conducted to establish the clinical effectiveness of these procedures in women who had symptomatic uterine fibroids and did not want to undergo a hysterectomy. This

study aims to determine the cost-effectiveness of UAE and myomectomy by performing an economic evaluation alongside the FEMME trial.

Methods

Overview of the Study Design

The FEMME trial protocol and two-year clinical results have been published elsewhere [11, 12]. Briefly, FEMME was a multicentre, randomised trial where 254 women were randomised to UAE or myomectomy. Women were eligible for the trial if they had symptomatic uterine fibroids amenable to myomectomy or UAE and excluded if they had significant adenomyosis, any malignancy, pelvic inflammatory disease or had had a previous open myomectomy or UAE. A substantial number of women were not recruited into the trial due to their preference for a particular treatment option. The primary outcome was fibroid-related quality of life measured by the score on the health-related quality-of-life (HR-QoL) domain of the Uterine Fibroid Symptom and Quality of Life (UFS-QOL) questionnaire. All patient-reported and clinical outcomes were compared between the two groups, under an intention-to-treat (ITT) principle, at two and four years. Two years was considered to be long enough to evaluate the sustained benefit of the intervention on the patient but not so short that this was confounded with recovery from surgery. Four years was chosen to see if the effect, if any, was maintained over a longer term. The FEMME trial showed that both treatments led to an improvement in HR-QoL scores. Women in myomectomy group reported higher scores than those in the UAE group. The hospital stay was shorter in the UAE group despite the need of re-interventions being higher. Complication rates from all initial procedures were similar.

Individual patient data from the FEMME trial were used for the economic evaluation. The perspective of the UK NHS over the time horizons of two years and four years was taken. The time horizon is in par with the clinical analysis.[11] Effectiveness of the procedures was defined as health-related quality of life measured by the EQ-5D-3L. Cost-effectiveness was expressed as incremental cost per QALY, where appropriate. All costs were adjusted to the price year 2018/2019. A discount rate of 3.5% was applied to both costs and outcomes, as recommended by the NICE.[13] As cost and outcomes that are predicted to occur in the future are valued less than present costs, discount rate adjusts

for difference in timing of costs compared to outcomes. Following an ITT principle, missing data were imputed using multiple imputation by chained equation (MICE) for the base case analysis and sensitivity analysis included a complete case analysis. Impact of varying unit cost of procedures on the mean total cost were also tested in the sensitivity analysis. Best practice guidance was followed for conducting and reporting the cost-effectiveness analysis [13, 14].

Resource Use, Costs and Health Outcomes

Data on resource use and health related quality of life were collected during the treatment and follow-up periods of the trial at baseline, six months, one year, two years and four years (Figure 1). Resource use items were categorised into two groups: treatment-related and post-treatment resource use items, depending on the timing of the treatment. Treatment-related resource use items were recorded from the time of pre-procedure fibroid assessment to the time participants were discharged after initial treatment. Post-treatment resource use items were recorded during the period from post-discharge from initial treatment to the follow-up time points.

For treatment-related resource use, unit costs were assigned to the procedures according to their Healthcare Resource Group (HRG). All initial admissions were assumed to be as elective inpatients and all repeat procedures were assumed to incur the same cost as the initial intervention. Length of stay (LOS) was determined as the difference between admission date and discharge date, including these days. Additional per diem cost was assigned to estimate costs associated with these excess bed days if the LOS exceeded the 'trim point'(i.e. the expected LOS for each HRG) [15]. HRG episode cost was assumed to include any medications recorded during the procedure or during the time in ward. Unit costs from the British National Formulary (BNF) was applied separately to any additional medications prescribed on discharge[16].

