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MRI-Guided Focused Ultrasound Surgery for Uterine Fibroid Treatment: A Cost-Effectiveness Analysis

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Abstract

Objective—To evaluate the cost-effectiveness of a treatment strategy for symptomatic uterine fibroids that employs Magnetic Resonance guided Focused Ultrasound (MRgFUS) as a first-line therapy relative to uterine artery embolization (UAE) or abdominal hysterectomy (HYST).

Materials and Methods—We developed a decision-analytic model to compare the cost-effectiveness of three treatment strategies: MRgFUS, UAE and HYST. Short and long-term utilities specific to each treatment were incorporated, allowing us to account for differences in quality of life across the strategies considered. Lifetime costs and quality-adjusted life-years (QALYs) were calculated for each strategy. An incremental cost-effectiveness analysis was performed, using a societal willingness-to-pay (WTP) threshold of \$50,000 per QALY to designate a strategy as cost-effective. Sensitivity analysis was performed on all key model parameters.

Results—In the base-case analysis, in which treatment for symptomatic fibroids started at age 40, UAE was the most effective and expensive strategy (22.81 QALYs, \$22,164), followed by MRgFUS (22.80 QALYs, \$19,796) and HYST (22.60 QALYs, \$13,291). MRgFUS was cost-effective relative to HYST, with an associated incremental cost-effectiveness ratio (ICER) of \$33,110/QALY. MRgFUS was also cost-effective relative to UAE – the ICER of UAE relative to MRgFUS (\$270,057) far exceeded the WTP threshold of \$50,000/QALY. In sensitivity analysis, results were robust to changes in most parameters, but were sensitive to changes in probabilities of recurrence and symptom relief following certain procedures, and quality of life associated with symptomatic fibroids.

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Conclusions—MRgFUS is cost-effective relative to both UAE and hysterectomy for the treatment of women with symptomatic fibroids.

INTRODUCTION

Uterine fibroids are the most common benign tumors in women of reproductive age, affecting 70–80% of women at some point in their lives, and leading to a significant reduction in their quality of life as a result of pelvic and abdominal pain, heavy menstrual bleeding, and fertility issues [1]. Most women with fibroids undergo pharmacological therapy prior to any other intervention. While traditional surgical treatments such as abdominal hysterectomy (HYST) and myomectomy (MYO) have been shown to improve symptoms for women who do not benefit from medication, they are also a significant source of economic burden for affected women and society [2].

The treatment of uterine fibroids accounts for 30–70% of hysterectomies carried out in the United States and annual healthcare costs for hysterectomy are estimated to be greater than \$2 billion [3]. Added onto the monetary cost of this procedure are the physical burden of an invasive surgery and the psychological burden of uterine removal for a benign disease, especially for younger women who may have wanted to preserve their fertility and femininity [4]. Despite the emergence in the last decade of non-surgical and less invasive options for fibroids including Uterine Artery Embolization (UAE), HYST and MYO remain the most common treatments for fibroids [5].

In 2004, Magnetic Resonance guided Focused Ultrasound Surgery (MRgFUS), a novel minimally invasive, and uterus-sparing option received clearance by the United States Food and Drug Administration (FDA) for treatment of uterine fibroids [6]. Focused ultrasound surgery is an in-situ thermal ablation method that uses highly focused sound waves to heat targeted tissues to a critical level ($>55^{\circ}\text{C}$) that results in cell death, leading to thermo-coagulation tissue necrosis. The addition of Magnetic Resonance Imaging (MRI) guidance, however, allows for excellent target definition, and very importantly, it can provide real-time “thermometry” with thermal mapping sequences that allow for confirmation of thermal dose delivery to the targeted tissue, and also confirm lack of thermal build up in non-targeted tissue. MRgFUS involves neither an arterial puncture as would UAE, nor any abdominal incisions as would HYST. Previous studies have concluded that MRgFUS is safe and effective in shrinking fibroids and producing symptom relief [7–9]. Unlike surgical treatments, it is a short outpatient procedure and there are few adverse events or minor complications associated with MRgFUS [10].

