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Cost-Effectiveness of Uterine-Preserving Procedures for the Treatment of Uterine Fibroid Symptoms in the United States

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Abstract

Objective—To evaluate cost-effectiveness of the following three treatments of uterine fibroids in a population of premenopausal women who wish to preserve their uteri: myomectomy, MR-guided focused ultrasound (MRgFUS) and uterine artery embolization (UAE).

Methods—A decision analytic Markov model was constructed. Cost-effectiveness was calculated in terms of U.S. dollars per quality adjusted life year (QALY) over five years. Two types of costs were calculated: direct costs only, and the sum of direct and indirect (productivity) costs. Women in the hypothetical cohort were assessed for treatment type eligibility, were treated based on eligibility, and experienced adequate or inadequate symptom relief. Additional treatment (myomectomy) occurred for inadequate symptom relief or recurrence. Sensitivity analysis was conducted to evaluate uncertainty in the model parameters.

Results—In the base-case, myomectomy, MRgFUS and UAE had the following combinations of mean cost and mean QALYs, respectively: (\$15,459, 3.957), (\$15,274, 3.953) and (\$18,653, 3.943). When incorporating productivity costs, MRgFUS incurred mean cost of \$21,232; myomectomy \$22,599; and UAE \$22,819. Using probabilistic sensitivity analysis (PSA) and

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excluding productivity costs, myomectomy was cost-effective at almost every decision threshold. Using PSA and incorporating productivity costs, myomectomy was cost-effective at decision thresholds above \$105,000/QALY; MRgFUS between \$30,000-\$105,000/QALY; and UAE below \$30,000/QALY.

Conclusions—Myomectomy, MRgFUS, and UAE were similarly effective in terms of QALYs gained. Depending on assumptions about costs and willingness-to-pay for additional QALYs, all three treatments can be deemed cost-effective in a five year time frame.

Keywords

Uterine fibroids; uterine-preserving treatments; myomectomy; uterine artery embolization (UAE); magnetic resonance-guided focused ultrasound (MRgFUS); cost-effectiveness; Markov model

I. Introduction

Uterine fibroids (UF) affect a significant proportion of premenopausal women in the United States, with cumulative incidence of 70% among white women and over 80% among black women.[1, 2] The estimated direct annual cost of \$4.1-9.4 billion (2010 USD) is over twice the amount spent on melanoma or cervical cancer treatment.[3, 4] Additionally, \$1.6-17.2 billion (2010 USD) is attributed to UF due to lost productivity (indirect costs).[3] While hysterectomy remains the most commonly performed procedure for UF, this choice is unacceptable for many women desiring uterine preservation and is especially problematic for Black women, the group most severely affected by this disease.[4-8]

The comparative effectiveness of procedural treatments for uterine fibroids remains understudied, and is identified as the top priority research question in an Agency for Healthcare Research and Quality report on the management of UF.[6] Although myomectomy is generally regarded as the standard of care for uterine-preserving procedural treatment, uterine artery embolization (UAE) and magnetic resonance-guided focused ultrasound (MRgFUS) have also been shown to yield comparable clinical symptom relief and facilitate faster recovery.[9-13]. Previous studies included MRgFUS in cost-effectiveness analyses but did not focus specifically on uterine-preserving procedural treatments, and only used clinical trial data and expert opinion to measure quality-of-life and health care costs associated with MRgFUS.[14, 15] Our study aims to fill this gap by using insurance claims data and published quality-of-life estimates to evaluate the cost-effectiveness of the three uterine-preserving treatment options: myomectomy, MRgFUS and UAE.

II. Materials And Methods

Model Structure

We developed a decision analytic Markov model to estimate the cost-effectiveness of three uterine-preserving treatment strategies for UF: 1) myomectomy as the sole treatment, where women would undergo myomectomy until they experienced adequate symptom relief; 2) the MRgFUS strategy, where myomectomy was used as a ‘second-line’ treatment if women were ineligible for MRgFUS or experienced inadequate symptom relief after first-line

MRgFUS treatment; and 3) the UAE strategy, with myomectomy used as ‘second-line’ treatment (Fig.1). We felt a Markov Model was the most appropriate choice of model as it allowed for the modeling of transitions between distinct health states, could easily incorporate data in the literature, and would be consistent with other modeling studies in the literature. [14, 15]

In the model, women could transition between health states at 6-month intervals. In the initial 6-month cycle, a woman was assessed for eligibility for treatment,[14] treated, and subsequently experienced either adequate or inadequate relief. We accounted for the possibility that patients could experience a major complication resulting from the procedure. We assumed women would undergo a relatively more invasive procedure (myomectomy) if they failed either of the less invasive treatments, as in O’Sullivan et al. and Zowall et al.’s cost-effectiveness models.[14, 15] The health trajectory of women in the hypothetical cohort was simulated for a five year time frame. The model incorporates the half-cycle corrections as is recommended for Markov models.[16]