For post-treatment related resource use, average costs of non-elective short stay (if two days or fewer) and long stay (if more than two days) were assigned to all readmissions until first follow up. Women who were not readmitted to hospital but had complications, infections or medications during the follow up period were assumed to attend outpatient

clinics. Inpatient admissions and outpatient clinic visits data recorded by hospital staff and data completed by the participants during the same period (first follow up at six months) were cross-checked to prevent double counting of resource use. All women who received reinterventions for fibroid removal during the follow up period were assumed to be performed as elective inpatients. Complications during treatment period or post-treatment period were assumed to be captured by the number of hospital admissions and associated excess bed days that were recorded alongside the complications, in order to avoid double counting.

Unit costs were valued using the NHS Reference Costs[17], Personal Social Services Resource Unit (PSSRU)[18] and BNF[16]. All costs were expressed in UK pounds sterling (£) for the price year 2018/19 using the NHS Cost Inflation Index (NHSCII). Total costs per patient were calculated by assigning unit costs to within-trial resource use for each patient. Further information on resource use items, unit costs and their sources are presented as supporting information (Table S1).

Patient-reported health related quality of life was measured using the EQ-5D-3L at various time points (baseline, six months, one year, two years and four years). The responses was used to calculate health utilities using a standard UK value set[19]. The utility values were then used to calculate QALYs for each participants using the area under the curve (AUC) method which considers linearity in utilities obtained at different time points [20]. Subsequently, QALYs over two years and over four years were estimated.

Missing Data

The following resource use assumptions were made for analysis:

- Medication: (i) median duration of treatment was assumed where data on treatment duration were missing; (ii) standard BNF dose were assumed where data on dosages were missing.
- Women who received initial fibroid assessment scans but did not undergo any procedure, yet remained on the trial and contributed cost or utility follow-up data (nine participants in the UAE group and four in the myomectomy group): (i) we did not make

assumptions on additional resource use for women who had no other resource use data throughout the study period (six in total from both groups); on women who had no other resource use data except from those during the follow-up (three from UAE group); and, on women who had additional fibroid imaging but no fibroid removal re-intervention during the follow-up (two from myomectomy group); (ii) we made the assumption that all women received fibroid imaging before re-intervention (hysterectomy and myomectomy) during the follow-up for those who had no resource use related to imaging (two from UAE group).

Baseline variables and observed outcomes associated with the probability of missingness was investigated using binomial logistic regression[21]. Missing data were assumed to be missing at random (MAR) and imputed using MICE[22]. It was performed on participants who withdrew, were left to follow up, had missing resource use at the main time points or any missing health utilities. Ten imputation datasets were generated with predictive mean matching. The total cost was imputed at sub-aggregate level of treatment and non-treatment costs and QALYs were imputed at aggregate-level of total QALYs.

Data Analysis

Our base-case analysis follows the ITT principle and was performed post multiple imputation. Cost and QALY data were analysed using Generalised linear models (GLMs). It is appropriate as it acknowledges the non-normal distribution of cost and outcomes data and allows specification of a distributional family and link function determined using the modified Park's test and other tests. [23] . Cost estimation adopted a gamma family and log link, adjusted for women's desire to be pregnant at the time of randomisation, the longest dimension of the largest fibroid and number of fibroids (randomisation minimisation variables used to balance the number of women allocated to each group). Similarly, QALYs estimation adopted a gaussian family and identity link, adjusting for minimisation variables as well as any potential effect modifiers of QALYs (baseline utilities and BMI). Marginal mean costs and QALYs were then predicted using the GLMs. The total cost and QALY differences between two groups were based on the marginal prediction.

Incremental cost effectiveness ration (ICER; ΔC/ ΔQ) was estimated by dividing the difference in mean total costs (incremental cost, denoted as $\Delta C = C_{UAE} - C_{Myomectomy}$) by the difference in mean total QALYs (incremental QALY, denoted as $\Delta Q = Q_{UAE} - Q_{Myomectomy}$). Cost-effectiveness was expressed as incremental cost per QALY. An intervention is considered to be cost-effective if below the willingness-to-pay threshold (£20,000 in the UK) [13]. However, ICERs can be difficult to interpret, especially in the case of dominance (e.g., intervention being less costly and more effective, and vice-versa) where it is negative. The NMB, a measure of the health benefit expressed in monetary terms obtained using the estimated ICER and a pre-defined cost-effectiveness threshold (λ), allows more intuitive interpretation of the result [23]. It was calculated using the formula, $NMB = (\Delta Q^* \lambda) - \Delta C$, where λ= willingness-to-pay threshold (£20,000 in the UK). An intervention is cost-effective if the NMB is positive, whereas a negative NMB implies that an intervention should be rejected, as its value is less than the additional cost of the benefit.