Prior cost-effectiveness analyses have compared MRgFUS with conventional treatments for fibroids [11–12]. However, the quality of life values assigned to women with symptomatic fibroids have often been derived from studies of women with menorrhagia [13], and no study has taken into account short and long-term decrements in quality of life associated with specific treatment modalities. Recently, we studied the health-related quality of life as reported by women who underwent different treatment modalities for the treatment of fibroids [14]. In this analysis, we used quality-of-life measurements derived from patient responses, to evaluate the cost-effectiveness of treatment strategies that employ MRgFUS as

a first-line treatment (M1) against strategies that use UAE (U1) or HYST as first-line treatment (H1). The goal of our cost-effectiveness analysis was to determine the optimal treatment strategy for uterine fibroids based on contemporary evidence.

MATERIALS AND METHODS

Institutional review board approval was not necessary, as this study was based solely on literature estimates and on publically available, de-identified data.

Overview of Treatment Strategies

Previous studies report that many women with symptomatic fibroids do not achieve adequate results or durability with a single treatment modality and will undergo repeat treatments [15–17], except when treated with hysterectomy. Considering this, we modeled three treatment strategies M1, U1, and H1, in which the first line treatment was abdominal MRgFUS, UAE, and HYST, respectively. We labeled the strategies as M1, U1, and H1 to emphasize that MRgFUS, UAE, and HYST are 1st line treatments; however, M1 and U1 may involve 2nd and 3rd line treatments that are different from 1st line treatment. Figure 1 summarizes each strategy.

The size of the uterus, number, size, type and location of fibroids often determines the type of fibroid treatment. Therefore, women who are considered for MRgFUS or UAE as 1st line treatment undergo imaging tests for eligibility assessment. If they are ineligible due to fibroid size or location, referral is made for the next least invasive treatment. The degree of invasiveness to the patient among treatment modalities is as follows: MRgFUS < UAE < MYO < HYST. In case of no symptom relief after treatment, re-treatment is with the next least invasive strategy, as shown in Figure 1. In case of fibroid recurrence, women are retreated by their initial (1st line) treatment modality. We limit the maximum treatments to three, with HYST as 3rd line treatment. In all three strategies, women are treated either until their symptoms resolve or until menopause at age 51. For women with age > 51 years (average age of menopause), fibroid symptoms are assumed to resolve of their own accord. Note that MYO was included as a second-line treatment only in strategy U1.

Model Overview

We used a microsimulation model with a 6-month cycle length to calculate quality-adjusted life-years (QALYs) and lifetime costs. All women enter the model at age of 40 years. Following treatment, women traverse through health states associated with each strategy. The possible health states include: 1) survival or death following the procedure, 2) presence or absence of post-procedure symptom relief, 3) recurrence or no recurrence of fibroids, and 4) death from natural causes. Those who reach the no-fibroid-recurrence state remain at risk for fibroid recurrence until menopause. Each health state had a specific cost and utility assigned. The model yielded strategy-specific lifetime costs and quality-adjusted life expectancy.

In keeping with standard methods for an incremental cost-effectiveness analysis [18], to calculate ICERs, strategies were first ranked based on increasing QALYs. If a strategy was more expensive than the next most effective strategy, it was considered dominated. ICERs

for all remaining strategies were then calculated. Because there is no single willingness-to-pay (WTP) threshold for medical procedures in the United States, we used a widely accepted \$50,000/QALY threshold for designation of a strategy as cost-effective [19]. Strategies were determined to be cost-effective if they had an associated ICER that was less than the designated WTP threshold. Costs and QALYs were discounted at a 3% annual rate. For each strategy, we simulated a cohort of 500,000 women in one simulation run. Model outcomes are averaged over 10 runs. The microsimulation model was built using TreeAge Pro 2009; TreeAge Software, Williamstown, MA.

Model Parameters

Transition Probabilities—Base case transition probabilities and ranges for sensitivity analysis were obtained through clinical trials, case-controlled studies and previous cost-effectiveness studies in MEDLINE (Table 1). When deciding which parameters to use in our base case analysis, multi-site randomized clinical trials took priority over single-site clinical trials. The latter took priority over retrospective case-controlled studies and previous cost-effectiveness analysis. We also gave higher priority to more recent studies. In the absence of existing data, model parameters were estimated by one of the radiologist co-authors (F.M.F.) and a gynecologist co-author (S.S.). All-cause mortality probabilities were based on 2007 U.S. life tables [20].