Model Parameters and Assumptions

Probabilities in the model reflecting how patients transitioned between health states were taken from the clinical literature. These values were obtained through a PubMed literature search for studies evaluating the effectiveness of myomectomy, MRgFUS, and/or UAE in U.S. women (July 2012). Estimates and their sources are listed in Table 1. When multiple values were available in the literature, we calculated weighted averages of that parameter (weighted by number of subjects) to use in the base-case analysis. If available, we used longer-term data from the same research group to estimate parameter values (for example, taking published 5-year results over 1-year results). When data were unavailable, we consulted a clinical expert (E.A.S). While published data is ideal, this is an accepted approach to fill in gaps in the literature for decision analytic modeling. [17, 18]

For MRgFUS, only three years of recurrence data were available.[19] In sensitivity analysis, we used a conservative estimate of 75% recurrence over 5 years, greater than the highest rate of five-year recurrence in the U.S. found for UAE (26%) and for myomectomy (14%). [20, 21]

Costs of treatment for myomectomy, MRgFUS, and UAE were obtained from the 2003-2010 *MarketScan Commercial Claims and Encounters* (CCAE) database.[22] *MarketScan* contains inpatient and outpatient healthcare utilization and outpatient prescription drug experience of several million employees and their dependents, covered under a variety of health plans. Screening costs were calculated as the sum of patient and health plan paid amounts for surgery preparation and testing during the 14 days prior to procedure. Procedure costs were calculated as the sum of payments made by patients and by insurers for claims made on the day of the surgery for outpatient procedures, or during the entire period of hospitalization for inpatient procedures. Treatment costs were defined as the sum of screening costs and procedure costs.

The analysis was conducted from the societal perspective. Productivity or indirect costs were calculated as the expected number of days missed from work after each procedure

multiplied by the average daily wage for women over the age of 25. To remain consistent with the *MarketScan* CCAE database used for treatment costs, all costs in the model were measured in 2010 US dollars, and were inflation-adjusted using the GDP Implicit Price Deflator.

Costs of major UF procedure-related complications for a U.S. population were not previously reported and the type of major complications or serious adverse events reported differed by study.[11, 13, 23, 24] Due to this fact, we estimated costs of complications for each procedure by focusing on the top 25% of costliest patients on the assumption that this portion of the cost distribution would capture those with major complications. The mean of all case costs was then subtracted from the distribution of the 25% most costly cases. This new distribution of costs was used for the increment of major complications.

Treatment effectiveness was measured in quality adjusted life years (QALYs). Health related quality-of-life values for women with symptomatic uterine fibroids were taken from Fennessy et al.'s study that used the waiting-trade-off method to obtain quality-of-life estimates for women pre-and post-treatment.[25] The study estimated pre- and post-treatment quality-of-life scores for women undergoing hysterectomy, UAE, and MRgFUS. As quality-of-life weights were not estimated for myomectomy, we used UAE scores to approximate the effectiveness of myomectomy and varied this assumption in sensitivity analysis. This assumption was supported by the reported equivalence of UAE and myomectomy in both disease-specific and general quality of life measures (UFS-QOL and SF-36)[26] We varied this assumption in sensitivity analysis. To estimate the quality-of-life score for inadequate symptom relief, we used a weighted average of the reported before-treatment scores. To account for the decreased quality-of-life that was expected to occur after complications, we assumed that women who experienced a major procedure-related complication would have a 20% decrement in quality-of-life at time of treatment, as in O'Sullivan et al. and Beinfeld et al.[14, 27]

Analyses

Costs and QALYs were discounted at a rate of 3%, as recommended in Gold et al., to account for current costs and QALYs being valued higher than future costs and QALYs.[28] In the base-case analysis, cost-effectiveness results were calculated deterministically, assuming no uncertainty in the model parameters. Incremental cost-effectiveness ratios (ICERs) were reported for the base-case results. Cost-effectiveness was calculated in terms of U.S. dollars per QALY using a decision threshold of \$50,000/QALY.[29]

The myomectomy-only strategy was considered as the reference strategy for analyses. As such, if neither the MRgFUS nor the UAE strategies were cost-effective compared to the myomectomy strategy, the myomectomy strategy would be considered the preferred strategy. Otherwise, the strategy with the highest ICER while remaining below the cost-effectiveness threshold would be considered the preferred strategy.

One-way sensitivity analyses were conducted to evaluate potential uncertainty in model parameters. This approach varied each parameter across its possible range, holding all other

parameter values constant at their base-case values. The model was deemed sensitive to a parameter if the preferred strategy changed over the sensitivity range.

In addition to the deterministic results, we reported results from probabilistic sensitivity analysis (PSA) to estimate the effect of varying individual parameters simultaneously. In this strategy, we utilized probability distributions assigned to individual parameters and then conducted simulations to determine the effects of variability of parameters on cost-effectiveness results. Each treatment cohort consisted of 10,000 hypothetical individuals. Parameter values were randomly selected based on the given distributions using Monte Carlo simulation.[30] Cost-effectiveness acceptability curves were constructed to investigate which strategy was preferred at different decision thresholds.[31] Ranges for one-way sensitivity analyses and distributions for probabilistic analyses are detailed in Table 1. All analyses were conducted using TreeAge Pro 2012 software.