A 1000-iteration bootstrap was undertaken to quantify for uncertainty around the incremental costs and QALYs and the resulting ICER. Results were presented using a cost-effectiveness plane. Cost-effectiveness acceptability curves (CEACs) were used to present uncertainty over a range of willingness to pay thresholds. All analysis was conducted using Stata version 16.0 (College Station, TX, US).

Sensitivity Analyses

We considered the impact of two scenarios on our results: (i.) complete case analysis, which assumes that data are missing completely at random (MCAR), and (ii.) varying the unit costs of procedures that took place during the initial intervention and re-interventions for fibroid removal in the study timeline. The unit cost for procedures were obtained from the English NHS reference costs which is based on HRG. HRG is a case-mix of clinically similar treatments which utilise a common set of health care resources[15].Thus, HRG tariffs are a reflection of NHS average costs. It may under-estimate or over-estimate our procedure costs and may not capture the differences in NHS practice across different FEMME sites. Therefore, a 20% increment and decrement were applied to unit cost of procedures to account for these differences.

Results

A total of 254 eligible women were randomised to UAE (n=127) and myomectomy (n=127) groups. Baseline characteristics of the two groups were similar (Table 1).

Treatment related (Table S2) resource use show that not all women received the procedure of their randomised group. In the UAE group, 14 received myomectomy and one received endometrial ablation (14 did not receive treatment or withdrew from the study). In the myomectomy group, 6 received UAE and 8 received hysterectomy (8 did not receive treatment or withdrew from the study). The majority of women underwent pre-procedure imaging using MRI (71% UAE and 79% myomectomy). UAE was associated with a median LOS of 2 days (IQR 2-3) compared to 4 days (IQR 3-5 days) with myomectomy. Almost all women were prescribed analgesics on discharge (91% in the UAE group and 97% in the myomectomy group). Post-treatment (Table S3) related resource use show women who underwent UAE were frequently readmitted to the hospital through-out the study period. Outpatient appointments and medications prescribed were similar between groups. More women in the UAE group (n=18) received re-interventions compared to myomectomy group (n=8) within the first two years. At the end of 4 years, 22 from the UAE group had re-intervention compared to 13 in the myomectomy group.

Women experienced improvements in their health domains over the follow-up period (Table S4). In particular, the improvement with the pain/discomfort and anxiety/depression domains was greater in myomectomy group than that observed with the UAE group.

There were low proportion of missing resource use cases at both years (4% and 8%). The EQ-5D-3L were missing for 32% and 45% of participants in two years and four years follow up, respectively.

At both years, total costs were higher in women who desired pregnancy at baseline and had longer fibroid dimension of the largest fibroid, whereas it was lower in those with

greater number of fibroids. Total QALYs were lower in women who desired pregnancy at baseline while those with longer fibroid dimension of the largest fibroid and greater number of fibroids had higher QALYs. QALYs decreased with increasing BMI. However, these results were not statistically significant.

The mean treatment cost for the UAE group was lower than that of the myomectomy group (£3,064 versus £3,862); Table 2). However, UAE was associated with a higher post-treatment cost over two years follow up compared to myomectomy group (£4,918 versus £3,431). A similar trend was observed with post-treatment cost over four years follow up (£5,288 versus £4,151). The total mean cost incurred over two years in UAE group was £7,958 compared with £7,314 in the myomectomy group. The four years total mean cost was £8,362 for UAE group and £8,010 for myomectomy group. Over two years, QALYS in the UAE group was 0.74 (95% CI 0.70 ; 0.78) compared with 0.83 (95% CI 0.79; 0.87) in the myomectomy group (Table 2). Similarly, at four years, the QALYs in the UAE group was 0.73 (95% CI; 0.69 to 0.76) QALYs and 0.82 (95% CI; 0.79 to 0.87) in the myomectomy group.