Quality of Life Measures-Utility Values—A “utility value” is a measure of quality of life, and provides a person’s relative preferences for different health states compared with death or the worst possible outcome. These values range from 0 (death) to 1 (perfect health). Short and long-term utility values assigned to specific health states were obtained from our recent study that surveyed women with uterine fibroids who had undergone MRgFUS, HYST or UAE, and obtained quality of life measures based on patient responses [14].

An additional 0.015 decrement was applied to women who underwent a final hysterectomy to account for the effect of the loss of fertility (i.e. early menopause) and femininity [4, 11]. Utility values used in our model are shown in Table 1.

Costs—We included all hospital and physician costs incurred including diagnostic and follow-up imaging and lab tests, office visits, procedures and hospital stays, as well as lost-productivity costs that refer to wages lost by the patient due to missed workdays. Outpatient procedures and physician costs were based on Medicare reimbursements for American Medical Association designated Common Procedural Terminology (CPT) codes. Hospital costs of inpatient procedures were based on Medicare reimbursements corresponding to specific diagnosis-related groups (DRG). Table 1 shows the costs associated with different treatments. Detailed justifications for our cost estimates and lost productivity calculations are as follows:

Screening: All 1st-line treatment modalities require initial screening which included two office visits (CPT: 99212, 99213) an ultrasound (CPT: 76856) and pertinent laboratory tests (CPT: 85025, 81025). In addition, patients undergoing MRgFUS and UAE receive an initial screening MRI (CPT: 72196).

Procedure: Procedure costs in Table 1 of the main text include hospital, and physician costs associated with each procedure. Inpatient costs of HYST and MYO procedure costs were calculated using DRG 742. Physician costs were calculated using CPT 58150 for HYST, and 58140 for abdominal MYO. In addition, we have added the cost of anesthesia, based on age-adjusted weight tables, to the procedural cost of HYST, MYO (not included in the cost shown in Table 1). Outpatient hospital and physician costs for UAE were calculated using CPT 37210. Because MRgFUS is a fairly recent method of treatment for fibroid treatment, current billing practice for this procedure is to substitute (“crosswalk”) a combination of several other CPT codes specific for radiation. We have used the crosswalk codes (CPT: 77295, 77334, 77370, 77300, 77470) provided by the developers of the ExAblate 2000 system (Insightec, Haifa, Israel) to calculate the outpatient hospital and physician cost of MRgFUS.

Inpatient hospital stay following HYST and MYO are accounted for in the cost of the procedure, as obtained through the DRG. However, as UAE is considered an outpatient procedure, we added the cost of an extra night of hospital stay, which was confirmed as standard practice by gynecologist co-author S.S. The cost of the extra night of hospital stay was obtained from Beinfeld et al. (46) and converted to 2011 U.S. dollars by using the medical care component of the consumer price index.

Lost Productivity: To calculate lost-productivity costs, the daily wage rate for women was obtained from the U.S. Bureau of Labor Statistics, Median Weekly Earnings of Wage and Salary Workers: Annual Averages 2010, and adjusted to 2011 dollars using the 2011 semiannual average consumer price index. The number of days missed per procedure was obtained from O’Sullivan et al. (17). Lost productivity cost for each procedure was calculated by multiplying the missed work days with the daily wage rate.

Follow-Up: Based on expert opinion, follow-up for HYST, MYO and MRgFUS included one office visit (CPT: 99213) two weeks after procedure. Follow-up for UAE included three office visits total, at 2 weeks, 6 months and 12 months, as well as one MRI (CPT: 72196) 6 months after the procedure. Each office visit and MRI appointment also had an additional half day productivity loss. In the case of fibroid recurrence, women incurred the cost of an office visit (CPT: 99213) and half day productivity loss.