III. Results

Base-case (Deterministic Results)

Results are reported in Table 2. Mean cost for myomectomy was \$15,459. Myomectomy was found to be the most effective strategy, incurring mean QALYs of 3.957. Mean cost for MRgFUS was lower at \$15,249. The MRgFUS strategy also incurred slightly lower mean QALYs of 3.953. The difference in effectiveness between myomectomy and MRgFUS, 0.004 QALYs, is the equivalent of living an additional 1.5 days in perfect health. The ICER for MRgFUS compared to myomectomy was \$46,250. Myomectomy was preferred, as the savings per QALY given up did not exceed the decision threshold.

For the UAE strategy, mean cost was \$18,653 and mean QALYs were 3.943. The difference in effectiveness between myomectomy and UAE was also minimal: 0.014 QALYs, or 5.1 days spent in perfect health. However, UAE was dominated by each of the other strategies, meaning it was more costly and less effective than both myomectomy and MRgFUS.

Including Lost Productivity Costs

When incorporating lost productivity costs into the base-case analysis, cost of the myomectomy strategy rose to \$22,599. MRgFUS was again found to be the least costly strategy with mean cost of \$21,232. This resulted in an ICER of \$341,750/QALY. This exceeded the decision threshold, making MRgFUS preferred over myomectomy. Mean costs for the UAE strategy rose to \$22,819. UAE was again dominated.

One-Way Sensitivity Analyses

Excluding productivity costs, the preferred treatment strategy was sensitive to the following model parameters: costs of treatment for all three strategies, probability of adequate relief for myomectomy and MRgFUS, probability of recurrence under MRgFUS and myomectomy, decrement of quality-of-life of complications, quality-of-life of adequate relief of myomectomy and UAE, quality-of-life of inadequate relief, the probability of major complications under MRgFUS, cost of complications for myomectomy and MRgFUS, the

daily wage rate and the discount rate. Threshold values for parameters that the model is sensitive to are listed in Table 3.

Including productivity costs in one-way analyses, the preferred treatment strategy was sensitive to the quality-of-life for adequate relief of myomectomy and UAE, daily wage rate, the treatment costs for all three treatment strategies, the recurrence rate of MRgFUS, and the probability of adequate relief under UAE. Results for threshold values are displayed in Table 3.

Probabilistic Sensitivity Analysis

In the PSA that examined only direct costs, MRgFUS was preferred over a small range of decision threshold values, approximately \$15,000 to \$25,000/QALY (Fig. 2a). However, myomectomy was preferred at all other values. Beyond \$25,000/QALY, the percentage of simulations with myomectomy being preferred was always below 40%. Conversely, MRgFUS was preferred roughly 35% of the time and UAE roughly 26% of the time. The most preferred strategy did not exceed the second most preferred strategy by more than 8% (42% vs. 34%) of the simulations over the reported threshold ranges.

In the PSA that incorporated lost productivity costs (Fig. 2b), UAE was preferred below threshold values of \$30,000/QALY with preferred percentages of simulations ranging from 42.4% to 35.4%. MRgFUS was then preferred until values of \$115,000/QALY, with preferred simulation percentages of 35.6% to 35.4%. The most preferred strategy did not exceed the second most preferred strategy by more than 9% (42% vs. 33%) of the simulations over the reported threshold ranges.

IV. Discussion

Our base-case scenario showed that myomectomy was preferred over MRgFUS and UAE. However, the difference in effectiveness between the three treatments was minimal. When incorporating productivity costs, the MRgFUS strategy became a cost-effective alternative to myomectomy. This reflects the reduction in missed days of work from shorter postop recovery. UAE remained dominated with and without lost productivity costs.

Comparing our results to other cost-effectiveness analyses is difficult, as other analyses included hysterectomy and non-procedural treatments, operated under different modeling structures, and used different data sources. Nonetheless, previous cost-effectiveness studies have also concluded that MRgFUS can be a cost-effective treatment for uterine fibroids.[14, 15] Unlike O'Sullivan et al.'s conclusions which were based largely on expert opinions around cost parameters, we find myomectomy to be less costly and more effective than UAE and MRgFUS.[14] Our study used insurance claims data for cost estimates of treatment, and Fennessy et al. (2011) for detailed quality-of-life estimates for different treatments.[25]

One-way sensitivity analyses reveal substantial uncertainty in model results. Not only does the preferred strategy change from varying a sizable portion of the model parameters, but all treatment strategies are preferred in certain circumstances. Additionally, the sensitive parameters change when including productivity costs. PSA results also exhibited uncertainty

in the preferred strategy, as they showed a change in the strategy with the highest percentage of preferred simulations within the \$50,000/QALY threshold irrespective of inclusion or exclusion of the productivity costs. All three strategies had a reasonably high percentage of preferred simulations across the decision threshold ranges. Given that the simulations are suggestive of comparable costs and effectiveness between the three treatments, factors such as patient preference could dictate the choice of the specific procedure.

Innovation and increased experience may create room for improvements and decreased costs among all three therapies. UAE and MRgFUS are newer techniques compared to myomectomy, so increased provider experience coupled with technical innovations could result in significant improvement as these technologies mature. For myomectomy, increasing use of robotic technology for endoscopic procedures could also improve patient outcomes, including decreased recovery time.