UAE was dominated by myomectomy. UAE was associated with higher costs (£645 difference; 95% CI -1,381; 2,580)and lower QALYs (-0.09 difference; 95% CI -0.11; -0.04), compared with myomectomy over a time-horizon of two years. Similarly, at four years UAE was associated with higher costs (£352 difference; 95%CI -1,825; 2,528), and lower QALYs (-0.09 difference; 95%CI -0.12; -0.05).

The cost-effectiveness plane (Figure 2) shows the uncertainty associated with the incremental mean differences of costs and QALYs in form of bootstrapped point estimates. There is little uncertainty that UAE is associated with lower QALYs when compared with myomectomy. There is some uncertainty around the magnitude of difference in costs between the two treatments. The cost-effectiveness acceptability curves (CEACs) confirm that myomectomy had higher probability (98% at two years; 96% at four years) of being cost-effective compared with UAE at willingness to pay thresholds of £20,000 and higher (Figure 2).

The results were mirrored in the complete case analysis (Table S5) performed as a scenario in sensitivity analyses. UAE arm had lower treatment cost compared to myomectomy arm (£3,073 vs 3,870) but higher non-treatment costs over two years (4,663 vs 3,384) and four years (5,057 vs. 4,127), respectively. UAE was associated with higher costs (£456 difference; 95% CI -1,823; 3,164) and lower QALYs (-0.06 difference; 95% CI (-0.11; -0.02) over a time horizon of two years. Similar results were observed over a time horizon of four years. The differences were not statistically significant. Difference in QALY was -0.06 for both years. Additionally, the sensitivity analysis varying costs of procedures provided results consistent to the base-case (Table S6). UAE was associated with higher costs and lower QALYs. Though ICERs are not reported in this case, we observed a change in its magnitude depending on 20% increment and decrement applied on the unit costs of procedures (Figure S6).

Discussion

Main findings

UAE was associated with higher costs and lower QALYs when compared with myomectomy over the two- and four-years time horizons. The difference in costs were small (£645 and £352 over the two- and four-years time horizons, respectively). The difference in QALYs over both time horizons was 0.09. The primary driver in costs were GP visits, outpatient appointments and inpatient admissions during the follow ups associated with re-interventions for fibroid removal. As the QALY combines the impact of treatment on mortality and morbidity into a single index, the difference of 0.09 can be interpreted as a gain of 33 days of perfect health in women who underwent myomectomy. The greater improvement in pain/discomfort and anxiety/depression domains of the EQ-5D-3L observed in myomectomy group was the primary driver of QALY difference. Myomectomy had 98% and 96% probability of being cost-effective at two and four years, respectively, when compared with UAE at willingness to pay thresholds of £20,000.

Strengths and limitations

This economic evaluation is based on the largest, multicenter RCT comparing UAE with myomectomy, which adhered to the good practice guidelines set out by NICE[13]. However, the cost-utility approach does not consider patient preference. The potential

trade-off between the additional QALYs associated with myomectomy, and the potential benefits of avoiding a surgical procedure associated with UAE is not known.