Complications: Major and minor complications were included if they required significant medical or surgical intervention and cost, and had greater than a 0.1% chance of occurrence in multiple studies. Complications costs included hospital, physician and lost-productivity costs associated with each procedure. Bladder, bowel and ureter injuries were included among the major complications associated with abdominal hysterectomy. Since bladder injury can be recognized intra-operatively or post-operatively, costs of these procedures were calculated separately. Intra-operative bowel injury costs included a general surgeon consult (average of 5 CPTs: 99251–99255) and intervention (CPT: 51925) in addition to the difference in hospital costs between HYST with major complications (DRG 742) and HYST without major complications (DRG 743). Based on expert opinion of the gynecologist co-author (S.S.), postoperative bladder injury costs include readmission to the hospital (DRG 674). To calculate the total cost of HYST related major complications, intro-operative and

post-operative bowel injury were weighted according to results from a large study from Finland that found 88% of bladder injury to be recognized intra-operatively (43). Cost of bowel and ureter injury were also calculated separately for intra and post operative complications and weighted accordingly in the total cost given in Table 1. Other peri-procedural major events associated with HYST included hemorrhage requiring transfusion, sepsis and pulmonary embolism. Cost of these events was assumed to be covered in the hospital cost difference between HYST with major complications (DRG 742) and HYST without major complications (DRG 743). Cost of minor complications of HYST included urinary tract and wound infections, hematomas and febrile events. These were covered in the reimbursement for HYST and did not extend beyond the hospital stay covered by Medicare. Since most major and minor complications occur within 0–30 days after procedure (43), lost productivity costs for major and minor complications of HYST were assumed to be included within the lost-productivity costs of the procedure.

We have not included any organ related injuries as a major complication of MYO based on a recent clinical trial (51) \. Instead, major complications included hemorrhage requiring transfusion, sepsis, ileus and pulmonary embolism occurring during hospital stay. Cost of these complications was calculated as the difference in hospital costs between MYO with major complications (DRG 742) and without major complications (DRG 743). Minor complications were similar to HYST and covered in the reimbursement for MYO.

Pulmonary embolism (PE) was the major complication of UAE included in our cost calculations. Based on a clinical trial which showed for uterine fibroid treatments, complications after surgical events occur during the hospital stay while medical event complications occur post-discharge, the cost of pulmonary embolism after UAE was calculated as a readmission to the hospital using CPT 78588 and DRG 078. Minor complication costs included an office visit and a procedure for dilatation and curettage (CPT 58120). PE resulted in 5 days of lost productivity while the dilatation and curettage required one day of missed work for the outpatient procedure.

For MRgFUS, we assumed no major or minor complications as these included short-term side effects that were treatable with over-the-counter medications.

Sensitivity Analysis

We performed a one-way sensitivity analysis and additional threshold analyses to examine the effect of uncertainty regarding input parameter values on model estimates of the ICERs. Table 1 shows the base-case parameter values and ranges evaluated in sensitivity analysis.

RESULTS

Base Case Analysis

The costs, effectiveness, and ICERs of M1, U1 and H1 are shown in Table 2. H1 resulted in the fewest QALYs and had the lowest total costs, followed by M1. U1 resulted in the greatest QALYs and highest cost. The ICER of M1 relative to H1 was \$33,110/QALY gained. U1 offered a minimal increase in QALYs compared to M1 but had substantially greater lifetime costs. The ICER for U1 relative to M1 was \$270,057/QALY gained, which

is above the WTP threshold. From a cost-effectiveness standpoint, M1 was therefore considered preferred relative to both H1 and U1.

We analyzed the breakdown of the costs associated with each strategy. Procedure costs made up the highest percentage of the total cost incurred for all three strategies. As shown in Figure 2, the procedural components of total costs were greatest for M1 (74%) and U1 (69%) as opposed to H1 (53%). The percentage due to lost productivity was highest for H1 (43%) as compared to M1 (14%) and U1 (16%). The component of total cost due to procedure-related complications was lowest for M1 (0.80%) as compared to U1 (1.0%) and H1 (1.6%). Follow-up costs for U1 made up 10% of the total cost, higher than all other strategies.

In addition, we tracked the procedural components of re-interventions and complications, in order to quantify the different treatment modalities involved in the three strategies. As shown in Table 3, on average, 93 and 71 out of 100 patients required re-intervention in the M1 and U1 strategies, respectively. Out of the 93 women who required re-interventions in the M1 strategy, 20 (21%) would receive surgical procedures, as compared to 23 out of 71 (33%) women who would receive surgical procedures in the U1 strategy. Since HYST is a one-time solution that has a 100% chance of symptom relief and 0% chance of fibroid recurrence, no re-intervention was required in the H1 strategy. However, with H1, on average 8 out of 100 women experienced major complications involving injury to internal organs such as the bladder, bowel and ureters, hemorrhage > 1000 mL, sepsis or pulmonary embolism; 29 out of 100 women had minor complications such as minor hemorrhage and infections. When MRgFUS is the first-line treatment (M1 strategy), risks of major and minor complications were considerably lower.