As in all decision analysis models, our results are dependent on modeling assumptions. We attempted to use as many published estimates for base-case parameter values and ranges as were available. We further attempted to use parameter values from studies that included premenopausal women from the United States, as fibroid tumor prevalence and severity may differ by country of residence and resultant racial diversity.[32] We incorporated 'real-world' cost data from insurance claims, as well as published quality-of-life data, into our model, allowing our analysis to take a more data-driven approach than prior studies that utilized unpublished industry trial data and assumed costs. Clinicians may find our collection of population-specific parameter values for probabilities of adequate relief, recurrence, quality-of-life data, and treatment costs, as useful as our cost-effectiveness results. Additionally, we assumed myomectomy to be the sole option for second-line treatment. While this may not be indicative of the general UF population [33], we felt this would be consistent with the preferences of a population wishing to preserve their uteri. We also assumed a fixed probability of eligibility for MRgFUS and UAE. Increasing the eligibility of MRgFUS would make it a more attractive option, as the average cost of first-line treatment would decrease. This would be even more the case when considering productivity costs, as the bulk of the increase in costs would be due to the productivity costs of the sizeable portion of patient ineligible for MRgFUS. Furthermore, we modeled only for 5 years, thus caution should be used when extrapolating our results beyond 5 years. We felt this time horizon to be best given the minimal amount of research reporting beyond 5 years. A woman's preference to preserve her uterus is expected to decline longer term and would make hysterectomy a viable option. However, this is beyond the scope of this research as our study assessed cost-effectiveness of only uterine-sparing options.

Our study has some limitations. This analysis did not quantitate the desire for future pregnancy into the cost-effectiveness model. While pregnancies have been reported after all three treatment types, a lack of reliable information on incorporating the effect of infertility into a quality-of-life measure and a lack of evidence on fertility outcomes for different uterinepreserving procedures led us to exclude fertility outcomes in analysis.[34] The impact of UAE and MRgFUS in particular on fertility outcomes remains understudied.[34-36] Additional research would be warranted in order to incorporate these important outcomes in future analyses.

We also assumed the costs of major complications for each treatment strategy, although we varied this in sensitivity analysis. Additionally, the available data did not allow us to stratify our analysis by type of myomectomy (abdominal, hysteroscopic, laparoscopic), which might influence the time to recovery and hence the indirect costs. Furthermore, since there was no data available on the comparability of uterine anatomy between these three procedures, we made the assumption that they were equivalent.

We elected to assess the costs and effectiveness of a five year period. Although studying a time frame longer than five years would be beneficial, longer-term effectiveness data was not available for MRgFUS, which was approved by FDA only in 2004. Additionally, we posited that women's preferences for uterine preservation could change after five years. For the few transition parameters not coming from five years of follow-up data, we made the implicit assumption that these parameters would not change between the reported follow-up and five years. Also, we did not find a reasonable way to incorporate patient preferences for undergoing a minimally invasive procedure as opposed to a surgical procedure into the model.

V. Conclusion

In summary, myomectomy was found to be cost-effective in base-case analysis excluding productivity costs. Including productivity costs, MRgFUS was found to be cost-effective. Model results were sensitive to most model parameters. No strategy was revealed to be the clearly preferred strategy in PSA. Value of information analyses would be warranted to determine which parameters future research should focus on in efforts to mitigate the sizeable uncertainty revealed in this analysis.

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References

1. Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. *Am J Obstet Gynecol.* 2003; 188(1): 100–107. [PubMed: 12548202]
2. Cramer SF, Patel A. The frequency of uterine leiomyomas. *Am J Clin Pathol.* 1990; 94(4):435–438. [PubMed: 2220671]
3. Cardozo ER, Clark AD, Banks NK, Henne MB, Stegmann BJ, Segars JH. The estimated annual cost of uterine leiomyomata in the United States. *Am J Obstet Gynecol.* 2012; 206(3):211 e211–219. [PubMed: 22244472]
4. Lee DW, Ozminkowski RJ, Carls GS, Wang S, Gibson TB, Stewart EA. The direct and indirect cost burden of clinically significant and symptomatic uterine fibroids. *Journal of occupational and environmental medicine / American College of Occupational and Environmental Medicine.* 2007; 49(5):493–506. [PubMed: 17495692]
5. Levy BS. Modern management of uterine fibroids. *Acta Obstet Gynecol Scand.* 2008; 87(8):812–823. [PubMed: 18607823]
- 6**. Gliklich, RE.; Leavy, MB.; Velentgas, P., et al. A Report on the Priority-Setting Process, Preliminary Data Analysis, and Research Plan. Vol. 31. Agency for Healthcare Research and Quality; Rockville, MD: 2011. Identification of Future Research Needs in the Comparative

Management of Uterine Fibroid Disease. This report commissioned by the Agency for Healthcare Research and Quality delineates the gaps in evidence on comparative effectiveness between available treatments for uterine fibroids. Our study aims to fill some of the evidence gaps identified by this study