Interpretation

Our results are in line with those of existing studies which compared UAE and myomectomy. These studies reported that UAE is dominated by myomectomy[4, 6, 9] even when productivity costs were included [4]. Moreover, UAE is only dominated by myomectomy over the longer term [5, 8]. In the short term, UAE had lower costs due to shorter procedural time, shorter length of hospital stays and faster resumption of usual activities[24, 25]. Our two-year result confirms that UAE had a lower treatment cost compared to myomectomy. The LOS is the key driver of treatment cost, which were captured only during the period from pre-procedure fibroid assessment stage to discharge. A longer LOS was observed in myomectomy group compared to UAE group (median 4 days compared with 2 days). Though definition of long term differs across the studies, the increase in resource use and costs, albeit a little difference in QALYs, were seen in UAE group after the first year of treatment [5]. The reason behind this continuous accumulation of cost in the long term related to UAE was an increased rate of re-intervention in UAE group after the first year [8]. Indeed, our results confirmed that women in the UAE group had higher re-intervention over the follow-up periods. In our study, the majority of the post-treatment costs were accrued within two years, only a small amount of additional post-treatment costs incurred between the two and four years. Though we did not calculate the cost of complications separately, it was captured within our treatment and post-treatment costs. Thus, we can be confident that women in the UAE group incurred greater post-treatment costs compared to myomectomy due to greater utilisation of healthcare resources and associated re-interventions for fibroid removal. This justifies the higher post-treatment costs ,which is based on costs accumulated after discharge till the end of follow up, in the UAE group of our study.

Conversely, some studies obtained different results in terms of cost-effectiveness[2, 7].Myomectomy was dominated by UAE instead. Findings reported mean costs and mean QALYs of UAE compared to myomectomy to be ($28,892 vs $35,057; 17.39 vs 17.31) [7]

and ($11,320.76 vs $13,399.09; 6.282 vs 6.229) [2]. Here, the difference in QALYs were marginal.

It should be noted that any comparison of the study with existing studies must be interpreted with caution as they differ in terms of settings, population, perspectives and their method of analysis including assumptions related to treatments, resource use, costs and outcomes. For instance, the dissimilarity in findings between the above-mentioned studies and our study can be due to the former being conducted in premenopausal women in the US and Canada from a societal and provider perspective, respectively. These studies also used a variety of clinical literature to support their assumptions. For example, the length of stay was obtained from a retrospective review conducted on women of reproductive age [2]. Due to this, a caveat that the results were extremely sensitive to several parameters and assumptions were provided.

There are more reasons that support the caution we have provided in interpretation and comparison of results. For example, myomectomy was frequently analysed with hysterectomy or only considered as a treatment option when less invasive methods failed to improve symptoms. No distinction was made between multiple treatment comparators in some cases. For example, a study grouped UAE, myomectomy and hysterectomy as 'current treatment' for comparison against MRgFU and assumed that 25%, 25% and 50% of women were allocated to the grouped treatments, respectively [10]. Moreover, treatment costs were assumed to be the same for all 'current treatment' and health-related quality of life following successful treatment was assumed to be the same for MRgFU and 'current treatment'. Previous studies focused on applying disutilities rather than cost to post-treatment complications as they assumed that patients would not experience significantly costly complications after discharge[26]. Majority of other economic evaluations comprised of model-based analysis deriving evidence from the literature, especially non-randomised studies, which sometimes present inconsistent and conflicting findings on the effectiveness and safety of the treatments.

Our cost-utility assessment establishes that UAE is dominated by myomectomy and therefore, would not be deemed a cost-effective alternative to displace myomectomy. The

costs differences were small, and both treatments led to an improvement in the quality of life. A greater improvement in the quality of life was associated with myomectomy. However, the cost-utility analysis framework restricts us from taking any into account any potential preference for a less invasive procedure. Some women may place added value on non-surgical procedure compared to a surgical procedure for various personal reasons.

Our result does not influence the choice between UAE and MRgHIFU, another non-surgical procedure, as the latter is only used in the UK with special arrangements or research purposes. Once it becomes more mainstream, appropriate economic evaluation will be able to compare the two treatments. Therefore, women seeking to undergo treatments other than hysterectomy should have the option to choose between UAE and myomectomy, given that they are fully informed.