Sensitivity Analysis

As the age for starting treatment increased from 40 to 49 years, the ICER for M1 improved (Figure 3). U1 was dominated (less effective and more expensive than) by M1 at all ages above 41. When the probability of symptom relief after MRgFUS was below 74% (base case 93%), U1 became the preferred strategy (Figure 4). Table 4 summarizes additional results from the one-way sensitivity analysis. When the probability of fibroid recurrence after UAE was above 4.7% (base case 3.2%), the ICER for M1 exceeded the WTP threshold of \$50,000/QALY gained threshold, making H1 the preferred strategy. Our results were sensitive to the long-term utility value associated with symptomatic fibroids. At the lowest utility value (0.528), H1 dominated M1. However, the ICER for U1 relative to H1 was \$253,036/QALY gained, above the WTP threshold. Thus, the preferred strategy changed from M1 to H1. Results were also sensitive to changes in the procedural cost of MRgFUS but not the cost of UAE, HYST and MYO. Above 200% of base case cost for MRgFUS, M1 was dominated by U1, and U1 became cost-effective (ICER compared to H1 = \$43,235/QALY gained).

M1 was consistently the preferred strategy within the parameter ranges examined in the sensitivity analysis for short-term utilities of specific treatments, long-term utilities associated with symptom relief, remaining costs, probabilities of major and minor complications and procedure related deaths.

Discussion

We found that MRgFUS, as the first line treatment for symptomatic fibroids, is preferred over both UAE and HYST from a cost-effectiveness standpoint. MRgFUS has an associated ICER of \$33,110/QALY relative to HYST, which is below the WTP threshold of \$50,000/QALY used in our analysis. With an associated ICER of \$270,057/QALY, UAE was above this WTP threshold and therefore not considered a cost-effective strategy. Notably, the cost-effectiveness of MRgFUS improves as the starting age for fibroid symptoms approaches 50.

In the sensitivity analysis, our findings remained stable as long as the probabilities of symptom relief following MRgFUS were above 74%. Below this threshold, U1 was preferred over M1. The lowest reported probability of symptom relief post-MRgFUS (71%) was from a 2006 study by Stewart et al. that treated patients under restricted guidelines [21]. A 2007 study with modified, less restrictive selection criteria for MRgFUS treatment reported higher probabilities of symptom relief following MRgFUS [9]. Our results were also sensitive to some cost estimates assigned to MRgFUS. Above 200% of the base case procedural cost of MRgFUS, U1 dominated M1.

Since 2008, two studies have investigated the cost-effectiveness of MRgFUS. In a 2009 analysis, O'Sullivan et al. concluded that using MRgFUS and UAE as first-line treatment (the same strategies we examined) were similar in term of cost-effectiveness with UAE having slightly higher total cost and QALYs [11]. While their incremental costs and ranking of QALY gained were similar to ours, they detected a greater gain in effectiveness with U1 relative to M1. One of the reasons for this may be that O'Sullivan et al did not include short-term disutilities related to treatments, and as a result, obtained greater gain in effectiveness for U1. In addition, the long-term utility associated with symptomatic fibroids in our base case scenario (0.82) is higher than the value of 0.67 used by O'Sullivan et al. When we decreased our long term value to 0.67 in the sensitivity analysis, U1 became cost-effective relative to M1 with an ICER of \$61,872/QALY gained, yielding the same conclusion as O'Sullivan et al. Thus, the difference in the conclusions between our study and the study by O'Sullivan et al may be largely driven by the difference in the long-term utilities associated with symptomatic fibroids. As MRgFUS is a fairly new technology that is rapidly changing, the difference between O'Sullivan et al's long-term utility value of 0.67 and our more recent value of 0.82 may reflect the improvement in patient experience with MRgFUS since its first use for clinical therapy. In addition, while the long-term utility values used in O'Sullivan et al is based on unpublished data from Insightec, the manufacturers of the ExAblate 2000® system used to perform MRgFUS, our use of utilities derived from comprehensive surveys strengthens our results. Another cost-effectiveness analysis (CEA) compared MRgFUS with the current treatment practice in the UK and concluded that including MRgFUS within the current UK practice is both cost-saving and more effective [12]. Despite the difference in health care systems, our results are similar in that including MRgFUS in a treatment plan can be cost-effective for uterine fibroid treatment.