7. Stewart EA, Nicholson WK, Bradley L, Borah BJ. The burden of uterine fibroids for African-American women: results of a national survey. *J Womens Health (Larchmt)*. 2013; 22(10):807–816. [PubMed: 24033092]
8. Borah BJ, Nicholson WK, Bradley L, Stewart EA. The impact of uterine leiomyomas: a national survey of affected women. *Am J Obstet Gynecol*. 2013 Oct; 209(4):e1–319.e20. [PubMed: 23891629]
9. Edwards RD, Moss JG, Lumsden MA, et al. Uterine-artery embolization versus surgery for symptomatic uterine fibroids. *N Engl J Med*. 2007; 356(4):360–370. [PubMed: 17251532]
- 10*. Fennessy FM, Tempany CM, Mcdannold NJ, et al. Uterine leiomyomas: MR imaging-guided focused ultrasound surgery--results of different treatment protocols. *Radiology*. 2007; 243(3): 885–893. This paper reviews the relatively new treatment procedure for uterine fibroids, magnetic resonance-guided focused ultrasound (MRgFUS). It summarizes results of the relevant clinical trials. [PubMed: 17446521]
11. Goodwin SC, Bradley LD, Lipman JC, et al. Uterine artery embolization versus myomectomy: a multicenter comparative study. *Fertil Steril*. 2006; 85(1):14–21. [PubMed: 16412720]
- 12**. Spies JB, Myers ER, Worthington-Kirsch R, Mulgund J, Goodwin S, Mauro M. The FIBROID Registry: symptom and quality-of-life status 1 year after therapy. *Obstet Gynecol*. 2005; 106(6): 1309–1318. This paper documents the effects on UF symptom severity and health-related quality of life on patients treated with uterine artery embolization (UAE). The study uses data from multicenter, prospective registry: Fibroid Registry for Outcomes Data (FIBROID) and found that UAE results in substantial improvement in symptom severity. [PubMed: 16319257]
13. Taran FA, Tempany CM, Regan L, Inbar Y, Revel A, Stewart EA. Magnetic resonance-guided focused ultrasound (MRgFUS) compared with abdominal hysterectomy for treatment of uterine leiomyomas. *Ultrasound Obstet Gynecol*. 2009; 34(5):572–578. [PubMed: 19852046]
- 14*. O'Sullivan AK, Thompson D, Chu P, Lee DW, Stewart EA, Weinstein MC. Cost-effectiveness of magnetic resonance guided focused ultrasound for the treatment of uterine fibroids. *Int J Technol Assess Health Care*. 2009; 25(1):14–25. This is one of the earliest studies that assessed cost-effectiveness of magnetic resonance-guided focused ultrasound (MRgFUS) compared with other treatment options including myomectomy, hysterectomy and pharmacotherapy. However, unlike our study that used real-world cost data, this study used cost data from clinical trials. [PubMed: 19126247]
15. Zowall H, Cairns JA, Brewer C, Lamping DL, Gedroyc WM, Regan L. Cost-effectiveness of magnetic resonance-guided focused ultrasound surgery for treatment of uterine fibroids. *Bjog*. 2008; 115(5):653–662. [PubMed: 18333948]
16. Naimark DMJ, Bott M, Krahn M. The half-cycle correction explained: two alternative pedagogical approaches. *Medical Decision Making*. 28(5):706–712. [PubMed: 18448700]
17. Weinstein MC, O'Brien B, Hornberger J, Jackson J, Johannesson M, McCabe C, Luce BR. ISPOR Task Force on Good Research Practices--Modeling Studies. Principles of good practice for decision analytic modeling in health-care evaluation: report of the ISPOR Task Force on Good Research Practices--Modeling Studies. *Value in Health*. 2003 Jan-Feb; 6(1):9–17. [PubMed: 12535234]
18. Briggs AH, Weinstein MC, Fenwick EA, Karnon J, Sculpher MJ, Paltiel AD. ISPOR-SMDM Modeling Good Research Practices Task Force. Model parameter estimation and uncertainty: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force--6. *Value in Health*. 2012 Sep-Oct; 15(6):835–42. [PubMed: 22999133]
19. Kim HS, Baik JH, Pham LD, Jacobs MA. MR-guided high-intensity focused ultrasound treatment for symptomatic uterine leiomyomata: long-term outcomes. *Acad Radiol*. 2011; 18(8):970–976. [PubMed: 21718955]
- 20*. Narayan A, Lee AS, Kuo GP, Powe N, Kim HS. Uterine artery embolization versus abdominal myomectomy: a long-term clinical outcome comparison. *J Vasc Interv Radiol*. 2010; 21(7): 1011–1017. This paper compares outcomes between uterine fibroids patients that underwent

uterine artery embolization (UAE) versus abdominal myomectomy, and finds that UAE outcomes are comparable or superior to myomectomy outcomes. [PubMed: 20570178]