Conclusion

In conclusion, UAE was dominated by myomectomy and would not be considered a cost-effective alternative to displace myomectomy from the perspective of the UK NHS. However, the cost-utility approach that has been adopted here does not consider any potential preference for less invasive procedure for the treatment of symptomatic uterine fibroids. Hence, given the small difference in costs between the two procedures, fully informed patient preference should be taken into account and women should have the option to choose between the two procedures. Future research should focus on methods to quantify fully informed patient preferences and incorporate it into subsequent economic analyses of medical, surgical and non-surgical interventions for uterine fibroids.

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Disclosure of Interests

MAL reports receiving personal fees from Gedeon Richter outside the submitted work. All authors declare they have no relevant conflict of interest.

Contribution to Authorship

All authors contributed to, read, and approved the final version for publication. DR, OW conceived the economic evaluation. OW led health economics. DR carried out the formal health economics analysis supervised by OW. DR and OW drafted this manuscript. LM, VC, WM conducted the statistical analysis in the trial. JD, IM, AMB, MAL, JM, OW, KM conceived the FEMME trial and obtained funding. KM was the chief investigator.

Details of Ethics Approval

The FEMME trial had a favourable ethical opinion from the National Research Ethics Service (NRES) Committee West Midlands - Coventry and Warwickshire, 15th June 2011, REC reference11/WM/0149.

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Figure Legends

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Tables

Table 1. Baseline characteristics

	Uterine Artery Embolization (n=127)	Myomectomy (n=127)
Demographics		
Age, mean (SD), n	40.2 (6.55)	42.7 (6.4)

Ethnic Group		
White (British/Other)	59 (46%)	57 (45%)
Black (Caribbean/African/other)	48 (38%)	54 (43%)
South Asian (Indian/Pakistani/Bangladeshi)	10 (8%)	5 (4%)
Mixed (White/Black/Asian/other)	6 (5%)	8 (6%)
Other	4 (3%)	3 (2%)
BMI (kg/m^2), mean (SD)	28.2 (6.2)	28.1 (5.3)
Obstetrics history and fibroid characteristics		
Desiring pregnancy at time of randomisation	61 (48%)	61 (48%)
Longest dimension of largest fibroid, cm		
<=7	64 (50%)	64 (50%)
>7	63 (50%)	63 (50%)
Mean (SD)	7.6 (3.2)	7.7 (4.2)
Number of fibroids		
1-3	84 (66%)	84 (66%)
4-10	37 (29%)	37 (29%)
>10	6 (5%)	6 (5%)
Median [IQR]	2 (1 to 5)	2 (1 to 5)
EQ-5D-3L, mean (SD)		
Baseline	*0.62 (0.34)*	*0.63 (0.32)*
6 months	*0.77 (0.30)*	*0.85 (0.17)*
1 year	*0.77 (0.30)*	*0.85 (0.23)*
2 years	*0.80 (0.29)*	*0.88 (0.20)*
4 years	*0.79 (0.30)*	*0.90 (83)*

Table 2. Base-case analysis results

Predicted mean cost for total cost components				
	UAE		Myomectomy	
	Cost (£) (SD)	95% CI	Cost (£) (SD)	95% CI

Treatment cost[a]	3,064 (80)	2,906	3,222	3,862 (99)	3,667	4,056
Post-treatment cost over 2 years[a]	4,918 (939)	3,076	6,759	3,431 (633)	2,191	4,671
Post-treatment cost over 4years[a]	5,288 (940)	3,445	7,131	4,151 (717)	2,745	5,557
2 years						
	Mean total cost (£) (95% CI)	Mean total QALY (95% CI)	Incremental cost (ΔC) (95% CI)	Incremental QALYs (ΔQ) (95% CI)	ICER[b] (ΔC/ ΔQ) (95% CI)	NMB[b] (ΔQ* λ) – ΔC, λ= £20,000
UAE	7,958 (6,304; 9,612)	0.74 (0.70; 0.78)	645 (-1,381; 2,580)	- 0.09 (-0.11; -0.04)	-7,167 (-39,597;19,764)	2,445 (-4,319; 15)
Myomectomy	7,314 (5,854; 8,773)	0.83 (0.79; 0.87)				
4 years						
UAE	8,362 (6640; 10083)	0.73 (0.69; 0.76)	352 (-1,825; 2,528)	-0.09 (-0.12; -0.05)	-3,911 (-31,357;23,566)	-2,152 (-4350; 221)
Myomectomy	8,010 (6,422; 9,598)	0.82 (0.79; 0.87)				

Footnote

SD: standard deviation; CI: Confidence interval; QALY: Quality-adjusted life year; ICER: Incremental cost-effectiveness ratios; NMB: Net monetary benefit

[a] Cost component for total cost.