From a patient's point of view, tradeoffs are involved in each of the first-line treatment strategies. While a treatment plan in which HYST is the first-line treatment is associated with the lowest lifetime cost and is the only strategy that requires no further intervention

after first-line treatment, the invasive nature of a surgical procedure, as well as the definite loss of fertility are points of consideration. Although patients who start their treatment plan with MRgFUS or UAE are likely to require a second treatment, the breakdown of procedural components in the re-intervention methods revealed that 67–79% of these re-interventions would be non-surgical, such as another round of MRgFUS or UAE, respectively. In addition, our results suggest that patients choosing HYST as first line treatment have substantially higher probabilities of major and minor complications. Only 14 and 16% of the total costs of M1 and U1 are due to lost productivity as compared to over half of the cost involved in H1. This result is largely due to long recovery times and time taken off from work related to HYST procedure.

Furthermore, MRgFUS is a promising option for women considering future pregnancy. There have been several reports of successful term pregnancies among women who underwent MRgFUS [22–23]. While there have been multiple reports of pregnancies post-MRgFUS, the largest series (which was reported to the FDA as part of post-approval medical device monitoring) found a higher rate of successful term delivery, a lower rate of cesarean section, and a lower rate of low-birth weight and stillbirths than that previously reported for pregnancy following UAE [24]. While the starting age of our model is 40, the rate of pregnancy in the United States after the age of 40 has been increasing, according to the latest report from Centers for Disease Prevention. [25] Therefore, such tradeoffs are often important points of consideration for pre-menopausal women.

The main limitation of our study is the small population size of MRgFUS clinical trials, as opposed to HYST and MYO studies that have data on thousands of women. In order to address this limitation, we used data from more recent and multi-center clinical trials in our base case scenario, and tested the effect of the variability in the literature in our sensitivity analysis. Another limitation is lack of inclusion of laparoscopic hysterectomy data. However, we did include comparison of a range of non-invasive (MRgFUS) to semi-invasive (UAE) to invasive, definitive (HYST) treatment strategies.

In conclusion, our findings suggest that for women with symptomatic fibroids, MRgFUS is cost-effective as a first-line therapy relative to both hysterectomy and uterine artery embolization (UAE). MRgFUS is a new procedure that is changing more rapidly than the alternative therapies. Thus, our estimates regarding number of repeat procedures and quality-of-life values after MRgFUS may be conservative, raising the possibility that MRgFUS may become even more cost-effective in the future. To our knowledge, this is the first CEA applying specific short-term quality of life decreases (disutilities) related to MRgFUS, UAE and HYST. This approach strengthens our results as we take into account the difference in the quality of life and duration of recovery following each treatment procedure.

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Figure 1. Overview of Treatment Strategies

Strategies for symptomatic fibroids are labeled as M1, U1 and H1 to indicate that MRgFUS, UAE and HYST are 1st line treatments in each strategy, respectively. Secondary to lack of symptom relief, women are retreated with the next least invasive strategy. If fibroids recur, the previous treatment modality is repeated. In all strategies, maximum treatments are limited to 3 with 3rd line treatment being HYST. * Women who are considered for treatment with MRgFUS or UAE undergo eligibility tests. Ineligible women are treated by the next least invasive strategy in the following order: MRgFUS < UAE < MYO < HYST. MRgFUS and UAE as 1st line treatments in the diagram represent women who are found eligible to undergo these procedures.

Figure 2. Total Lifetime Costs by Component

Breakdown of total lifetime cost associated with each starting treatment strategy. Screening costs include eligibility assessment tests. Procedure costs include starting strategy and any re-intervention strategies, and make up the largest component of each total. Follow-up costs are lab and imaging test costs incurred after symptom free stage until time of death. Lost productivity costs include wages lost due to absence from work during recovery.

Figure 3. Sensitivity Analysis Results for Age of Starting Treatment

Graph shows ICER for M1 at different treatment starting ages. Treatment starting age is 40 in base case scenario. ICER decreases as treatment starting age decreases. At age 49 and above, M1 becomes the dominant strategy with the lowest cost and highest QALYs. Shading indicates starting ages at which U1 is dominated.