- 21*. Spies JB, Bruno J, Czeyda-Pommersheim F, Magee ST, Ascher SA, Jha RC. Long-term outcome of uterine artery embolization of leiomyomata. *Obstet Gynecol.* 2005; 106(5 Pt 1):933–939. This study assessed 5-year outcomes in uterine fibroids patients being treated with uterine artery embolization, and found that while UAE provides durable symptom relief, about 25% of the patients had failed symptom relief, or had recurrence within the 5-year period. [PubMed: 16260509]
22. Truven Health Analytics. Bethesda, MD: 2003-2010. MarketScan Commercial Claims and Encounters database.
23. Lamorte AI, Lalwani S, Diamond MP. Morbidity associated with abdominal myomectomy. *Obstet Gynecol.* 1993; 82(6):897–900. [PubMed: 8233261]
24. Spector A, Roth AR, Baker CM, Mauro L, Murphy-Skrynarz K. Complications after uterine artery embolization for leiomyomas. *Obstetrics & Gynecology.* 2002; 100(5):8p. [PubMed: 12100798]
- 25*. Fennessy FM, Kong CY, Tempany CM, Swan JS. Quality-of-life assessment of fibroid treatment options and outcomes. *Radiology.* 2011; 259(3):785–792. The paper estimated utilities for the following three uterine fibroids treatment procedures: abdominal hysterectomy, magnetic resonance (MR) imaging-guided focused ultrasound surgery, and uterine artery embolization (UAE). [PubMed: 21364084]
26. Spies JB, Bradley LD, Guido R, Maxwell GL, Levine BA, Coyne K. Outcomes from leiomyoma therapies: comparison with normal controls. *Obstetrics & Gynecology.* 2010 Sep; 116(3):641–52. [PubMed: 20733447]
27. Beinfeld MT, Bosch JL, Isaacson KB, Gazelle GS. Cost-effectiveness of uterine artery embolization and hysterectomy for uterine fibroids. *Radiology.* 2004; 230(1):207–213. [PubMed: 14695395]
28. Gold, MR.; Siegel, JE.; Russel, LB.; Weinstein, MC. Cost-effectiveness in health and medicine. Oxford University Press; New York: 1996.
29. Hirth RA, Chernew ME, Miller E, Fendrick AM, Weissert WG. Willingness to pay for a qualityadjusted life year: in search of a standard. *Medical Decision Making.* 20(3):332–342. [PubMed: 10929856]
30. O'Hagan A, Stevenson M, Madan J. Monte Carlo probabilistic sensitivity analysis for patient level simulation models: efficient estimation of mean and variance using ANOVA. *Health Economics.* 16(10):1009–1023. [PubMed: 17173339]
31. Van Hout BA, Al MJ, Gordon GS, Rutten FF. Costs, effects and C/E-ratios alongside a clinical trial. *Health Economics.* 1994; 3(5):309–319. [PubMed: 7827647]
32. Zimmermann A, Bernuit D, Gerlinger C, Schaefer M, Geppert K. Prevalence, symptoms and management of uterine fibroids: an international internet-based survey of 21,746 women. *BMC Womens Health.* 2012; 12:6. [PubMed: 22448610]
33. Reed SD, Newton KM, Thompson LB, Mccrummen BA, Warolin AK. The incidence of repeat uterine surgery following myomectomy. *J Womens Health (Larchmt).* 2006; 15(9):1046–1052. [PubMed: 17125423]
34. Mara M, Maskova J, Fucikova Z, Kuzel D, Belsan T, Sosna O. Midterm clinical and first reproductive results of a randomized controlled trial comparing uterine fibroid embolization and myomectomy. *Cardiovasc Intervent Radiol.* 2008; 31(1):73–85. [PubMed: 17943348]
35. ACOG practice bulletin. Alternatives to hysterectomy in the management of leiomyomas American College of Obstetricians and Gynecologists. *Obstetrics & Gynecology.* 2008 Aug; 112(2 Pt 1): 387–400. [PubMed: 18669742]
36. Mara M, Fucikova Z, Maskova J, Kuzel D, Haakova L. Uterine fibroid embolization versus myomectomy in women wishing to preserve fertility: preliminary results of a randomized controlled trial. *European Journal of Obstetrics, Gynecology, & Reproductive Biology.* 2006 Jun 1; 126(2):226–33.
37. Gorny KR, Woodrum DA, Brown DL, et al. Magnetic resonance-guided focused ultrasound of uterine leiomyomas: review of a 12-month outcome of 130 clinical patients. *J Vasc Interv Radiol.* 2011; 22(6):857–864. [PubMed: 21482137]

38. Broder MS, Goodwin S, Chen G, et al. Comparison of long-term outcomes of myomectomy and uterine artery embolization. *Obstetrics & Gynecology*. 100(5 Pt 1):864–868. [PubMed: 12423842]
39. Carls GS, Lee DW, Ozminkowski RJ, Wang S, Gibson TB, Stewart E. What are the total costs of surgical treatment for uterine fibroids? *J Womens Health (Larchmt)*. 2008; 17(7):1119–1132. [PubMed: 18687032]
40. Highlights of Women's Earnings in 2010. U S Bureau of Labor Statistics; Washington D.C: 2011.