[b] ICERs and NMB are not normally calculated when an intervention is dominated by its comparator. However, we present it for completeness.

*All monetary units have been rounded to the nearest pound.

Figure 1. Resource use and health related quality of life data collection schedule

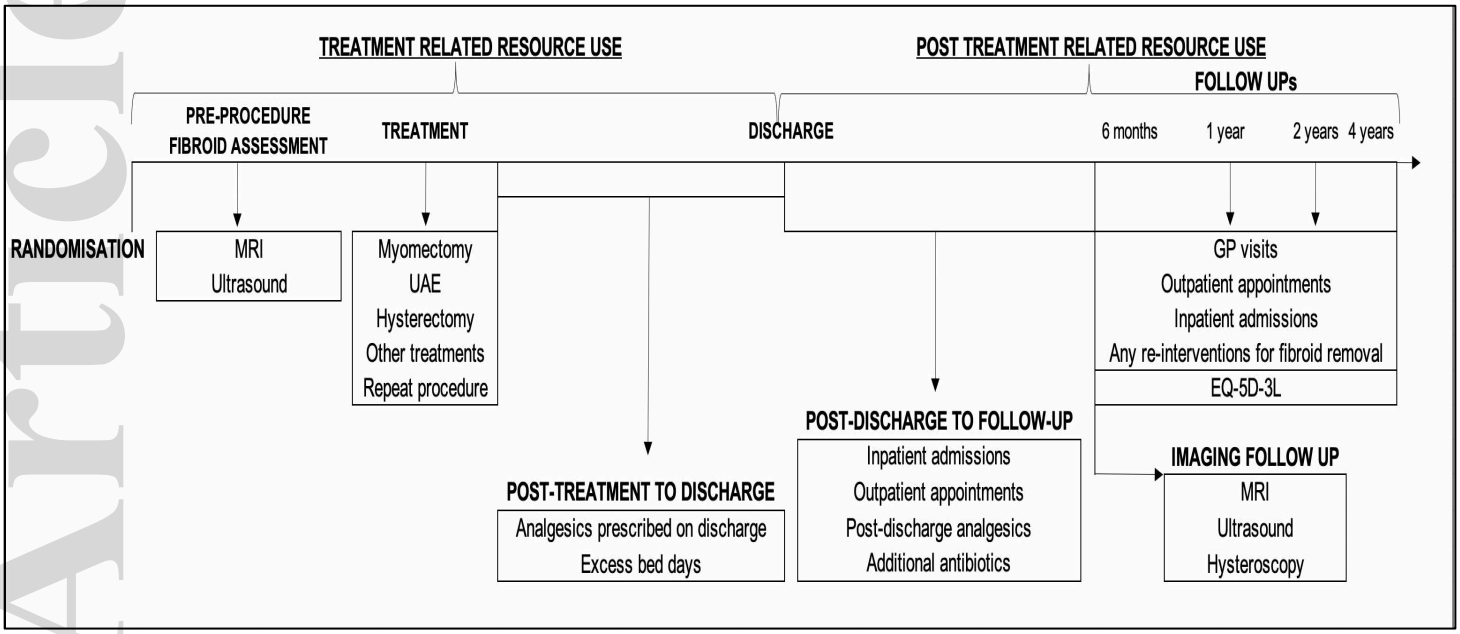

Figure 2. Cost-effectiveness planes and cost-effectiveness acceptability curves (CEACs) for 2 years and 4 years