Figure 4. Sensitivity Analysis Results for Probability of Symptom Relief

Graph shows the change in ICER for M1 and U1 as a function of the probability of symptom relief after MRgFUS (base case 0.93).

Table 1**Model Transition Probabilities**

Parameters	Base Case Estimates	Ranges used in sensitivity analysis	Source
Probabilities			
Treatment Eligibility (%)			
HYST	100	-	Expert opinion
MYO	100	-	Expert opinion
UAE	90	88.6–100	[26–27]
MRgFUS	35	25–75	[21, 28–29]
Procedure Related Death (%)			
HYST	0	0–0.03	[29–32]
MYO	0	0	[33–34]
UAE	0	0	[31, 33, 35]
MRgFUS	0	0	[21, 29]
Symptom Relief (0–6 months)			
HYST	100	89–100	[11, 31]
MYO	92	88–93	[33–34]
UAE	92	80–92	[31, 33, 36–37]
MRgFUS	93	71–93	[21, 38]
Fibroid Recurrence			
HYST	0	0	Expert opinion,
MYO	3.2	3.2–5	[36, 39]
UAE	3.2	2–6.9	[31, 36–37]
MRgFUS	7.4	6–7.4	[11, 38]
Major Complications (HYST)			
Bowel Injury	0.2	-	[32]
Bladder Injury	0.9	-	[32]
Ureter Injury	0.3	-	[32]
Other *	6.7	5.8–8.5	[31–32]
Major Complications (MYO) *	6.6	6.6–7.9	[36, 40]
Major Complications (UAE) *	0.5	0–0.66	[11, 31, 41]
Major Complications (MRgFUS)	0	-	[10, 21, 38]
Minor Complications			
HYST	29	14.8–29.3	[30–31]
MYO	11	-	[40]
UAE	6.5	-	[11]
MRgFUS	0	-	[10, 21, 38]
Utilities			
Long-Term Utilities			
Symptomatic Fibroids	0.815	0.528–1	[14]
Symptom Relief from Fibroids	0.944	0.811–1	[14]

Parameters	Base Case Estimates	Ranges used in sensitivity analysis	Source
Post Menopause**	1	-	[14]
Death	0	-	[14]
Short-Term Disutilities [†]			
Post-HYST	0.311	-	[14]
Post-MYO	0.311	-	[14]
Post-UAE	0.085	-	[14]
Post-MRgFUS	0.0623	-	[14]
Costs (2011 US\$)[#]			
Screening Cost for HYST/MYO	\$466	233–932	
Screening Cost for UAE/MRgFUS	\$1,474	737–2,948	
Procedure Cost for HYST	\$7,125	3,526–14,250	
Procedure Cost for MYO	\$7,452	3,726–14,904	
Procedure Cost for UAE	\$10,225	5,087–20,-346	
Procedure Cost for MRgFUS	\$6,148	3,047–12,296	
Annual Follow-Up Cost [#]	\$197	98.5–394	
Follow-Up Cost (UAE 1 st Year)	\$1,673	837–3,346	
Bowel Injury (HYST Major Complication)	\$3,700	1850–7400	
Bladder Injury (HYST Major Complication)	\$3,484	1742–6968	
Ureter Injury (HYST Major Complication)	\$11,118	5559–22236	
Cost of Other Major Complications (HYST)	\$2,094	1047–4188	
Cost of Major Complications (MYO)	\$2,094	1047–4188	
Cost of Major Complications (UAE)	\$6,482	3241–12964	
Cost of Major Complications (MRgFUS)	0	-	
Cost of Minor Complications (HYST/MYO) [#]	0	-	
Cost of Minor Complications (UAE)	\$1,643	822–3286	
Cost of Minor Complications (MRgFUS)	0	-	
Missed Work Days			
Due to HYST	39.8	-	[11]
Due to MYO	38.9	-	[11]
Due to UAE	10	-	[11]
Due to MRgFUS	2	-	[11]
Daily Wage for Women	\$145.64	-	
Discount Rate	0.03	-	

* Other major complications of HYST include pulmonary embolism, hemorrhage >1000 mL, sepsis. Major complications of MYO are pulmonary embolism, hemorrhage, sepsis, PE, laparotomy conversion. Major complication of UAE is pulmonary embolism. See the Methods sections for details.