Summary Points

- In order to assess the cost-effectiveness between three uterine-sparing procedures for the treatment of uterine fibroids, we developed a decision analytic Markov model:
 - Myomectomy as the sole treatment
 - MRgFUS as first-line treatment and myomectomy as second-line treatment
 - UAE as first-line treatment and myomectomy as second-line treatment
- Probabilities in the model reflecting how patients transitioned between health states were taken from the relevant clinical literature, while costs of treatment for myomectomy, MRgFUS, and UAE were obtained from the 2003-2010 *MarketScan Commercial Claims and Encounters* database.
- Productivity or indirect costs were calculated as the expected number of days missed from work after each procedure multiplied by the average daily wage for women over the age of 25.
- Cost-effectiveness was calculated in terms of U.S. dollars per QALY using a decision threshold of \$50,000/QALY.
- The mean costs and QALY in the base-case analyses were \$15,459 and 3.957 for myomectomy; \$15,249 and 3.953 for MRgFUS; and \$18,653 and 3.943 for UAE. Myomectomy was found to be preferred based on the decision threshold.
- Including productivity costs increased costs of myomectomy, MRgFUS, and UAE to \$22,599, \$21,232 and \$22,819, respectively. MRgFUS was found to be cost-effective.
- One-way sensitivity analyses revealed the results to be sensitive to a large proportion of model parameters.
- Results from PSA excluding productivity costs showed myomectomy to be cost-effective at almost every decision threshold. However, including productivity costs resulted in UAE to be cost-effective below \$30,000/QALY, MRgFUS to be cost-effective between \$30,000-\$105,000/QALY, and myomectomy to be cost-effective above \$105,000/QALY.
- Value of information analyses would be warranted to determine which parameters future research should focus on efforts to mitigate the sizeable uncertainty revealed in this analysis.
- Depending on assumptions about costs and willingness-to-pay for additional QALY, all three treatments can be deemed cost-effective in a five year time frame

Figure 1. Model Schematic

*Those who experience inadequate relief or fibroid recurrence will undergo myomectomy treatment ('second-line' treatment).

**Complications can occur after treatment.

Figure 2.

- a.** Percentage of Simulations found to be Cost-Effective, at Various Decision Threshold Values, Productivity Costs Excluded
- b.** Percentage of Simulations found to be Cost-Effective, at Various Decision Threshold, Productivity Costs Included

Table 1

Parameter Estimates and Ranges Used in Modeling

Parameter	Base-case	Range	Reference	Distribution	Distribution Details [†]
<i>Probabilities</i>					
<i>Proportion Eligible for Treatment</i>					
MRgFUS	0.35	(fixed)	[14], Assumption	(none)	(none)
Myomectomy	1	(fixed)	[14], Assumption	(none)	(none)
UAE	0.9	(fixed)	[14], Assumption	(none)	(none)
<i>Probability of Adequate Relief</i>					
MRgFUS	0.868 [*]	0.792-0.929	[37], [25]	Uniform	0.792 / 0.929
Myomectomy	0.799 [*]	0.75-0.9	[11], [38]	Uniform	0.75 / 0.9
UAE	0.851 [*]	0.812-0.92	[12], [38], [11]	Uniform	0.812 / 0.92
<i>Probability of Recurrence</i>					
MRgFUS	0.072	0.036-0.130	[19], Assumption	Uniform	0.36 / 0.13
Myomectomy	0.009 [*]	0.003-0.014	[38], [20]	Uniform	0.003 / 0.014
UAE	0.016 [*]	0.007-0.044	[12, 21], [20]	Uniform	0.007 / 0.044
<i>Probability of Major Complications</i>					
MRgFUS	0.030 [*]	0.008-0.083	[37], [13]	Uniform	0.008 / 0.083
Myomectomy	0.021 [*]	0.017-0.023	[11], [23]	Uniform	0.017 / 0.023
UAE	0.036 [*]	0.003-0.077	[12], [11]	Uniform	0.003 / 0.077
<i>Costs</i>					
<i>Screening and Procedure Costs</i>					
MRgFUS	\$6,864	\$4,358-\$21,084	[22]	Gamma	\$6,864 / 6,817
Myomectomy	\$11,112	\$7,018-\$13,011	[22]	Gamma	\$11,112 / 8,747
UAE	\$12,229	\$5,955-\$15,686	[22]	Gamma	\$12,229 / 13,373
<i>Cost of Complications</i>					
All treatments	\$10,148	\$3,890-\$11,363	[22]	Gamma	\$10,148 / 16,068
<i>Quality-of-life</i>					
QoL for Inadequate Symptom Relief	0.8375 [*]	0.67-1.00	[25], [14]	Beta	0.8375 / 0.2
QoL for Symptom Relief, MRgFUS	0.925	0.797-1.00	[25]	Beta	0.925 / 0.128

Parameter	Base-case	Range	Reference	Distribution	Distribution Details [‡]
QoL for Symptom Relief, Myomectomy	0.925	0.716-1.00	Assumption	Beta	0.925 / 0.204
QoL for Symptom Relief, UAE	0.92	0.716-1.00	[25]	Beta	0.92 / 0.204
Decrement in Utility from Complications	20%	0-40%	[14]	Uniform	0.0 / 40%
<i>Productivity</i>					
Missed Workdays, MRgFUS	1.2	0.4-2.0	[13]	Uniform	0.4 / 2.0
Missed Workdays, Myomectomy	38.09 [*]	37-38.8	[11], [39]	Uniform	37 / 38.8
Missed Workdays, UAE	9.54 [*]	7.4-9.9	[11, 39]	Uniform	7.4 / 9.9
Daily Wages, Women Ages 25+ [‡]	\$140.80	\$70.20-\$307	[40]	Triangle	\$70.2 / \$307