** 0.015 decrement is applied post-HYST to account for loss of fertility and femininity.[4, 11]

[†] Utility is equal to 1 – disutility.

[#] See Methods section for CPT and DRG codes used to calculate costs and details of lost productivity calculations. The costs of anesthesia (not shown) were calculated based on age adjusted weights and added to procedure costs. Follow up costs were accrued annually until menopause. Cost of minor complications associated with HYST/MYO is accounted for in DRG 742.

Table 2

Base Case Results

Strategy	Total Cost (\$)	Incremental Cost (\$)	Total QALYs	QALYs Gained	ICER (Cost/QALY gained)
H1	13,291	-	22.604	-	-
M1	19,796	6,505	22.801	.196	\$ 33,110
U1	22,164	2,368	22.810	.009	\$ 270,057

Table shows results from the base case scenario. Starting strategies are given in order of increasing QALYs. Strategies are compared incrementally where each strategy was compared with the next most effective one based on QALYs. Total cost includes lifetime screening, procedural, complications, follow-up, and lost-productivity costs. ICER is calculated by dividing the cost difference by the QALY difference.

Table 3

Summary of Additional Outcomes

Treatment Strategy	M1	U1	H1
Re-Interventions per 100 Women	93	71	0
Due to Fibroid Recurrence	79(85%)	58(82%)	-
Due to no symptom relief	14(15%)	13(18%)	-
Types of Re-Interventions			
HYST	8(8%)	5(7%)	-
MYO	12(13%)	18(26%)	-
UAE	36(39%)	48(67%)	-
MRgFUS	37(40%)	-	-
Complications per 100 Women	12	16	37
Total Major	2(17%)	3(19%)	8(22%)
Total Minor	10(83%)	13(81%)	29(78%)

Table summarizes additional outcomes from base case scenario. The number of re-interventions, percent likelihood of fibroid recurrence, lack of symptom relief and each re-intervention strategy is quantified. Re-interventions after starting treatment strategy may be due to fibroid recurrence or lack of symptom relief. Major and minor complications represent the likelihood of events following procedures.

Table 4

Sensitivity Analysis Results

Parameter	ICER (M1 versus H1)	ICER (U1 vs. M1)	Change in Preferred Strategy (WTP \$50,000)
Low			
High			
Probability of Fibroid Recurrence (%)			
MYO			
1.4	28,961	130,224	-
5	37,272	731,536	-
UAE			
2	22,673	72,458	-
8.3	153,997	DOMINATED	H1
MRgFUS			
6	27,998	DOMINATED	-
9	39,912	63,304	-
Treatment Eligibility (%)			
UAE			
88.6	33,510	363,302	-
100	29,860	116,368	-
MRgFUS			
25	34,715	573,420	-
75	26,080	130,322	-
Utilities			
Symptomatic Fibroids			
0.528	DOMINATED	253,036 [#]	H1
0.815 [*]	33,110	270,057	-
Symptom Relief			
0.811	15,778	DOMINATED	-
0.944 [*]	33,110	270,057	-
Cost (2011 \$)			
HYST			
3,563(50%)	49,909	278,918	-
14,250 (200%)	DOMINANT	252,419	-
MYO			
3,726 (50%)	29,871	231,896	-
14,904 (200%)	39,555	346,018	-
UAE			
5,087 (50%)	10,131	33,072	-
20,346 (200%)	78,373	736,877	-
MRgFUS			

Parameter	ICER (M1 versus H1)	ICER (U1 vs. M1)	Change in Preferred Strategy (WTP \$50,000)
Low			
High			
3,074 (50%)	22,851	499,871	-
12,296 (200%)	DOMINATED	43,235 [#]	U1

Table shows results of sensitivity analysis. Literature values were tested to determine the robustness of the results. If a parameter was sensitive across the range of literature values, further values were tested to determine the value at which the ICER crosses the \$50,000/QALY gained and \$100,000/QALY gained threshold.

[#] In cases where MRgFUS was dominated, ICER for UAE was calculated by dividing the cost difference between U1 and H1 by the difference in QALYs gained.

* indicates base case