MRgFUS=Magnetic Resonance-Guided Focused Ultrasound; UAE=Uterine Artery Embolization; QoL=Quality-of-life;

^{*} Weighted Average (Weighted by number of subjects in each study)

[‡] Daily Wage Rate not used in base-case calculations; wages are included in sensitivity analysis

[‡] Distribution details are provided in a manner based on distribution type: uniform=min / max; triangle= min / max; gamma= mean / standard deviation; beta= mean / standard deviation

Table 2
Incremental Cost-Effectiveness Ratios, Base-case Results

Strategy	Mean Cost	Mean QALY	ICER
<i>Productivity Costs Excluded (Reference=Myomectomy)</i>			
Myomectomy	\$15,459	3.957	-
MRgFUS	\$15,274	3.953	\$46,250 [†]
UAE	\$18,653	3.943	Dominated
<i>Productivity Costs Included (Reference=Myomectomy)</i>			
Myomectomy	\$22,599	3.957	-
MRgFUS	\$21,232	3.953	\$341,750 [†]
UAE	\$22,819	3.943	Dominated

MRgFUS=Magnetic Resonance-Guided Focused Ultrasound; UAE=Uterine Artery Embolization; QALY=quality adjusted life years;
 ICER=incremental cost-effectiveness ratio

[†]Denotes a strategy cheaper and less effective than the reference, which inverts the decision rule (ICER above the threshold are cost-effective)

Table 3
Results from One-Way Sensitivity Analysis of sensitive model parameters

Productivity Costs Excluded			
Parameter	Estimate	Threshold	Preferred Strategy
Quality-of-life of adequate relief, Myomectomy	0.925	> 0.794	Myomectomy
		> 0.757 and < 0.794	MRgFUS
		< 0.757	UAE
Quality-of-life of adequate relief, UAE	0.920	> 0.812	UAE
		< 0.812	Myomectomy
Daily Wages for Women Ages 25+	\$140.80	> \$305	UAE
		< \$305	MRgFUS
Quality-of-life of inadequate relief	0.8375	> 0.693	MRgFUS
		< 0.693	Myomectomy
Cost of Treatment, Myomectomy	\$11,112	> \$12,406	MRgFUS
		< \$12,406	Myomectomy
Cost of Treatment, MRgFUS	\$6,864	> \$6,803	Myomectomy
		< \$6,803	MRgFUS
Cost of Treatment, UAE	\$12,229	> \$8,186	MRgFUS
		< \$8,186	UAE
Cost of complications, Myomectomy	\$10,148	> \$10,834	MRgFUS
		< \$10,834	Myomectomy
Cost of complications, MRgFUS	\$10,148	> \$9,059	Myomectomy
		< \$9,059	MRgFUS
Decrement in Quality-of-life of complications	20%	> 30.9%	MRgFUS
		< 30.9%	Myomectomy
Probability of Adequate Relief, Myomectomy	0.799	> 0.796	Myomectomy
		< 0.796	MRgFUS
Probability of Adequate Relief, MRgFUS	0.868	> 0.871	MRgFUS
		< 0.871	Myomectomy
Probability of Recurrence, Myomectomy	0.009	> 0.009	MRgFUS
		< 0.009	Myomectomy

Productivity Costs Excluded

Parameter	Estimate	Threshold	Preferred Strategy
Probability of Recurrence, MRgFUS	0.072	> 0.071	Myomectomy
		< 0.071	MRgFUS
Probability of Major Complications, MRgFUS	0.030	> 0.028	Myomectomy
		< 0.028	MRgFUS
Discount Rate	3%	> 3.2%	MRgFUS
		< 3.2%	Myomectomy

Productivity Costs Included

Parameter	Estimate	Threshold	Preferred Strategy
Quality-of-life of adequate relief, Myomectomy	0.925	> 0.81	Myomectomy
		> 0.774 and < 0.81	MRgFUS
		< 0.774	UAE
Quality-of-life of adequate relief, UAE	0.920	> 0.802	UAE
		< 0.802	MRgFUS
Daily Wages for Women Ages 25+	\$140.80	> \$305	UAE
		< \$305	MRgFUS
Cost of Treatment, MRgFUS	\$6,864	> \$10,298	Myomectomy
		< \$10,298	MRgFUS
Cost of Treatment, Myomectomy	\$11,112	> \$12,693	MRgFUS
		< \$12,693	Myomectomy
Cost of Treatment, UAE	\$12,229	> \$11,304	MRgFUS
		< \$11,304	UAE
Probability of Adequate Relief, UAE	0.851	> 0.902	UAE
		< 0.902	MRgFUS
Probability of Recurrence, MRgFUS	0.072	> 0.10	Myomectomy
		< 0.10	MRgFUS

MRgFUS=Magnetic Resonance-Guided Focused Ultrasound; UAE=Uterine Artery Embolization;